Original Article

Effect of preoperative autologous platelet-rich plasmapheresis on postoperative bleeding in patients undergoing heart valve surgery

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Background: Cardiovascular surgeries often require deep hypothermic circulatory arrest and cardiopulmonary bypass (CPB), which can disrupt blood clotting and lead to excessive bleeding. Traditional treatments involve transfusing blood and blood products, which can have adverse effects and place significant strain on the global blood supply. Research suggests that autologous platelet-rich plasmapheresis (aPRP) may reduce the need for transfusions by preserving blood components. However, the impact of aPRP on postoperative blood loss and clinical outcomes in cardiovascular surgery remains controversial. This study aimed to examine the effects of aPRP on postoperative blood loss and recovery in patients undergoing heart valve surgery.

Methods: A total of 183 patients were divided into either aPRP or control groups. The aPRP group received aPRP before CPB, whereas the control group did not. The primary endpoint was postoperative bleeding between the groups. The secondary endpoints were postoperative bleeding risk factors and clinical outcome assessment. Logistic regression analysis with covariate adjustment was used to calculate these risk factors.

Results: A total of 76 patients (41.5%) in the aPRP group and 107 patients (58.5%) in the control group were included in the analysis. No significant difference was found in the occurrence of postoperative bleeding [odds ratio (OR) =0.53, 95% confidence interval (CI): 0.28–1.00, P=0.05], and the aPRP group had fewer complications than the controls (OR =0.28, 95% CI: 0.10–0.68, P=0.009). However, after adjusting for the New York Heart Association (NYHA) classification, diabetes, arrhythmology, mean activated clotting time (ACT_{mean}), CPB, bleeding, thoracotomy, and body mass index (BMI), there was a significant difference in postoperative bleeding (adjusted OR =0.47, 95% CI: 0.22–0.98, P=0.04) and complications (adjusted OR =0.23, 95% CI: 0.07–0.64, P=0.008) between the two groups.

Conclusions: Preoperative aPRP can improve postoperative outcomes and reduce complications in patients undergoing heart valve surgery.

Keywords: Autologous platelet-rich plasmapheresis (aPRP); heart valve surgery; postoperative bleeding; multiple regression analyses

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Introduction

Background

Deep hypothermic circulatory arrest and cardiopulmonary bypass (CPB) often disrupt normal coagulation during cardiovascular surgeries and impair perioperative hemostasis (1). To minimize bleeding, traditional therapies typically involve transfusion of allogeneic blood to blood products, such as platelets, red blood cells (RBCs), and fresh frozen plasma. However, according to the current guidelines, excessive blood and blood product transfusion may have adverse effects, including the potential spread of hepatitis C and human immunodeficiency virus, especially in low-income countries (2). Moreover, transfusions are often required because of thrombocytopathy, fibrinolysis, and coagulation factor deficiency during prolonged CPB, all of which can cause further surgical complications (3,4).

Heart valve surgery is associated with an increased risk of bleeding and high postoperative mortality and morbidity (5). The causes of hemostatic impairment are multifactorial and include hemodilution, consumptive coagulopathy, platelet dysfunction, and fibrinolysis (6). Moreover, platelet dysfunction makes it challenging to achieve adequate hemostasis after administration of the heparin antagonist protamine and can contribute to postoperative bleeding (7). The global demand for transfusion is rising and is expected to outrun the available blood supply, ultimately increasing healthcare costs (8). Therefore, developing better, safer, and more cost-effective methods of conserving blood is essential to reduce the need for donor blood transfusions and the amount of intraoperative blood loss.

Autologous platelet-rich plasma (aPRP) exchange, an innovative technique for autologous blood transfusion, offers an alternative to conventional blood conservation methods and has been successfully used in cardiovascular surgery to preserve platelet integrity (9), minimize the exposure of platelets and coagulation factors during CPB and associated fibrinolysis (10,11), and manage serum volume. Furthermore, aPRP transfusion after protamine administration has been shown to assist in restoring normal hemostasis and, consequently, maintaining tissue microcirculation and endothelial integrity. Zhou *et al.* conducted a retrospective review of 685 cases in 2013 and a prospective randomized controlled trial (RCT) of 80 patients in 2015 to investigate the role of aPRP during ascending and transverse aortic arch repair surgery (5,12). Both studies suggested that pre-CPB and postoperative aPRP transfusions decrease the need for allogeneic blood transfusions. Moreover, the safety and efficacy of aPRP transfusions for preventing hematological dysfunction caused by extracorporeal circulation has been validated (6). Nonetheless, there is no lack of some reports indicating the possibility of drawbacks, for instance aPRP association with an increased postoperative risk of acute kidney injury subsequent to acute aortic dissection repair (9,11).

Rationale and knowledge gap

There is still an ongoing debate regarding the optimal target population, effective collection method, and appropriate quantity, as well as its effects on postoperative bleeding and clinical outcomes (13). A study examining aPRP without cell salvage found no advantage in terms of decreasing blood loss or improving hemostatic parameters (14), indicating that cell salvage may compensate for plateletpheresis and CPB-related complications through aPRP-activated procoagulant and complement removal. Furthermore, aPRP was not shown to reduce blood loss or the transfusion requirement of blood products in other studies (3,15).

Highlight box

Key findings

- Autologous platelet-rich plasma (aPRP) before cardiac surgery can enhance postoperative results and lower the likelihood of complications in patients.
- Patients with diabetes and thoracotomy had a higher risk of postoperative bleeding, whereas female, body mass index and mean platelet count suggested potential benefits in reducing postoperative bleeding.

What is known and what is new?

- Traditional methods rely on allogeneic blood transfusions during cardiovascular surgeries, posing risks such as viral transmission and surgical complications.
- Despite ongoing controversies, careful patient screening, maintaining hemodynamic stability during collection, appropriate collection timing, and coagulation monitoring can greatly improve aPRP safety and efficacy.

What is the implication, and what should change now?

- aPRP shows potential for advancement and is anticipated to have a significant impact on the field of cardiac surgery, warranting further research to clarify its effectiveness and optimal usage in cardiovascular surgery.

Objective

Based on these controversial results, we conducted a retrospective study to investigate the potential effects of aPRP in cardiovascular surgery on postoperative blood loss and clinical outcomes. We present this article in accordance with the STROCSS reporting checklist (16) (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-794/rc).

Methods

Ethical approval

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the ethics committee of Zhongshan Hospital (Xiamen), Fudan University (approval No. B2023-040) on 23 May 2023 and registered with the Chinese Clinical Trial Registry (registration No. ChiCTR2300071798) on 9 June 2023. Given the retrospective design of the study, the requirement for informed consent was waived.

Data sources

Patient data were obtained from the hospital's electronic medical records system and included baseline preoperative patient data, including age, sex, body mass index (BMI), concomitant diseases, American Society of Anesthesiologists (ASA) status, New York Heart Association (NYHA) classification, and laboratory test results. An anesthesia recording system was used to acquire intraoperative information regarding the aPRP process, surgical technique, valve type, CPB duration, and intraoperative bleeding. The following postoperative patient data were also collected after admission to the intensive care unit (ICU) and ward: postoperative bleeding, duration of mechanical ventilation, thoracic puncture drainage, duration of pericardial and mediastinal drainage tube maintenance, and postoperative complications, such as incision site infection, lung infection, liver and kidney insufficiency, unplanned thoracotomy, and hemostasis.

The following definitions and criteria were used in this study:

(I) Arrhythmia was diagnosed when the preoperative electrocardiogram showed indications of various abnormal heart rhythms, such as ventricular premature beats, atrial fibrillation, sinus tachycardia, sinus bradycardia, or atrioventricular block.

(II) Nephropathy was defined as an estimated glomerular filtration rate (eGFR) less than 90 mL/min/1.73 m^2, as indicated by preoperative laboratory tests.

(III) Criteria for stopping mechanical ventilation: (i) the cause of mechanical ventilation has improved or been removed; (ii) the preoperative oxygenation index is greater than 150–200; (iii) hemodynamic stability has been achieved; and (iv) a successful spontaneous breathing trial (SBT) has been conducted.

(IV) Criteria for removal of pericardial and mediastinal drainage tube: (i) the patient's respiratory circulation is stable; (ii) the drainage rate is less than 50 mL/24 hours; (iii) the color of the drainage fluid gradually changes to light red or yellow.

(V) ICU exit criteria: (i) the patient's respiratory circulation is stable and (ii) the patient does not benefit from continued intensive care.

Patient population

This study was a retrospective cohort analysis of the clinical data of patients who underwent valve repair or replacement surgery on Zhongshan Hospital (Xiamen), Fudan University between September 2020 and February 2023. We included patients aged 18–80 years who underwent heart valve repair or replacement surgery under general anesthesia with the use of extracorporeal circulation and who had an ASA physical status between II–III and preoperative platelet count >100×10^9/L.

The exclusion criteria were as follows: (I) patients presenting with severe coagulation dysfunction prior to surgery, leading the attending physician to determine that aPRP collection was not appropriate; (II) platelet counts <100×10^9/L; (III) patients who require preoperative antiplatelet therapy; (IV) patients with severe perioperative renal insufficiency (eGFR <30 mL/min/1.73 m^2); and (V) patients with severe perioperative hepatic insufficiency (prothrombin ratio <15%). A total of 183 patients met the eligibility criteria and were enrolled in this study. The patients were then divided into two groups: the aPRP group, who received aPRP, and the control group, who did not.

Study endpoint

The primary endpoint of this study was postoperative

bleeding. The secondary endpoints were identifying the risk factors associated with postoperative bleeding and evaluating clinical outcomes according to the ICU and ward data. The following outcomes were assessed: duration of mechanical ventilation, time until pericardial and mediastinal drainage tube removal, length of stay in the ICU, length of postoperative hospitalization, and in-hospital complications. Pericardial and mediastinal drainage volumes were measured on the day following the surgery and on postoperative days 1 and 2. Postoperative massive bleeding was defined as pericardial and mediastinal drainage flow >1,000 mL within 72 hours after surgery or the need for emergency surgery to control bleeding (17).

Anesthesia procedure

All patients received standardized monitoring. Upon admission, the right jugular vein and radial artery were punctured for invasive blood pressure monitoring. Anesthesia was induced using target-controlled infusions of propofol (2–3 mcg/mL), sufentanil (0.5–1 mcg/kg), and rocuronium (0.5–1 mg/kg), and ventilation was achieved after tracheal intubation. These drugs were administered intravenously throughout surgery.

aPRP harvesting technique

Prior to heparin administration, PRP, platelet-poor plasma (PPP), and RBCs were collected from the jugular vein using the Haemonetics Component Collection System® (Haemonetics Corporation, Boston, MA, USA). After the reversal of heparin, PRP and PPP were reinfused under strictly sterile conditions. The aPRP treatment was administered to the aPRP group, but not the control group. All other parameters were similar in both the groups. About 2–3 harvesting cycles were performed to collect sufficient aPRP (approximately 100 mL). The same amount of colloid was infused as the volume of blood removed. Hemoglobin (Hb) levels were measured to guide the reinfusion of the collected RBCs and maintain Hb levels >100 g/L. The PPP and concentrated RBCs were stored in the refrigerator, whereas the PRP was shaken at a frequency of 60 rpm at room temperature (20–24 ℃) using an oscillator machine (18,19).

Statistical analysis

Baseline data were expressed as standardized mean differences (SMDs), with SMD >0.1 considered statistically significant. The mean values of international normalized ratio, platelet count, and activated clotting time (ACT) were recorded and introduced into the model. Quantitative variables are presented as the mean ± standard deviation or median (interquartile range), whereas categorical variables are presented as frequencies or percentages. Multiple regression analyses was used to determine the independent factors associated with postoperative bleeding. In this study, we collected data on the outcome effect, continuous predictor variable, mean activated clotting time (ACT_{mean}), covariate treatment, NYHA, diabetes, arrhythmology, thoracotomy, and BMI. Possible nonlinear relationships between the change in ACT_{mean} and other aPRP-related effects were examined using a logistic regression model with restricted cubic splines (RCS) analysis. The model with the lowest Akaike information criterion value was selected for the RCS. Of the 3 and 7 knots tested, the RCS with 3 knots at the 10th, 50th, and 90th percentiles provided the best overall fit. The reference value was set based on the RCS shape.

When interpreting the results of the RCS analysis, the median value of the predictor variable was selected as the reference value. If the curve exhibited a U-, inverted U-, or L-shape, the inflection point was set as the cut-off value. The inflection point represented a turning point or boundary between the different patterns of association between the predictor variable and the outcome. If this inflection point was clearly identifiable, the data were divided into two distinct segments. This segmented logistic regression allowed for a more nuanced understanding of the relationship between the predictor variable and the outcome in each segment, as it accounted for distinct patterns of association in different parts of the curve. The adjusted odds ratios (aORs) derived from the logistic regression segments were also calculated. All statistical tests were 2-sided, and statistical significance was set at <0.05. All statistical analyses were performed using R software (version 4.2.2; R Core Team, Vienna, Austria), including the rms package, and STATA software (StataCorp., College Station, TX, USA).

Results

Baseline characteristics

Of the 183 patients, 76 patients (41.5%) received aPRP (aPRP group) and 107 patients did not (control group). The

Table 1 Baseline data

Characteristics	Control (N=107)	aPRP (N=76)	SMD
Age (years)	57.22±12.6	57.76±12.49	0.04
Sex			
Male	62 (57.9)	37 (48.7)	–0.19
Female	45 (42.1)	39 (51.3)	0.19
BMI (kg/m^2)	22.4±2.9	22.8±2.8	0.12
ASA classification			
II	21 (19.6)	9 (11.8)	–0.24
III	86 (80.4)	67 (88.2)	0.24
NYHA classification			
II	20 (18.7)	9 (11.8)	–0.21
III	87 (81.3)	67 (88.2)	0.21
Hypertension			
None	77 (72.0)	50 (65.8)	–0.13
Yes	30 (28.0)	26 (34.2)	0.13
Diabetes			
None	99 (92.5)	73 (96.1)	0.18
Yes	8 (7.5)	3 (3.9)	–0.18
Arrhythmology			
None	99 (92.5)	65 (85.5)	–0.20
Yes	8 (7.5)	11 (14.5)	0.20
Nephropathy			
None	101 (94.4)	75 (98.7)	0.38
Yes	6 (5.6)	1 (1.3)	–0.38
Double valve			
None	61 (57.0)	34 (44.7)	–0.25
Yes	46 (43.0)	42 (55.3)	0.25
Surgery type			
Thoracoscope	39 (36.4)	13 (17.1)	–0.51
Open	68 (63.6)	63 (82.9)	0.51

Data are presented as mean ± standard deviation or n (%). BMI, body mass index; ASA, American Society of Anesthesiologists; NYHA, New York Heart Association; aPRP, autologous platelet-rich plasma; SMD, standardized mean difference.

aPRP group consisted of 37 males (48.7%) with a mean age of 57.76 (12.49) years, whereas the control group consisted of 62 males (57.9%) with a mean age of 57.22 (12.6) years. The first patient underwent surgery on 18 September 2020 and the last patient on 3 February 2023 (*Table 1*).

Intraoperative outcomes

The postoperative mechanical ventilation time, ICU stay length, postoperative hospital stays length, thoracotomy rate, and tracheotomy rate did not differ between the two groups. However, the duration of pericardial mediastinal drainage tube extraction (P<0.001) was significantly longer in the control group than in the aPRP group (*Tables 2,3*).

Postoperative outcomes

Compared to the control group, the aPRP group experienced less bleeding on the second day post-surgery (P=0.03). No significant difference was found in the occurrence of postoperative bleeding [odds ratio (OR) =0.53, 95% confidence interval (CI): 0.28–1.00, P=0.05]. However, after adjusting for NYHA class, diabetes, arrhythmology, ACT_{mean}, CPB, bleeding, thoracotomy, and BMI (*Table 4*, *Figure 1*), there was a significant difference in postoperative bleeding (adjusted OR =0.47, 95% CI: 0.22–0.98, P=0.04) (*Table 5*, *Figure 1*).

Incidence of complications

The aPRP group had fewer complications than the controls (OR =0.28, 95% CI: 0.10–0.68, P=0.009). After adjusting for NYHA classification, diabetes, arrhythmology, ACT_{mean}, CPB, bleeding, thoracotomy, and BMI (*Table 4*, *Figure 1*), there was a significant difference in complications (adjusted OR =0.23, 95% CI: 0.07–0.64, P=0.008) between the two groups (*Table 5*).

Logistic regression analysis

After adjusting the ORs derived from the segmented logistic regression analysis, covariate imbalances in sex, ASA

Table 2 Perioperative baseline

Characteristics	Control (N=107)	aPRP (N=76)	P value
Postoperative bleeding (mL)			0.07
<1,000	64 (59.8)	56 (73.7)	
≥1,000	43 (40.2)	20 (26.3)	
Postoperative bleeding (mL)			
D0	435.17±358.97	432.50±268.41	0.25
D1	298.02±183.82	300.91±223.29	0.61
D2	233.44±242.79	141.08±104.07	0.03
Tracheotomy			0.76
None	99 (92.5)	72 (94.7)	
Yes	8 (7.5)	4 (5.3)	
Thoracotomy			0.11
None	64 (59.8)	55 (72.4)	
Yes	43 (40.2)	21 (27.6)	
Postoperative hospital stay (day)	12.5±6.3	11.6±7.9	0.41
ICU stay (day)	4.5±5.9	3.7±4.7	0.33
Drainage tube extraction time (day)	8.6±4.9	6.1±3.7	<0.001
Mechanical ventilation time (hour)	60±50.4	50.4± 36	0.15
CPB time (minute)	139.6±36.6	146.6±49.3	0.30
PT (second)			
Preoperative	13.2±3.9	12.8±2.4	0.39
POD0	15.0±1.5	14.8±1.4	0.54
POD1	13.9±1.4	13.7±2.0	0.48
POD2	14.6±1.5	14.5±2.9	0.87
PT_{mean}	14.2±1.6	14.0±1.6	0.40
INR			
Preoperative	1.2±0.4	1.1±0.2	0.24
POD0	1.3±0.2	1.3±0.1	0.71
POD1	1.2±0.1	1.2±0.2	0.56
POD2	1.3±0.1	1.3±0.3	0.95
INR_{mean}	1.3±0.2	1.2±0.1	0.39
PLT ($\times10^9$/L)			
Preoperative	202.2±72.4	207.2±76.3	0.65
POD0	113.0±43.1	114.9±53.3	0.80
POD1	118.2±49.3	117.7±65.0	0.95
POD2	106.5±46.7	102.6±55.7	0.62
PLT_{mean}	135.0±48.1	135.6±57.7	0.94

Table 2 (*continued*)

Table 2 (*continued*)

Characteristics	Control (N=107)	aPRP (N=76)	P value
ACT (second)			
Preoperative	154.9±16.8	153.2±12.2	0.45
POD0	161.4±125.8	148.6±14.2	0.30
POD1	156.7±16.6	157.9±11.7	0.57
ACT_{mean}	118.2±31.6	114.9±7.9	0.30

Data are presented as mean ± standard deviation or n (%). aPRP, autologous platelet-rich plasma; ICU, intensive care unit; CPB, cardiopulmonary bypass; PT, prothrombin time; PLT, platelet count; INR, international normalized ratio; ACT, activated clotting time of whole blood; POD, postoperative day.

Table 3 Logistic regression with best subsets variable reduction

Postoperative bleeding	Univariable		Multivariable	
	OR (95% CI)	P value	OR (95% CI)	P value
Treatment				
Control	–	–	–	–
aPRP	0.53 (0.28–1.0)	0.05	0.52 (0.23–1.13)	0.11
Sex				
Male	–	–	–	–
Female	0.45 (0.24–0.85)	0.01	0.35 (0.15–0.76)	0.009
Age (years)	1.01 (0.98–1.03)	0.67	0.97 (0.94–1.00)	0.09
BMI (kg/m^2)	0.88 (0.78–0.98)	0.03	0.83 (0.72–0.95)	0.01
ASA classification				
II	–	–	–	–
III	1.06 (0.47–2.51)	0.89	0.81 (0.28–2.42)	0.70
NYHA classification				
II	–	–	–	–
III	1.80 (0.75–4.78)	0.21	–	–
Hypertension				
None	–	–	–	–
Yes	0.86 (0.44–1.67)	0.67	–	–
Diabetes				
None	–	–	–	–
Yes	5.67 (1.57–26.66)	0.01	14.95 (2.80–107.41)	0.003
Arrhythmology				
None	–	–	–	–
Yes	2.33 (0.89–6.19)	0.08	–	–

Table 3 (*continued*)

Table 3 (*continued*)

Postoperative bleeding	Univariable		Multivariable	
	OR (95% CI)	P value	OR (95% CI)	P value
Nephropathy				
None	–	–	–	–
Yes	0.75 (0.11–3.61)	0.74	–	–
INR_{mean} (second)	18.61 (2.17–231.91)	0.01	4.15 (0.28–90.10)	0.33
PLT_{mean} ($\times10^9$/L)	0.98 (0.97–0.99)	<0.001	0.98 (0.97–0.99)	0.001
ACT_{mean} (second)	1.00 (0.98–1.01)	0.89		
Double valve				
None	0.63 (0.34–1.17)	0.14	–	–
Yes	–	–	–	–
Surgery type				
Open	–	–	–	–
Thoracoscope	0.54 (0.26–1.09)	0.09	–	–
Intraoperative bleeding (mL)	1.00 (1.00–1.00)	0.03	1.00 (1.00–1.00)	0.06
Mechanical ventilation time (hour)	1.16 (0.99–1.40)	0.09	–	–
Drainage tube extraction time (day)	1.11 (1.04–1.22)	0.008	–	–
CPB time (minute)	1.00 (1.00–1.01)	0.34	1.00 (0.99–1.01)	0.80
Thoracotomy				
None	–	–	–	–
Yes	3.16 (1.67–6.05)	<0.001	2.55 (1.15–5.77)	0.02

aPRP, autologous platelet-rich plasma; BMI, body mass index; ASA, American Society of Anesthesiologists; NYHA, New York Heart Association; INR, international normalized ratio; PLT, platelet count; ACT, activated clotting time; CPB, cardiopulmonary bypass; OR, odds ratio; 95% CI, 95% confidence interval.

Table 4 Effect of ACT_{mean} level on effect: adjusted odds ratios from segmented logistic regression analysis

Characteristic	Unadjusted		Adjusted	
	OR (95% CI)	P	OR (95% CI)	P
ACT_{mean} (<119.45 second)	1.05 (0.98, 1.13)	0.18	1.31 (0.89, 2.01)	0.18
ACT_{mean} (≥119.45 second)	0.99 (–, –)	0.58	0.69 (–, –)	0.58

ORs were adjusted for treatment, NYHA, diabetes, arrhythmology, thoracotomy, and BMI. ACT, activated clotting time; OR, odds ratio; CI, confidence interval; NYHA, New York Heart Association; BMI, body mass index.

II, NYHA II, diabetes, and tracheotomy were observed between the groups. Nonetheless, imbalanced covariates were accounted for in the effect size estimation. Patients with diabetes (OR =14.95, 95% CI: 2.80–107.41, P=0.003) and thoracotomy (OR =2.55, 95% CI: 1.15–5.77, P=0.02) had a higher risk of bleeding, female (OR =0.35, 95% CI: 0.15–0.76, P=0.009), BMI (OR =0.83, 95% CI: 0.72–0.95, P=0.01) and mean platelet count (PLT_{mean}) (OR =0.98, 95% CI: 0.97–0.99, P=0.001) suggesting potential benefits in reducing postoperative bleeding (*Table 3*, *Figures 2*,*3*).

Discussion

This retrospective cohort study demonstrated that the preoperative use of aPRP before heart valve surgery may reduce postoperative bleeding and was associated with fewer postoperative complications. Multivariate regression analysis showed that diabetes and thoracotomy increased the risk of postoperative bleeding, while female sex, BMI and PLT_{mean} were associated with a decreasing in postoperative bleeding. Thus, reduced postoperative bleeding was a surrogate marker for improved outcomes during heart valve surgery.

Our results indicate that aPRP improves the clinical outcomes, consistent with studies conducted by Sandhu *et al.* and Andersen *et al.* (7,13). Researchers have proposed that aPRP therapy may offer enhanced benefits to surgical patients with low-risk and stable preoperative conditions, which may have contributed to improving the clinical outcomes, consistently with the current study, in which patients with stable preoperative conditions were enrolled. However, some studies suggested that aPRP is particularly beneficial for high-risk patients who experience extensive platelet activation and destruction during heart surgery (11,20). Inconsistent with our results, Wajon *et al.* found that aPRP in patients undergone reoperation did not reduce postoperative bleeding or improve clinical outcomes (14) and proposed that these patients were not suitable for aPRP therapy owing to severe myocardial reserve dysfunction. Additionally, the aPRP collection process can cause hypotension and activate leukotrienes and complements released after platelet activation, thus worsening microcirculatory disorders and coronary artery ischemia and ultimately leading to postoperative cardiac output reduction and heart failure exacerbation (21). However, the timing of aPRP administration also impacts clinical outcomes. Honda *et al.* demonstrated that autologous platelet separation and collection during the early stage of heparinization was safe and effective, did not disturb the surgical process, and avoided hypotension (22). However, whether the infusion of heparin-rich platelet plasma at the end of CPB increases the difficulty of surgical hemostasis and the risk of postoperative bleeding remains controversial (23).

Unlike previous studies, we observed a difference in the volume of mediastinal drainage 3 days after surgery between the two groups. Although our study found that aPRP had no significant effect on platelet counts after

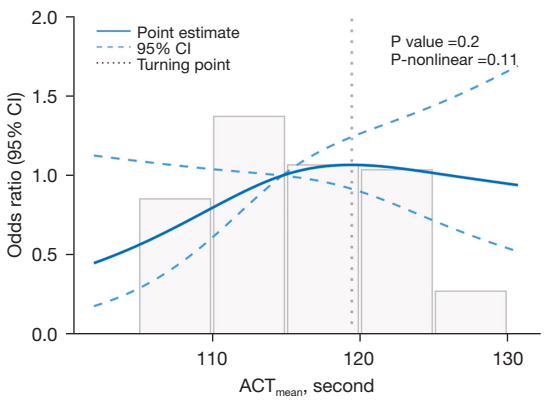

Figure 1 Association between ACT_{mean} and effect with the RCS function. 95% CI, 95% confidence interval; ACT, activated clotting time; RCS, restricted cubic spline.

Table 5 Logistic regression for efficacy/effectiveness analysis

Characteristic	Primary outcome (postoperative bleeding)			Secondary outcome complication		
	OR	95% CI	P value	OR	95% CI	P value
Treatment (unadjusted)						
Control	–	–	–	–	–	–
aPRP	0.53	0.28–1.00	0.05	0.28	0.10–0.68	0.009
Treatment (adjusted)*						
Control	–	–	–	–	–	–
aPRP	0.47	0.22–0.98	0.04	0.23	0.07–0.64	0.008

*, adjusted for NYHA, diabetes, arrhythmology, ACT_{mean}, CPB, bleeding, thoracotomy, BMI. aPRP, autologous platelet-rich plasma; OR, odds ratio; CI, confidence interval; NYHA, New York Heart Association, ACT, activated clotting time, CPB, cardiopulmonary bypass; BMI, body mass index.

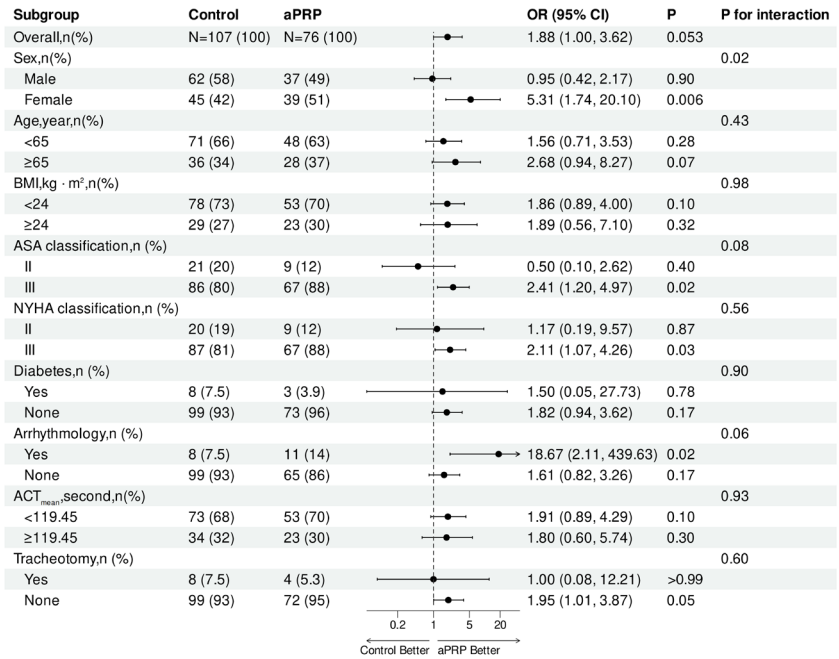

Figure 2 Subgroup analysis before calibration (multivariate logistic model). aPRP, autologous platelet-rich plasma; BMI, body mass index; ASA, American Society of Anesthesiologists; NYHA, New York Heart Association; ACT, activated clotting time; OR, odds ratio; CI, confidence interval.

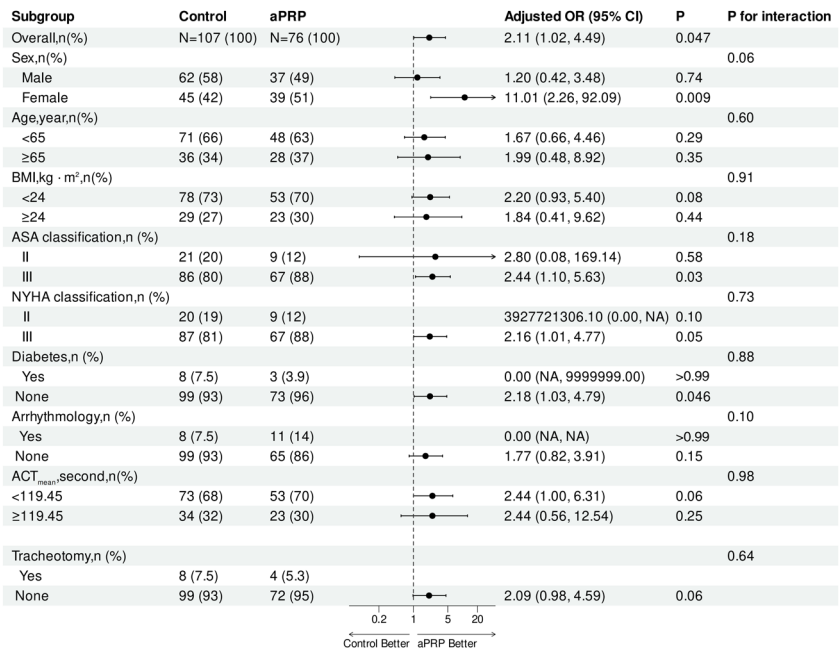

Figure 3 Subgroup analysis after calibration (multivariate logistic model). aPRP, autologous platelet-rich plasma; BMI, body mass index; ASA, American Society of Anesthesiologists; NYHA, New York Heart Association; ACT, activated clotting time; OR, odds ratio; CI, confidence interval; NA, not available.

surgery, after adjusting for variables and conducting multivariate risk analysis, we found that aPRP could reduce postoperative bleeding and decrease the retention time of the pericardial and mediastinal drainage tube. We speculate that the platelet-protective effect of aPRP may be attributed to the observed reduction in the postoperative drainage volume. A possible mechanism may be related to the high concentration of platelets, growth factors and cytokines [such as transforming growth factor (TGFb) and vascular endothelial growth factor (VEGF)] in aPRP, which mediate the repair and regeneration of cells during the early stages of cardiac injury (7,14). Additionally, platelets are known to play an anti-inflammatory role, reduce protein consumption, and maintain sufficient plasma colloidal osmotic pressure to decrease pleural effusion (5), which may explain the shortened retention time of pericardial and mediastinal drainage tubes.

At present, an exhaustive view of the various mechanisms triggered by postoperative aPRP transfusion is still far from to be provided, because of the multiple factors potentially involved, including those stored within platelet alpha granules, such as the chemokines interleukin 8 (IL-8), beta-thromboglobulin, platelet factor 4, and RANTES protein, the adhesion molecules P-selectin, and the growth factors platelet-derived growth factor (PDGF), TGFb, VEGF, stromal-derived growth factor 1 (CXCL12), and epidermal growth factor (EGF) (24), without considering the leukocyte presence.

Our study focused on the overall incidence of postoperative complications, including postoperative wound infections, poor healing, postoperative cerebral infarction, and postoperative liver and kidney failure. Although influenced by many factors, it was evident that the use of aPRP decreased the incidence postoperative complications. Numerous studies have confirmed aPRP can reduce C-reactive protein and inflammatory factors (25), such as interleukins 1 and 6 (IL-1, IL-6), and tumor necrosis factor alpha (TNFα) (26,27), which subsequently promotes re-epithelialization and improves clinical outcomes. Indeed, various studies focused on specific outcomes needed in the future, and with subgroup analyses revealing that preoperative aPRP is associated with a decreased risk of postoperative bleeding in patients suffering from diabetes. However, the underlying mechanism remains to be elucidated. For instance, in *in vitro* and *in vivo* animal studies (28), aPRP has been shown to inhibit ferroptosis and significantly improve the migration and regeneration ability of fibroblasts and vascular endothelial cells as induced by high glucose, but further randomized controlled trials are mandatory to validate this. Importantly, discrepancies in the sample size, target population, and platelet collection timing across studies have also contributed to contradictory research outcomes.

This study had several limitations. First, we did not perform a functional evaluation of the collected platelets or quantify the degree of platelet activation and loss during CPB. Second, although we attempted to minimize the impact of multicollinearity on the outcome variables by employing the logistic regression model of the RCS, bias could not be completely avoided. Additionally, standards for allogeneic blood transfusion among physicians are subjective. Since both inadequate and excessive transfusions can affect the evaluation of allogeneic blood transfusion volume, the volume of allogeneic blood transfusion was not a primary observation indicator in this study.

Conclusions

Although the benefit of PRP technology remains controversial, the safety and efficacy of aPRP can be significantly enhanced by thorough patient screening for indications, maintaining hemodynamic stability during the collection process, making reasonable arrangements for aPRP collection time, and monitoring coagulation function. Thus, the application of aPRP remains a promising avenue for future research and is poised to have a significant impact in the field of cardiac surgery.

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Footnote

Reporting Checklist: The authors have completed the STROCSS reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-794/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-794/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the ethics committee of Zhongshan Hospital (Xiamen), Fudan University (approval No. B2023-040) on 23 May 2023. Given the retrospective design of the study, the requirement for informed consent was waived.

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