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*Article*

# Association between Thrombocytopenia and Outcomes in Patients Undergoing Redo Valvular Surgery Utilizing Cardiopulmonary Bypass

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## Abstract

**Objective**: To figure out the incidence of postoperative thrombocytopenia among adult cases undergoing redo valvular surgery with cardiopulmonary bypass (CPB) and to discern its ramifications on early postoperative outcomes. **Methods**: A cohort comprising 188 cases undergoing redo valvular surgery with CPB between March 2018 and July 2023 was analyzed. It was attempted to stratify cases into two groups on the basis of presence of thrombocytopenia that was defined as a nadir platelet count $<71 \times 10^3/\mu L$ within 72 hours (n = 45), or absence of thrombocytopenia (n = 143). Comparative evaluation was performed concerning postoperative mortality and morbidity. Logistic regression models were employed to unveil the relationship of thrombocytopenia with clinical outcomes. **Results**: Thrombocytopenia manifested in 45 (23.94%) cases. Univariate analysis disclosed a significant association of percent change in platelet count with mortality (odds ratio (OR), 1.039, 95% confidence interval (CI), 1.005 to 1.074, $p = 0.024$), postoperative pneumonia (OR, 1.058, 95% CI, 1.023 to 1.095, $p = 0.001$), prolonged mechanical ventilation (OR, 1.048, 95% CI, 1.026 to 1.071, $p < 0.001$), extended intensive care unit (ICU) stay (OR, 1.029, 95% CI, 1.010 to 1.049, $p = 0.003$), protracted post-operative hospitalization (OR, 1.031, 95% CI, 1.011 to 1.051, $p = 0.002$), postoperative renal replacement therapy (OR, 1.042, 95% CI, 1.017 to 1.069, $p = 0.001$), and re-thoracotomy attributable to hemorrhage (OR, 1.040, 95% CI, 1.000 to 1.080, $p = 0.047$). Multivariate analysis demonstrated that thrombocytopenia, regarded as a categorical variable, was independently correlated with an escalated likelihood of prolonged postoperative hospital stay (OR, 4.926, 95% CI, 1.740 to 13.948, $p = 0.003$). **Conclusions**: Thrombocytopenia appeared to be closely linked to escalated in-hospital mortality and postoperative morbidity rates among cases undergoing redo valvular surgery employing CPB. Further investigations with larger, prospective cohorts are essential to validate these outcomes and unravel potential underlying mechanisms.

## Keywords

platelets; thrombocytopenia; redo valvular surgery; cardiopulmonary bypass; post-operation

## Introduction

Recent investigations have unveiled the involvement of platelets not only in hemostasis and thrombosis, but also in inflammation and innate immunity [1–4]. Thrombocytopenia, frequently occurring following cardiac surgery [5,6], exerts a substantial influence on postoperative morbidity and mortality [5,7,8]. As life expectancy rises and medical techniques advance, there is a growing demand for redo valvular surgery [9,10]. Furthermore, there has been a notable elevation in the use of bioprosthetic valves, which are susceptible to structural valve degeneration and may necessitate re-valve replacement [11,12]. While prior research explored platelet dynamics following coronary artery bypass grafting and cardiopulmonary bypass (CPB) [7,8], little is known about the incidence of thrombocytopenia among cases receiving redo valvular surgery with CPB and its impact on perioperative complications. This retrospective study aimed to assess the frequency and pattern of platelet count decline and investigate the repercussions of postoperative thrombocytopenia on early outcomes in patients undergoing redo valvular surgery.

## Materials and Methods

### *Study Population*

Consecutively, adult patients undergoing elective redo valvular surgery with CPB at the Department of Cardiac Surgery of Peking University International Hospital that was headquartered in Beijing (China) during the period from March 2018 to July 2023, were involved. The inclusion criteria encompassed individuals who had previously undergone redo valvular surgeries with CPB, while exclusion criteria were delineated to exclude cases under 18 years

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of age, those necessitating emergency procedures, intraoperative mortalities, recent antibiotic usage within 2 weeks preceding surgery, preoperative reliance on dialysis, presence of infective endocarditis, utilization of immunosuppressants for systemic autoimmune disorders or myeloid malignancies, diagnosis of cancer, severe hepatic insufficiency, hypersplenism, consumption of antiplatelet agents within 1 week prior to surgery, and confirmation of heparin-induced thrombocytopenia (HIT) prior to surgery. A total cohort of 188 patients was ultimately involved, stratified into distinct groups based on the postoperative platelet count for analysis.

### *Data Collection and Definitions*

Data comprising demographic profiles, intraoperative specifics, and postoperative records were attained from the electronic medical record system. Thrombocytopenia, delineated by a platelet count dipping below $71 \times 10^3/\mu L$ postoperatively, was regarded significant due to its alignment with the 25th percentile of the lowest platelet count found within 72 hours following surgery [7]. The primary outcome was in-hospital mortality, while secondary endpoints encompassed postoperative pneumonia, prolonged mechanical ventilation, protracted stay in the intensive care unit (ICU), extended hospitalization post-surgery, necessity for postoperative renal replacement therapy, and the occurrence of re-thoracotomy prompted by hemorrhage. Parameters for defining prolonged mechanical ventilation, ICU stay, and postoperative hospital stay were contingent upon surpassing the 75th percentile. Identification of postoperative pneumonia entailed meeting criteria, such as positive culture of respiratory secretions or manifestation of new or progressive, persistent infiltrates on X-rays [13].

### *Statistical Analysis*

Expression of continuous variables was in the format of mean values accompanied by their respective standard deviations, and it was attempted to compare normally distributed data between groups through Student's *t*-test. Presentation of abnormally distributed data was through median along with interquartile range (25th–75th percentile) and their analysis analyzed using the Mann-Whitney U test. Describing categorical variables was in the format of count and percentage, and their comparison was implemented through Chi-squared test, Bonferroni correction, continuity correction, or Fisher's exact test as appropriate. Thrombocytopenia was treated as a categorical variable, while platelet nadir at 72 hours, absolute change in platelet count (defined as the difference between postoperative and preoperative values), and percent change in platelet count (defined as the absolute change divided by the preoperative value) were regarded as continuous variables. The association of thrombocytopenia with outcomes was figured out univariate logistic regression analysis. A multivariable regression model was subsequently developed, adjusting for several variables, encompassing age, body mass index (BMI), preoperative serum creatinine, platelet count, white blood cell count, intraoperative blood loss, red blood cell transfusion, plasma transfusion, and surgical time. It was attempted to calculate odds ratios (ORs) plus 95% confidence intervals (CIs). $p$ subordinate 0.05 was utilized to signify statistical analysis. It was attempted to analyze data through SPSS 26.0 software (IBM Corp., Chicago, IL, USA) developed via IBM Corp. that was headquartered in Armonk (USA).

## Results

### *Patients' Characteristics*

The study encompassed 188 patients, with a median age of 58.00 years (interquartile range: 48.25 to 67.00 years, range: 19–79 years), with women constituting 57.45% of the cohort. The median duration between the two cardiac procedures stood at 14.50 years (interquartile range: 9.00 to 22.00 years). Following redo valvular surgery, 11 cases succumbed during their hospitalization, 4 developed pneumonia, 45 necessitated prolonged mechanical ventilation, 45 experienced extended stays in the ICU, 43 endured prolonged post-operative hospital stay, 7 underwent reintubation, 7 required exploratory thoracotomy for hemorrhage, and 22 underwent renal replacement therapy. The average follow-up period mirrored the mean length of hospitalization post-surgery, which was equal to $15.04 \pm 11.32$ days.

### *Comparison of Preoperative, Intraoperative Factors and Outcomes between Thrombocytopenia and Non- Thrombocytopenia Group*

Patients with postoperative thrombocytopenia were older ($p = 0.002$), and had lower BMI ($p = 0.007$). The estimated glomerular filtration rates (eGFR) ($p = 0.001$), preoperative platelet count ($p < 0.001$), and white blood cell count ($p = 0.020$) in the thrombocytopenia group were all significantly lower than those without thrombocytopenia, while the preoperative serum creatinine was higher than that in the non-thrombocytopenia group ($p = 0.011$). Patients in the thrombocytopenia group had longer surgical time ($p = 0.001$), CPB duration ($p = 0.006$), more blood loss ($p < 0.001$), more red blood cells ($p < 0.001$) and plasma ($p < 0.001$) transfusion than the non-thrombocytopenia group. The clinical characteristics of thrombocytopenia and non-thrombocytopenia groups are accessible in Table 1.

Analysis of the postoperative clinical data between the two cohorts unveiled significant differences. Patients experiencing thrombocytopenia exhibited substantially prolonged mechanical ventilation duration ($p < 0.001$), ex-

**Table 1. Demographic and clinical profiles of cases subjected to redo valvular surgery utilizing cardiopulmonary bypass.**

| Characteristics | All cases (n = 188) | Platelet nadir <71 × $10^3$/μL (n = 45) | Platelet nadir ≥71 × $10^3$/μL (n = 143) | *p* |
|---|---|---|---|---|
| Age, y | 58.00 (48.25, 67.00) | 63.00 (54.25, 70.50) | 57.00 (46.00, 65.00) | 0.002 |
| Female sex, n (%) | 108.00 (57.45) | 27.00 (60.00) | 81.00 (56.64) | 0.691 |
| BMI, kg/m$^2$ | 21.56 (19.66, 23.55) | 20.33 (18.54, 23.08) | 21.88 (19.83, 23.90) | 0.007 |
| Interval, y | 14.50 (9.00, 22.00) | 15.50 (10.00, 24.00) | 14.00 (8.00, 22.00) | 0.356 |
| Diabetes (type 1 or 2), n (%) | 14.00 (7.45) | 0.00 (0.00) | 14.00 (9.79) | 0.063 |
| Smoking, n (%) | 20.00 (10.64) | 6.00 (13.33) | 14.00 (9.79) | 0.693 |
| Hypertension, n (%) | 19.00 (10.11) | 6.00 (13.33) | 13.00 (9.09) | 0.589 |
| COPD, n (%) | 2.00 (1.06) | 1.00 (2.22) | 1.00 (0.70) | 0.972 |
| LVEF, % | 62.00 (56.00, 70.00) | 62.50 (55.00, 69.98) | 62.00 (56.00, 69.50) | 0.566 |
| Preoperative eGFR, mL/min/1.73 m$^2$ | 84.89 (62.42, 100.07) | 72.59 (52.96, 93.76) | 87.21 (67.36, 103.14) | 0.001 |
| Preoperative serum creatinine, μmol/L | 75.00 (61.00, 95.00) | 90.00 (66.25, 121.25) | 73.00 (60.00, 88.00) | 0.011 |
| Baseline platelets, ×$10^3$/μL | 159.50 (118.00, 197.75) | 103.00 (85.25, 128.50) | 173.00 (140.00, 208.00) | <0.001 |
| Preoperative white blood cell count, ×$10^3$/μL | 5.11 (3.79, 6.67) | 4.24 (3.16, 6.37) | 5.45 (4.01, 6.85) | 0.020 |
| Preoperative hemoglobin, g/L | 115.00 (98.25, 131.00) | 109.00 (93.50, 130.75) | 116.00 (100.00, 131.00) | 0.067 |
| Surgical time, hour | 6.18 (5.03, 7.50) | 6.83 (5.91, 8.64) | 5.92 (4.94, 7.04) | 0.001 |
| CPB duration, min | 190.00 (140.00, 243.00) | 221.00 (159.00, 288.50) | 173.00 (133.00, 231.00) | 0.006 |
| Cross-clamp time, min | 129.50 (91.00, 169.25) | 153.00 (98.25, 180.75) | 124.00 (90.00, 163.00) | 0.139 |
| Intraoperative blood loss, mL | 700.00 (500.00, 1037.50) | 1000.00 (600.00, 1775.00) | 600.00 (445.00, 900.00) | <0.001 |
| Red blood cells transfusion, U | 4.00 (2.00, 8.00) | 8.00 (4.00, 11.50) | 4.00 (2.00, 4.00) | <0.001 |
| Plasma transfusion, mL | 400.00 (0.00, 600.00) | 600.00 (400.00, 1200.00) | 400.00 (0.00, 600.00) | <0.001 |
| Platelet transfusion, U | 1.00 (0.00, 1.00) | 1.00 (0.00, 1.00) | 1.00 (0.00, 1.00) | 0.451 |

BMI, body mass index; COPD, chronic obstructive pulmonary disease; LVEF, left ventricular ejection fraction; eGFR, estimated glomerular filtration rate; CPB, cardiopulmonary bypass.

tended stay in the ICU ($p < 0.001$), and prolonged hospitalization following surgery ($p < 0.001$) relative to those without thrombocytopenia. Moreover, the incidence of requiring renal replacement therapy was notably higher in cases with thrombocytopenia relative to their non-thrombocytopenic counterparts ($p = 0.047$). Detailed clinical outcomes are accessible in Table 2.

### *Postoperative Thrombocytopenia Incidence*

The incidence of postoperative thrombocytopenia was notable. Moreover, 171 of the 188 (90.96%, 171/188) patients had a platelet nadir <150 × $10^3$/μL within 72 hours of CPB, while 102 (54.26%, 102/188) patients had <100 × $10^3$/μL, 45 (23.94%, 45/188) patients had <71 × $10^3$/μL, and 18 (9.57%, 18/188) patients had <50 × $10^3$/μL. The mean platelet drop was 38.67%. Thrombocytopenia before surgery was common, as 85 (12.7%, 85/188) patients had a pre-operative platelet count <150 × $10^3$/μL, 29 (15.43%, 29/188) had a platelet count <100 × $10^3$/μL, and 7 (3.72%, 7/188) had a platelet count <71 × $10^3$/μL. No patient of the 45 with post-operative thrombocytopenia was found to have HIT. The drop in platelet count was noted from the day of surgery to day 3 with recovery on day 4 (Fig. 1). There were 27 patients with thrombocytopenia (<71 × $10^3$/μL) on day 4, of whom 4 (14.81%, 4/27) died in hospital.

### *Analysis of Association between Postoperative Thrombocytopenia and Clinical Outcomes*

Univariate analysis revealed that thrombocytopenia could be a categorical variable that was associated with postoperative pneumonia, prolonged mechanical ventilation, prolonged ICU stay, and prolonged post-operative hospital stay. Platelet nadir as a continuous variable was inversely related to the six secondary outcomes. Absolute change in platelets was associated with prolonged mechanical ventilation and postoperative renal replacement therapy. Percent change in platelets was associated with all primary and secondary outcomes. All associations were statistically significant (all $p < 0.05$, Table 3). In the multivariable analysis, thrombocytopenia was associated with increased rates of prolonged postoperative hospital stay (OR, 4.926, 95% CI, 1.740 to 13.948, $p = 0.003$) after adjusting for covariates. Platelet nadir and absolute change in platelets were associated with prolonged mechanical ventilation (OR, 0.972, 95% CI, 0.953 to 0.992, $p = 0.006$; OR, 1.024, 95% CI, 1.004 to 1.045, $p = 0.016$). Percent change in platelets was associated with re-thoracotomy due to hemorrhage (OR, 1.126, 95% CI, 1.000 to 1.268, $p = 0.049$). No statistical significance in adjusted models was identified for the remaining primary and secondary end points (Table 4).

**Table 2. Comparative examination of postoperative outcomes in cases with and without thrombocytopenia.**

| Characteristics | Platelet nadir <71 × $10^3$/μL (n = 45) | Platelet nadir ≥71 × $10^3$/μL (n = 143) | *p* |
|---|---|---|---|
| In-hospital death, n (%) | 5.00 (11.11) | 6.00 (4.20) | 0.174 |
| Pneumonia, n (%) | 1.00 (2.22) | 3.00 (2.10) | 1.000 |
| Mechanical ventilation, h | 48.00 (20.50, 125.50) | 19.00 (17.00, 25.00) | <0.001 |
| ICU stay, d | 6.00 (4.00, 11.00) | 3.00 (2.00, 4.00) | <0.001 |
| Postoperative hospital stay, d | 19.00 (10.00, 32.00) | 10.00 (8.00, 14.00) | <0.001 |
| Renal replacement therapy, n (%) | 9.00 (20.00) | 13.00 (9.09) | 0.047 |
| Re-thoracotomy due to hemorrhage, n (%) | 4.00 (8.89) | 3.00 (2.10) | 0.100 |

ICU, intensive care unit.

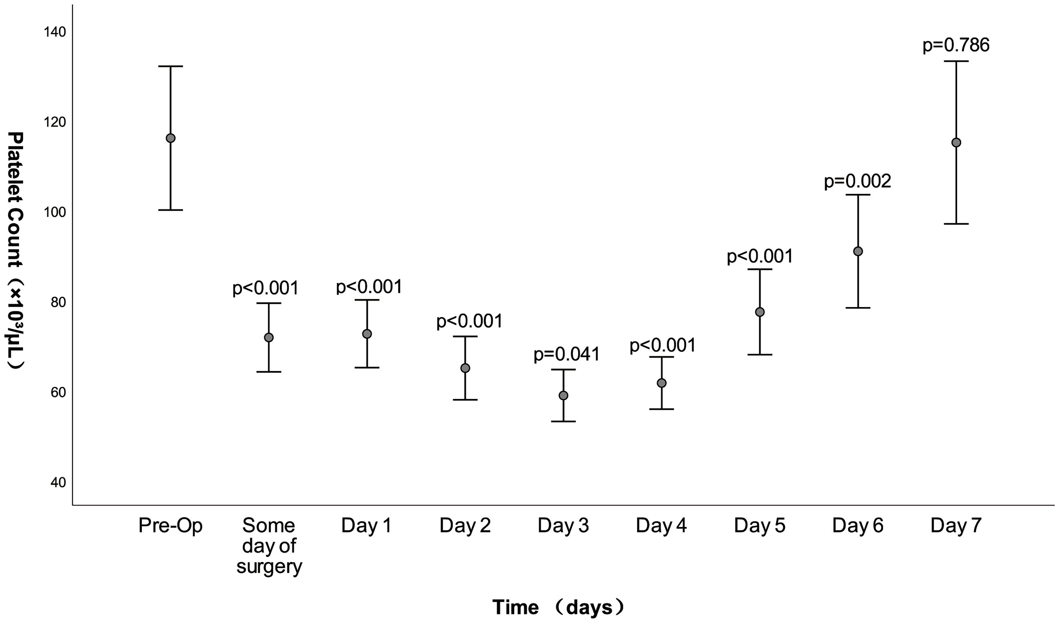


**Fig. 1. Platelet count in patients with thrombocytopenia.**

## Discussion

The primary purpose of this investigation was to elucidate the frequency of thrombocytopenia occurrence in cases undergoing iterative valvular surgeries with CPB and its consequential impact on mortality and morbidity. While existing literature has extensively examined thrombocytopenia subsequent to initial cardiac interventions involving CPB, there exists a notable dearth in studies examining its prevalence and implications in the context of redo cardiac surgeries [14–17]. Within this study cohort, comprising exclusively cases undergoing iterative valvular surgeries with CPB, with valve procedures being the predominant type, and the analysis unveiled a prevalent occurrence of postoperative thrombocytopenia, concomitant with escalated rates of mortality and morbidity.

Monitoring of platelet count after cardiac surgery is vital. Platelet count and function play notable functions in hemostasis, inflammation, and modulating immunological processes [2]. Anticoagulant therapy after cardiac valvular surgery is imperative, in which monitoring of platelets is valuable for periprocedural medication management. Additional attention to platelet count could contribute to timely identify high-risk cases for poor outcomes. Moreover, the presence of thrombocytopenia is essential for diagnosing HIT, which makes platelet monitoring inevitable.

Postoperative thrombocytopenia is common in cardiac surgery with CPB. The reported incidence of postoperative thrombocytopenia varied from 30% to 94% [5–8]. Divergence in diagnostic criteria for thrombocytopenia and the heterogeneous nature of cardiac surgical interventions may account for these distinctions. Remarkably, the present investigation unveiled a remarkable incidence of thrombocytopenia subsequent to redo valvular procedures. Additionally, cases in the postoperative thrombocytopenia subset manifested traits commonly linked to advanced age, decreased BMI, diminished preoperative platelet and white blood cell counts, alongside elevated serum creatinine level, in accordance with prior observations in similar cardiac procedural contexts [7,8,18].

**Table 3. Univariate analysis of association between postoperative thrombocytopenia and clinical outcomes.**

| Adverse outcome | Thrombocytopenia | | Platelet nadir | | Absolute change in platelets | | % change in platelets | |
|---|---|---|---|---|---|---|---|---|
| | Odds Ratio (95% CI) | *p* value | Odds Ratio (95% CI) | *p* value | Odds Ratio (95% CI) | *p* value | Odds Ratio (95% CI) | *p* value |
| In-hospital death | 2.228 (0.600–8.276) | 0.232 | 0.985 (0.967–1.003) | 0.110 | 1.009 (0.998–1.020) | 0.126 | 1.039 (1.005–1.074) | 0.024 |
| Pneumonia | 10.090 (2.550–39.926) | 0.001 | 0.949 (0.924–0.974) | <0.001 | 1.007 (0.996–1.018) | 0.220 | 1.058 (1.023–1.095) | 0.001 |
| Mechanical ventilation >46 hours | 6.639 (3.147–14.008) | < 0.001 | 0.965 (0.952–0.978) | <0.001 | 1.008 (1.001–1.015) | 0.019 | 1.048 (1.026–1.071) | <0.001 |
| ICU stay >5 days | 5.750 (2.743–12.055) | < 0.001 | 0.970 (0.958–0.982) | <0.001 | 1.001 (0.994–1.008) | 0.796 | 1.029 (1.010–1.049) | 0.003 |
| Postoperative hospital stay >18 days | 7.398 (3.463–15.808) | < 0.001 | 0.976 (0.965–0.987) | <0.001 | 1.005 (0.998–1.012) | 0.181 | 1.031 (1.011–1.051) | 0.002 |
| Renal replacement therapy | 2.500 (0.990–6.315) | 0.053 | 0.985 (0.972–0.998) | 0.029 | 1.010 (1.002–1.019) | 0.018 | 1.042 (1.017–1.069) | 0.001 |
| Re-thoracotomy due to hemorrhage | 4.553 (0.979–21.171) | 0.053 | 0.968 (0.944–0.993) | 0.011 | 1.002 (0.987–1.018) | 0.752 | 1.040 (1.000–1.080) | 0.047 |

CI, confidence interval; ICU, intensive care unit.

**Table 4. Multivariate analysis of association between postoperative thrombocytopenia and clinical outcomes.**

| Adverse outcome | Thrombocytopenia | | Platelet nadir | | Absolute change in platelets | | % change in platelets | |
|---|---|---|---|---|---|---|---|---|
| | Odds Ratio (95% CI) | *p* value | Odds Ratio (95% CI) | *p* value | Odds Ratio (95% CI) | *p* value | Odds Ratio (95% CI) | *p* value |
| In-hospital death | 0.575 (0.055–5.985) | 0.643 | 0.992 (0.959–1.025) | 0.620 | 1.005 (0.974–1.037) | 0.760 | 1.019 (0.965–1.076) | 0.495 |
| Pneumonia | 2.370 (0.314–17.885) | 0.403 | 0.967 (0.930–1.006) | 0.095 | 1.028 (0.991–1.067) | 0.137 | 1.035 (0.984–1.089) | 0.179 |
| Mechanical ventilation >46 hours | 2.332 (0.758–7.173) | 0.140 | 0.972 (0.953–0.992) | 0.006 | 1.024 (1.004–1.045) | 0.016 | 1.027 (0.997–1.057) | 0.077 |
| ICU stay >5 days | 1.641 (0.576–4.680) | 0.354 | 0.984 (0.967–1.001) | 0.067 | 1.015 (0.997–1.033) | 0.095 | 1.022 (0.994–1.050) | 0.122 |
| Postoperative hospital stay >18 days | 4.926 (1.740–13.948) | 0.003 | 0.984 (0.968–1.000) | 0.054 | 1.013 (0.996–1.029) | 0.128 | 1.017 (0.991–1.043) | 0.200 |
| Renal replacement therapy | 1.808 (0.358–9.140) | 0.474 | 0.980 (0.957–1.003) | 0.094 | 1.017 (0.994–1.040) | 0.143 | 1.034 (0.993–1.075) | 0.102 |
| Re-thoracotomy due to hemorrhage | 1.603 (0.068–37.526) | 0.769 | 0.925 (0.854–1.001) | 0.054 | 1.077 (0.995–1.165) | 0.065 | 1.126 (1.000–1.268) | 0.049 |

CI, confidence interval; ICU, intensive care unit. Several variables were adjusted which include the age, body mass index (BMI), preoperative serum creatinine, platelet count, white blood cell count, intraoperative blood loss, red blood cells transfusion, plasma transfusion and surgical time.

Studies have outlined that platelets undergo quantitative alterations throughout CPB [6,7,16,17,19]. Throughout CPB, alterations in platelet count and function ensue due to factors, involving hemodilution, hypothermia, shear stress, prolonged interaction with artificial surfaces, and the administration of pharmacological agents like heparin and protamine. Notably, our observations revealed prolonged CPB duration in cases in the thrombocytopenia cohort, aligning with prior investigations. Moreover, a decline was noted in platelet count within the initial 72-hour postoperative timeframe, followed by a subsequent rebound by day four, mirroring trends documented in prior research [6,7,17,20–22]. The incidence of HIT in cases receiving cardiac surgery is 1–3% [23–25]. In the present investigation, no patients could be identified to have HIT that could be attributable to limited samples.

The present investigation demonstrated that percent change in platelets was associated with mortality, postoperative pneumonia, prolonged mechanical ventilation, prolonged ICU stay, prolonged post-operative hospital stay, postoperative renal replacement therapy, and re-thoracotomy due to hemorrhage. Platelet surface receptors (TLR4, TLR2, $\alpha$IIb$\beta$3, GPIb, *etc.*) engage in direct interaction of platelets and bacteria. Moreover, platelet granules secret microbicidal agents that may lyse bacteria directly and abundant proteins, which may regulate the immune response [26]. Platelets may interact with the endothelium, neutrophils, monocytes, and lymphocytes, and platelets thus contribute to the regulation of both adaptive and innate immune responses, as well as inflammation [27]. These outcomes might be potential mechanisms that thrombocytopenia may result in a higher incidence of postoperative pneumonia and prolonged mechanical ventilation. In addition, it was unveiled that the success rate of extubation was higher at the stage when the platelet count was higher in clinical settings. This suggests that monitoring platelet count may help reduce the rate of reintubation due to inappropriate assessment of the condition. This has certain clinical implications for the perioperative management of such patients.

In recent studies, thrombocytopenia was associated with postoperative acute kidney injury (AKI) [8,28]. Platelets were initially recruited to the sites of acute injury, where they could interact with leukocytes and endothelial cells [29]. Platelets were found to recruit and activate leukocytes and stimulate endothelial cells during the inflammatory reaction, thereby promoting inflammation [30]. In AKI, platelets are also involved in renal hemodynamic processes, causing hypoxemic kidney tissue injury [31]. Both systemic inflammation and ischemia–reperfusion induce changes in the renal microcirculation and microcirculation, mainly resulting in poorly controlled hemostatic and inflammatory responses, thereby triggering irreversible damage to kidney tissues [32]. This may explain why a lower platelet count is linked to the escalated incidence of postoperative renal replacement therapy. Furthermore, the elevated preoperative serum creatinine level noted in the thrombocytopenia group could also be a contributing factor to the escalated need for renal replacement therapy.

In a retrospective examination encompassing 589 cases undergoing cardiac surgery with CPB [33], it was discerned that platelet function, as quantified by multiple electrode aggregometry, displayed a dependency on platelet count, with preoperative platelet count and function emerging as predictive factors for postoperative bleeding. Similarly, insights attained from the PLATFORM study, a prospective cohort encompassing 490 adult cardiac surgery cases, underscored the substantive correlation of post-CPB platelet function assessment with subsequent bleeding occurrences [34]. Furthermore, Ichikawa *et al.* [35], through a post-hoc analysis of 97 CPB-assisted cardiac surgery cases, identified a notable association of diminished platelet count at surgery's conclusion with the escalated postoperative bleeding. Our outcomes align with these conclusions, revealing an association of thrombocytopenia with the requirement for re-thoracotomy to address hemorrhage. Hence, timely administration of platelet transfusions upon detecting low platelet levels could potentially mitigate the necessity for re-thoracotomy in cases of bleeding.

### *Limitations*

Initially, it is imperative to acknowledge that this study adopted a retrospective approach, necessitating validation through precisely designed prospective investigations. It is crucial to recognize potential biases, including selection bias and measurement errors, which may impinge upon the robustness of the findings. Secondly, the study's sample size was modest, and the follow-up was confined to a singular institution. Consequently, residual biases and potential confounding variables inevitably persist, and definitive causal relationships remain elusive. Moreover, the exploration of thrombocytopenia across various types of valvular surgeries remains cursory. Hence, comprehensive prospective studies conducted on a larger scale are essential to deeply figure out the risk factors and prognostic implications of postoperative thrombocytopenia among cases undergoing redo valvular surgery.

## Conclusions

This investigation concentrated on examination of the intricate relationship of thrombocytopenia with surgical complications, particularly in the context of redo valvular surgery with CPB. Noteworthy was the significant prevalence of postoperative thrombocytopenia in this cohort. Moreover, thrombocytopenia emerged as a pivotal factor associated with escalated mortality and morbidity rates in cases undergoing redo valvular surgeries utilizing CPB. Employing continuous platelet monitoring regarded as a strategic approach for the timely identification of high-risk cases, reflecting the necessity of multidisciplinary, multimodal perioperative interventions.

## Availability of Data and Materials

The original contributions presented in the study are included in the article, and further inquiries can be directed to the corresponding author.

## Author Contributions

CZ: conception, design, data management, statistical analysis, manuscript writing, and manuscript editing. YX: conception, data management, manuscript editing, supervision or mentorship. JX: provision of study materials or patients, manuscript editing, supervision or mentorship. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

## Ethics Approval and Consent to Participate

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Review Board of Peking University International Hospital (protocol code 2024-KY-0001-01, 2024-02-22). Informed consent was obtained from all subjects involved in the study.

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## Conflict of Interest

The authors declare no conflict of interest.

## References

[1] Mandel J, Casari M, Stepanyan M, Martyanov A, Deppermann C. Beyond Hemostasis: Platelet Innate Immune Interactions and Thromboinflammation. International Journal of Molecular Sciences. 2022; 23: 3868.

[2] Maouia A, Rebetz J, Kapur R, Semple JW. The Immune Nature of Platelets Revisited. Transfusion Medicine Reviews. 2020; 34: 209–220.

[3] El Filaly H, Mabrouk M, Atifi F, Guessous F, Akarid K, Merhi Y, *et al*. Dissecting Platelet's Role in Viral Infection: A Double-Edged Effector of the Immune System. International Journal of Molecular Sciences. 2023; 24: 2009.

[4] Hicks SM, Lee CSM, Ali SA, Choi PY, Gardiner EE. The molecular basis of immune-based platelet disorders. Clinical Science. 2020; 134: 2807–2822.

[5] Squiccimarro E, Jiritano F, Serraino GF, Ten Cate H, Paparella D, Lorusso R. Quantitative and Qualitative Platelet Derangements in Cardiac Surgery and Extracorporeal Life Support. Journal of Clinical Medicine. 2021; 10: 615.

[6] Hamid M, Akhtar MI, Naqvi HI, Ahsan K. Incidence and pattern of Thrombocytopenia in cardiac surgery patients. JPMA. the Journal of the Pakistan Medical Association. 2017; 67: 1019–1023.

[7] Griffin BR, Bronsert M, Reece TB, Pal JD, Cleveland JC, Fullerton DA, *et al*. Thrombocytopenia After Cardiopulmonary Bypass Is Associated With Increased Morbidity and Mortality. The Annals of Thoracic Surgery. 2020; 110: 50–57.

[8] Kertai MD, Zhou S, Karhausen JA, Cooter M, Jooste E, Li YJ, *et al*. Platelet Counts, Acute Kidney Injury, and Mortality after Coronary Artery Bypass Grafting Surgery. Anesthesiology. 2016; 124: 339–352.

[9] Kilic A, Acker MA, Gleason TG, Sultan I, Vemulapalli S, Thibault D, *et al*. Clinical Outcomes of Mitral Valve Reoperations in the United States: An Analysis of The Society of Thoracic Surgeons National Database. The Annals of Thoracic Surgery. 2019; 107: 754–759.

[10] Bianco V, Kilic A, Gleason TG, Aranda-Michel E, Habertheuer A, Wang Y, *et al*. Reoperative Cardiac Surgery Is a Risk Factor for Long-Term Mortality. The Annals of Thoracic Surgery. 2020; 110: 1235–1242.

[11] Kim KM, Shannon F, Paone G, Lall S, Batra S, Boeve T, *et al*. Evolving trends in aortic valve replacement: A statewide experience. Journal of Cardiac Surgery. 2018; 33: 424–430.

[12] Isaacs AJ, Shuhaiber J, Salemi A, Isom OW, Sedrakyan A. National trends in utilization and in-hospital outcomes of mechanical versus bioprosthetic aortic valve replacements. The Journal of Thoracic and Cardiovascular Surgery. 2015; 149: 1262–9.e3.

[13] Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. American Journal of Infection Control. 2008; 36: 309–332.

[14] Kizilay M, Elbir F, Aglar AA, Vural U, Balci AY, Yekeler İ. An overlooked fact: thrombocytopenia following bioprosthetic aortic valve replacement. Kardiochirurgia i Torakochirurgia Polska. 2019; 16: 19–26.

[15] Di Dedda U, Ranucci M, Porta A, Bari V, Ascari A, Fantinato A, *et al*. The combined effects of the microcirculatory status and cardiopulmonary bypass on platelet count and function during cardiac surgery. Clinical Hemorheology and Microcirculation. 2018; 70: 327–337.

[16] Argiriadou H, Antonitsis P, Gkiouliava A, Papapostolou E, Deliopoulos A, Anastasiadis K. Minimal invasive extracorporeal circulation preserves platelet function after cardiac surgery: a prospective observational study. Perfusion. 2020; 35: 138–144.

[17] Mujtaba SS, Ledingham S, Shah AR, Schueler S, Clark S, Pillay T. Thrombocytopenia After Aortic Valve Replacement: Comparison Between Sutureless Perceval S Valve and Perimount

Magna Ease Bioprosthesis. Brazilian Journal of Cardiovascular Surgery. 2018; 33: 169–175.

[18] Xie E, Liu J, Liu Y, Liu Y, Xue L, Fan R, *et al*. Association between platelet counts and morbidity and mortality after endovascular repair for type B aortic dissection. Platelets. 2022; 33: 73–81.

[19] van Straten AHM, Hamad MAS, Berreklouw E, ter Woorst JF, Martens EJ, Tan MESH. Thrombocytopenia after aortic valve replacement: comparison between mechanical and biological valves. The Journal of Heart Valve Disease. 2010; 19: 394–399.

[20] Agarwal S, Johnson RI, Kirmani BH. Pre- and Post-Bypass Platelet Function Testing With Multiple Electrode Aggregometry and TEG Platelet Mapping in Cardiac Surgery. Journal of Cardiothoracic and Vascular Anesthesia. 2015; 29: 1272–1276.

[21] Weitzel NS, Weitzel LB, Epperson LE, Karimpour-Ford A, Tran ZV, Seres T. Platelet mapping as part of modified thromboelastography (TEG®) in patients undergoing cardiac surgery and cardiopulmonary bypass. Anaesthesia. 2012; 67: 1158–1165.

[22] Bønding Andreasen J, Hvas AM, Ravn HB. Marked changes in platelet count and function following pediatric congenital heart surgery. Paediatric Anaesthesia. 2014; 24: 386–392.

[23] Selleng S, Malowsky B, Itterman T, Bagemühl J, Wessel A, Wollert HG, *et al*. Incidence and clinical relevance of anti-platelet factor 4/heparin antibodies before cardiac surgery. American Heart Journal. 2010; 160: 362–369.

[24] Warkentin TE, Sheppard JI, Sun JCJ, Jung H, Eikelboom JW. Anti-PF4/heparin antibodies and venous graft occlusion in post-coronary artery bypass surgery patients randomized to postoperative unfractionated heparin or fondaparinux thromboprophylaxis. Journal of Thrombosis and Haemostasis. 2013; 11: 253–260.

[25] Pishko AM, Cuker A. Heparin-Induced Thrombocytopenia in Cardiac Surgery Patients. Seminars in Thrombosis and Hemostasis. 2017; 43: 691–698.

[26] Deppermann C, Kubes P. Platelets and infection. Seminars in Immunology. 2016; 28: 536–545.

[27] Thomas MR, Storey RF. The role of platelets in inflammation. Thrombosis and Haemostasis. 2015; 114: 449–458.

[28] Yan S, Gao S, Lou S, Zhang Q, Wang Y, Ji B. Risk Factors of Thrombocytopenia After Cardiac Surgery with Cardiopulmonary Bypass. Brazilian Journal of Cardiovascular Surgery. 2023; 38: 389–397.

[29] Zuchtriegel G, Uhl B, Puhr-Westerheide D, Pörnbacher M, Lauber K, Krombach F, *et al*. Platelets Guide Leukocytes to Their Sites of Extravasation. PLoS Biology. 2016; 14: e1002459.

[30] Gleissner CA, von Hundelshausen P, Ley K. Platelet chemokines in vascular disease. Arteriosclerosis, Thrombosis, and Vascular Biology. 2008; 28: 1920–1927.

[31] Stokes KY, Granger DN. Platelets: a critical link between inflammation and microvascular dysfunction. The Journal of Physiology. 2012; 590: 1023–1034.

[32] Jansen MPB, Florquin S, Roelofs JJTH. The role of platelets in acute kidney injury. Nature Reviews. Nephrology. 2018; 14: 457–471.

[33] Ranucci M, Baryshnikova E, For The Surgical And Clinical Outcome Research Score Group. The interaction between preoperative platelet count and function and its relationship with postoperative bleeding in cardiac surgery. Platelets. 2017; 28: 794–798.

[34] Ranucci M, Pistuddi V, Di Dedda U, Menicanti L, De Vincentiis C, Baryshnikova E. Platelet function after cardiac surgery and its association with severe postoperative bleeding: the PLATFORM study. Platelets. 2019; 30: 908–914.

[35] Ichikawa J, Osada Y, Kodaka M, Nishiyama K, Komori M. Association Between Platelet Count and Postoperative Blood Loss in Patients Undergoing Cardiac Surgery With Cardiopulmonary Bypass and Fresh Frozen Plasma Administration Guided by Thromboelastometry. Circulation Journal. 2018; 82: 677–683.