# ORIGINAL ARTICLE

# Postoperative Thrombocytopenia and Coagulopathy in Cardiac Surgery with Cardiopulmonary Bypass: Incidence and Outcomes after Non-Red Cell Blood Product Transfusion

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**Background**: Cardiopulmonary bypass (CPB) activates inflammatory and fibrinolytic pathways, potentially disrupting hemostasis. Transfusion of non-red cell blood product is a conventional method of restoring hemostasis and treating coagulopathy and thrombocytopenia, the two common adverse outcomes of CPB.

**Objective**: To determine the incidence and outcomes of postoperative thrombocytopenia and coagulopathy in adult Thai cardiac surgery patients with CPB receiving non-red cell blood product transfusions.

**Materials and Methods**: The present study included patients aged 18 years and older that underwent cardiac surgery with CPB at Siriraj Hospital between January 2017 and June 2018. Enrolled patients were divided into four groups, no non-red cell blood products in Group 1, platelets (PLT) only in Group 2, fresh frozen plasma (FFP) and/or cryoprecipitate (cryo) in Group 3, and PLT, FFP and/or cryo in Group 4. Patients, clinical status and histories, intraoperative outcomes, and perioperative outcomes were collected and assessed for all groups. Postoperative thrombocytopenia was defined by PLT counts less than 100,000 cells/mm<sup>3</sup>. Coagulopathy was defined by prothrombin time (PT) or activated partial thromboplastin time (aPTT) greater than 1.5 of its institutional reference values. Non-red cell blood product transfusions for cardiac patients were determined by their attending physician.

**Results**: Of the 360 patients included, 61.7% were male, with a mean (±SD) age of 65.3±11.7 years, and BMI of 24.1±4.0 kg/m<sup>2</sup>. Most patients were classified as ASA-PS class 3 (71.9%), had elective surgeries (96.4%), history of antiplatelet use (65.8%), and coronary artery bypass graft (CABG) surgical procedure (56.9%). Postoperative thrombocytopenia was significantly more prevalent in Group 1 at 11.6%, followed by Group 3 at 9.5%, Group 4 at 3.7%, and Group 2 at 0% (p=0.010). Post-operative coagulopathy was more prevalent in Group 3 at 4.8%, followed by Group 2 at 4.1%, Group 1 at 3.9%, and Group 4 at 0.7%. Group 4 had a significantly greater incidence of anticoagulant use at 17.8% (p=0.007) and significantly longer CPB durations compared to the other groups at 146.6±74.7 minutes (p<0.01).

**Conclusion**: The researchers' study confirmed that preoperative antithrombotic use prior to cardiac surgical procedures and longer CPB duration influences physicians' decision to transfuse. The present study recommended prohibiting prophylactic administration of FFP and PLT as well as implementing restrictive non-red cell blood product transfusion strategies.

Keywords: Thrombocytopenia; Coagulopathy; Non-red Cell Blood Product Transfusion; Cardiopulmonary Bypass; Cardiac Surgery

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About 20% to 40% of cardiac surgery patients require transfusion to address postoperative

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Department of Anesthesiology, Faculty of Medicine Siriraj Hospital, Mahidol University, 2 Wanglang Road, Siriraj, Bangkoknoi, Bangkok 10700, Thailand.

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Khamtuikrua C, Lawanwisut C, Sujirattanawimol K, Suksompong S. Postoperative Thrombocytopenia and Coagulopathy in Cardiac Surgery with Cardiopulmonary Bypass: Incidence and Outcomes after Non-Red Cell Blood Product Transfusion. J Med Assoc Thai 2023;106:671-9. DOI: 10.35755/jmedassocthai.2023.07.13862 bleeding<sup>(1,2)</sup>. This percentage is even higher for major complex surgeries<sup>(1)</sup>. Cardiopulmonary bypass (CPB) activates inflammatory, hemostatic, and fibrinolytic pathways through blood-membrane interactions and shearing through its extracorporeal circuits<sup>(3,4)</sup>. This severely disrupts and impairs hemostasis with adjunctive heparin-protamine use under hypothermic, hemodiluted conditions<sup>(3,5,6)</sup>, increasing the demand for red cell and non-red cell blood product transfusions<sup>(5)</sup>. These outcomes are exacerbated by non-modifiable factors such as physiology, age, prior cardiac surgeries, CPB duration, critical preoperative status, impaired renal, or hepatic function, and modifiable factors such as preoperative anticoagulants or antiplatelet use, preoperative anemia, preoperative thrombocytopenia, or CPB hemoglobin level<sup>(1,3)</sup>.

The systemic effects of major CPB-cardiac surgeries trigger platelet (PLT) dysfunction, fibrinolysis, coagulation factor deficiencies, heparin rebound, metabolic derangements, untreated bleeding, and much more<sup>(1,2,4,7-9)</sup>. Thrombocytopenia and coagulopathy are the two common adverse outcomes after CPB and volume replacement<sup>(10)</sup>. Complications may arise from hemostatic deterioration such as postoperative bleeding, surgical re-exploration, post-surgical infection, stroke, acute kidney injury (AKI), morbidities, and mortality<sup>(2-5,7-12)</sup>.

Red cell and non-red cell transfusions are conventional methods of restoring hemostasis and treating coagulopathy and thrombocytopenia<sup>(2,3,7,13)</sup>. Fresh frozen plasma (FFP), cryoprecipitate (cryo), PLT, and fibrinogen concentrate such as prothrombin complex concentrate (PCC) are often administered prophylactically to correct laboratory values or minimize risk of bleeding<sup>(9,13,14)</sup>. Such unstandardized means of administration results in under- or overdosing<sup>(2,8)</sup>. This, coupled with conflicting results regarding potential adverse effects (AEs) from transfusion such as transfusionassociated cardiac overload (TACO), lung injury (TRALI), immunomodulation, stroke, vasoplegia, and death<sup>(2,6,9,14)</sup> fuels growing concerns about current transfusion practices.

Studying patients' hemostatic conditions and determining clinically safe transfusion thresholds will help minimize inappropriate and unnecessary transfusion practices, perioperative complications in CPB cardiac surgeries, and ensure timely interventions<sup>(1,8,15)</sup>.

The authors sought to determine the incidence and outcomes of thrombocytopenia and coagulopathy in adult Thai cardiac surgery patients with CPB receiving non-red cell transfusions.

# **Materials and Methods**

# Study design and participants

The present study was a single-center, retrospective chart study that included patients aged 18 years or older that underwent cardiac surgery with CPB at Siriraj Hospital between January 2017 and June 2018. Patients with more than two value procedures, aortic surgery, repeated cardiac surgery, mechanical circulatory support after CPB such as intra-aortic balloon pump (IABP) or extracorporeal membrane oxygen (ECMO), or that had incomplete anesthetic records were excluded. Enrolled patients were divided into four groups based on transfused products, no non-red cell blood products were in Group 1; PLT only in Group 2; FFP and/or cryo in Group 3; and PLT, FFP, and/or cryo in Group 4. Patient characteristics such as age, biological gender, body weight and height; clinical status based on the American Society for Anesthesiologists physical status (ASA-PS) classification, history of antiplatelets or anticoagulants, operative duration, CPB duration, surgical procedure type, and surgical condition as elective versus emergency; intraoperative outcomes as operation characteristics, operative time, CPB time, antifibrinolytic dosage, non-red cell blood component transfusion type, and body temperature upon arrival at cardiac surgical intensive care unit (CSICU); perioperative outcomes as prothrombin time (PT), activated partial thromboplastin time (aPTT), PLT count, drainage volume, resternotomy due to surgical bleeding, morbidities, and mortality, were collected and assessed for all groups. The authors received approval from the Institutional Review Board of the Faculty of Medicine, Siriraj Hospital, Mahidol University (COA no. Si 142/2018).

# Non-red cell blood product transfusion management

All procedures were performed by the same team of surgeons, anesthesiologists, and perfusionists. Tranexamic acid (TXA) was administered to each patient in different dosages and regimens as a single bolus or continuous infusion per the anesthesiologists' decision. Prior to CPB initiation, 3 mg/kg of heparin was administered to ensure activated clotting time (ACT) of more than 480 minutes. Optimal hypothermic nadir temperatures for CPB were agreed upon within the team. All patients were rewarmed to a nasopharyngeal temperature of 36.8°C to 37.0°C. Post-CPB, warmed red cell and non-red cell blood products were transfused per the attending surgeons' or anesthesiologists' decision.

# Definitions

Postoperative thrombocytopenia was defined by PLT counts of less than 100,000 cells/mm<sup>3</sup>. Coagulopathy was defined by PT or aPTT greater than 1.5 of the institutional reference values.

# Statistical analyses

A sample size of 359 patients was calculated based on the coagulopathy incidence recorded after cardiac surgery by Griffin et al.<sup>(4)</sup> and Li et al.<sup>(12)</sup> with a 5% acceptable error and a type I error of 0.05.

#### Table 1. Demographic and perioperative data

Variable	Study group				Total	p-value
	Group 1 (n=155)	Group 2 (n=49)	Group 3 (n=21)	Group 4 (n=135)	(n=360)	
Age (years); mean±SD	$64.8 \pm 11.4^{\text{D}}$	$69.2 \pm 9.9^{\text{D}}$	56.0±12.4 <sup>E</sup>	65.9±11.7 <sup>D</sup>	65.3±11.7	< 0.01
Biological sex; n (%)						0.690
Male	98 (63.2)	29 (59.2)	15 (71.4)	80 (59.3)	222 (61.7)	
Female	57 (36.8)	20 (40.8)	6 (28.6)	55 (40.7)	138 (38.3)	
BMI (kg/m <sup>2</sup> ); mean±SD	$24.1 \pm 3.6$	$24.0 \pm 3.8$	$24.7 \pm 4.6$	$23.9 \pm 4.4$	$24.1 \pm 4.0$	0.889
ASA-PS; n (%)						< 0.01
Class 3	130 (83.9)	42 (85.7)	11 (52.4)	76 (56.3)	259 (71.9)	
Class 4	25 (16.1)	7 (14.3)	10 (47.6)	59 (43.7)	101 (28.1)	
Condition of surgery; n (%)						< 0.01
Elective	155 (100)	49 (100)	21 (100)	122 (90.4)	347 (96.4)	
Emergency	0 (0.0)	0 (0.0)	0 (0.0)	13 (9.6)	13 (3.6)	
History of antithrombotic drugs; n (%)						< 0.01
No	49 (31.6)	6 (12.2)	10 (47.6)	33 (24.4)	98 (27.2)	
Antiplatelets	97 (62.6)	40 (81.6)	9 (42.9)	78 (57.8)	224 (62.2)	
Anticoagulants	4 (2.6)	0 (0.0)	1 (4.8)	20 (14.8)	25 (6.9)	
Both	5 (3.2)	3 (6.1)	1 (4.8)	4 (3.0)	13 (3.6)	
Method of intravenous administration tranexamic	acid; n (%)					0.647
Single bolus	135 (87.1)	42 (85.7)	20 (95.2)	115 (85.2)	312 (86.7)	
Infusion	20 (12.9)	7 (14.3)	1 (4.8)	20 (14.8)	48 (13.3)	
Tranexamic acid dosage (mg/kg); mean±SD	$22.0 \pm 11.0^{D}$	$28.1 \pm 13.3^{\text{E}}$	$18.4 \pm 8.5^{\circ}$	$20.5 \pm 9.0^{\text{D}}$	22.1±10.8	< 0.01
Type of surgical procedures; n (%)						< 0.01
CABGs	89 (57.4)	44 (89.8)	8 (38.1)	64 (47.4)	205 (56.9)	
Valve surgery	49 (31.6)	3 (6.1)	9 (42.9)	45 (33.3)	106 (29.4)	
Both	10 (6.5)	2 (4.1)	2 (9.5)	25 (18.5)	39 (10.8)	
Other <sup>A</sup>	7 (4.5)	0 (0.0)	2 (9.5)	1 (0.7)	10 (2.8)	
Operative duration (minutes); mean±SD	$171.8 \pm 61.2^{E}$	$225.1 \pm 88.5^{\text{D}}$	223.6±86.1 <sup>D</sup>	267.9±115.8 <sup>D</sup>	218.1±99.9	< 0.01
CPB duration (minutes); mean±SD	$86.3 \pm 29.0^{E,C}$	$108.5 \pm 44.8^{D}$	$129.4 \pm 65.1^{\text{D,F}}$	146.6±74.7 <sup>D</sup>	$114.5 \pm 60.8$	< 0.01
Post-operative thrombocytopenia; n (%)	18 (11.6)	0 (0.0)	2 (9.5)	5 (3.7)	25 (6.9)	0.010
Post-operative coagulopathy <sup>B</sup> ; n (%)	6 (3.9)	2 (4.1)	1 (4.8)	1 (0.7)	10 (2.8)	0.337
Hypothermia <sup>B</sup> ; n (%)	94 (60.6)	30 (61.2)	14 (66.7)	85 (63.0)	223 (61.9)	0.944
Platelet count <sup>B</sup> ; median (minimum, maximum)	149 (68, 273) <sup>D</sup>	202 (108, 311) <sup>E</sup>	162 (83, 249) <sup>D</sup>	162 (74, 412) <sup>D</sup>	166 (68, 412)	< 0.01
Reoperation; n (%)	4 (2.6)	1 (2.0)	0 (0.0)	6 (4.4)	11 (3.1)	0.609
Death; n (%)	0 (0.0)	1 (2.0)	1 (4.8)	4 (3.0)	6 (1.7)	0.152

SD=standard deviation; BMI=body mass index; ASA-PS=American Society of Anesthesiologist Physical Status; CABGs=coronary artery bypass graft surgery; CPB=cardiopulmonary bypass

<sup>A</sup> Other types of surgical procedures entail atrial or ventricular septal defect surgeries, <sup>B</sup> Incidence of hypothermia, platelet count (×10<sup>3</sup> cells/mm<sup>3</sup>), and coagulopathy were measured upon patients' arrival to the cardiac intensive care unit (CICU). <sup>D-F</sup> Data in rows without a common superscript reveals a difference (p<0.05), as analyzed by one-way ANOVA.

Normally distributed continuous data were presented as mean  $\pm$  standard deviation (SD) and compared using unpaired t-test, 1-way ANOVA followed by multiple comparisons. Non-normally distributed continuous data were presented as median (minimum, maximum) and compared using Kruskal-Wallis test. Categorical data were presented as integers and percentages and compared through chi-square test, Fisher's exact test. Statistical significance was defined by p-value less than or equal to 0.05. All data were analyzed using IBM SPSS Statistics, version 28.0 (IBM Corp., Armonk, NY, USA).

#### Results

### **Demographics and baseline characteristics**

Of the 360 patients included in the present study, 61.7% were male, with a mean (±SD) age of  $65.3\pm11.7$  years, and BMI of  $24.1\pm4.0$  kg/m<sup>2</sup>. No significant difference in biological gender or BMI was observed across the groups, but Group 3

 Table 2. Demographic and perioperative data between patients

 with/without thrombocytopenia in Group 1 patients

Variables	Thrombo	p-value	
	No (n=137)	Yes (n=18)	
Age (years); mean±SD	$64.6 \pm 11.8$	$66.0 \pm 8.5$	0.625
Sex; n (%)			0.473
Male	88 (64.2)	10 (55.6)	
Female	49 (35.8)	8 (44.4)	
BMI (kg/m <sup>2</sup> ); mean±SD	$24.3 \pm 3.5$	22.9±3.8	0.127
ASA-PS; n (%)			0.455
Class 3	116 (84.7)	14 (77.8)	
Class 4	21 (15.3)	4 (22.2)	
Antithrombotic medication; n (%)			0.150
No	44 (32.1)	5 (27.8)	
Antiplatelets	87 (63.5)	10 (55.6)	
Anticoagulants	3 (2.2)	1 (5.6)	
Both	3 (2.2)	2 (11.1)	
Type of surgical procedures; n (%)			0.266
CABGs	81 (59.1)	8 (44.4)	
Valve surgery	43 (31.4)	6 (33.3)	
Both	7 (5.1)	3 (16.7)	
Other <sup>A</sup>	6 (4.4)	1 (5.6)	
Operative duration (minutes); mean±SD	169.9±61.7	186.7±63.0	0.298
CPB duration (minutes); mean±SD	85.9±27.3	89.9±40.9	0.689

SD=standard deviation; BMI=body mass index; ASA-PS=American Society of Anesthesiologist Physical Status; CABGs=coronary artery bypass graft surgery; CPB=cardiopulmonary bypass

<sup>A</sup> Other types of surgical procedures entail atrial or ventricular septal defect surgeries

was significantly younger (p<0.01) (Table 1). Most patients were classified as ASA-PS class 3 (71.9%), had elective surgeries (96.4%), history of antiplatelet use (65.8%), and coronary artery bypass graft (CABG) surgical procedures (56.9%). Group 2 had significantly greater incidence of ASA-PS class 3 at 85.7% (p<0.01), history of antiplatelet use at 81.6% (p<0.01), CABG at 89.8% (p<0.01), and TXA dosage at 28.1±13.3 mg/kg (p<0.01). Group 4 had a significantly greater incidence of anticoagulant use at 14.8% (p<0.01). No statistical difference was observed across different methods of intravenous TXA administration (p=0.647). Group 1 had the significantly shortest mean operative and CPB durations of 171.8±61.2 and 86.3±28.0 minutes, respectively (p<0.01 for both). Group 2 also had a significantly shorter CPB duration compared to Group 4. Group 4 patients had significantly longer operative at 267.9±115.8 minutes (p<0.01) and CPB at 146.6±74.7 minutes (p<0.01) durations compared

 Table 3. Demographic and perioperative data between patients

 with/without coagulopathy in Group 1 patients

Variables	Coagulopathy		p-value
	No (n=149)	Yes (n=6)	
Age (years); mean±SD	$64.8 \pm 11.6$	$64.2 \pm 8.0$	0.898
Sex; n (%)			0.121
Male	96 (64.4)	2 (33.3)	
Female	53 (35.6)	4 (66.7)	
BMI (kg/m <sup>2</sup> ); mean±SD	$24.2 \pm 3.5$	$20.7 \pm 2.5$	0.016
ASA-PS; n (%)			0.971
Class 3	125 (83.9)	5 (83.3)	
Class 4	24 (16.1)	1 (16.7)	
Antithrombotic medication; n (%)			0.002
No	47 (31.5)	2 (33.3)	
Antiplatelets	96 (64.4)	1 (16.7)	
Anticoagulants	3 (2.0)	1 (16.7)	
Both	3 (2.0)	2 (33.3)	
Type of surgical procedures; n (%)			0.137
CABGs	88 (59.1)	1 (16.7)	
Valve surgery	45 (30.2)	4 (66.7)	
Both	9 (6.0)	1 (16.7)	
Other <sup>A</sup>	7 (4.7)	0 (0.0)	
Operative duration (minutes); mean±SD	172.7±62.5	150.8±42.8	0.398
CPB duration (minutes); mean <u>+</u> SD	86.7±29.3	76.0±20.5	0.376

SD=standard deviation; BMI=body mass index; ASA-PS=American Society of Anesthesiologist Physical Status; CABGs=coronary artery bypass graft surgery; CPB=cardiopulmonary bypass

<sup>A</sup> Other types of surgical procedures entail atrial or ventricular septal defect surgeries

to other groups. Further details are listed in Table 1.

# Incidence of post-operative thrombocytopenia and coagulopathy

Post-operative thrombocytopenia was significantly more prevalent in Group 1 at 11.6% followed by Group 3 at 9.5%, Group 4 at 3.7%, and Group 2 at 0%. While statistically insignificant, post-operative coagulopathy was more prevalent in Group 3 at 4.8%, followed by Group 2 at 4.1%, Group 1 at 3.9%, and Group 4 at 0.7%. A significantly greater incidence of postoperative thrombocytopenia was observed in Group 1 (p=0.01), albeit statistically insignificant (p=0.337). A similar trend was seen for postoperative coagulopathy (Table 1).

# Patients without non-red cell transfusion

There was no statistical difference in the incidence of antithrombotic medication between patients with or without thrombocytopenia in Group 1

(p=0.15) (Table 2). A significantly greater incidence of preoperative anticoagulant use was observed in Group 1 patients with coagulopathy (p=0.002) (Table 3).

#### Transfusion outcomes, morbidities, and mortalities

Median PLT counts were highest in Group 2 at  $202 \times 10^3$  cells/mm<sup>3</sup>, followed by Group 3 and Group 4 at  $162 \times 10^3$  cells/mm<sup>3</sup>, and Group 1 at  $149 \times 10^3$  cells/mm<sup>3</sup> (p<0.01). No statistical differences in incidence of hypothermia (p=0.944), reoperation (p=0.609), or death (p=0.152) were observed across the study groups.

#### Discussion

The authors determined the incidence and outcomes of thrombocytopenia and coagulopathy in adult Thai cardiac surgery patients with CPB. While overall prevalence of coagulopathy and thrombocytopenia across the four groups were low (2.8% and 6.9%, respectively), the incidence of abnormal clotting factors and thrombocytopenia in patients that did not receive transfusion were higher (3.9% and 11.6%, respectively). A significantly greater frequency of perioperative anticoagulant use was observed in patients with coagulopathy that did not receive transfusion. Median PLT count was highest in patients that received PLT transfusions. Patients who received PLT, FFP, and/or cryo had significantly longer operative and CPB durations.

#### **Complex cardiac surgeries with CPB**

Complex cardiac surgical procedures like CABG are typically conducted under CPB, which requires complete heparinization<sup>(16)</sup>. Restoring hemostasis is difficult despite preoperative administration of TXA and heparin reversal due to the systemic effects of CPB promoting coagulation factor and PLT uptake<sup>(1,5,16)</sup>. This often leads to bleeding once cardiopulmonary circulation resumes<sup>(1)</sup> and subsequent allogenic blood product transfusion<sup>(5)</sup>.

#### Thrombocytopenia

Thrombocytopenia has a 10% to 90.2% incidence depending on defined PLT counts or decreased PLT nadirs within fixed time periods<sup>(4,7,10,17)</sup>. PLT thresholds for thrombocytopenia used in previous studies ranged from less than 75,000 to less than 150,000 cells/mm<sup>3(4,8,10,12,17,18)</sup>, and 30% to 50% for PLT nadir reductions 48 to 72 hours after cardiac surgery with CPB<sup>(4,5)</sup>. The effects of thrombocytopenia entail increased bleeding risk,

chest drainage volume, postoperative transfusion, blood destruction, PLT activation, hospital and intensive care unit (ICU) stay, morbidity, as well as 30-day and 1-year mortality<sup>(4,5,10,12,18,19)</sup>. Extended CPB duration<sup>(4,20)</sup> and other adverse outcomes such as heparin-induced thrombocytopenia (HIT) and druginduced thrombocytopenia (DIPT) can cause further complications<sup>(12,17)</sup>. Predictors for postoperative thrombocytopenia include old age (older than 60 years), intraoperative blood transfusion, low preoperative PLT count, and long CPB duration<sup>(10)</sup>. Patients also had lower BMI, more complex surgeries, lower nadir temperature, and lower heparin dosages<sup>(10)</sup>. Median PLT counts and postoperative thrombocytopenia incidence in the researchers' study aligned with those found previously<sup>(4,12)</sup>.

The linkage between thrombocytopenia and CABG is more controversial. Some studies report prolonged mechanical ventilation time, AKI, and stroke in cardiac surgery patients with CPB<sup>(4,12)</sup>. Other studies found no increased 28-day or inhospital mortality perioperatively after adjusting for confounders<sup>(12)</sup>, or linkage between PLT count and CABG procedures towards short- or long-term mortality across 348,341 CABG patients<sup>(21)</sup>. The researchers' study also noted no significant difference in CABG or ASA-PS class incidence between patients with or without thrombocytopenia in Group 1 patients.

### Coagulopathy

Coagulopathy varies according to its definition, surgery type and technique, pre-existing conditions, and CPB duration<sup>(8)</sup>. It is a large contributing factor to postoperative bleeding and transfusion, prolonged hospitalization, morbidities, life-threatening complications, and mortality after complex cardiac surgeries due to its influence on anti- and procoagulant proteins<sup>(3,5,8,9,11)</sup>. Significantly greater incidence of postoperative coagulopathy has been linked to preoperative anticoagulant use like heparin, extended CPB, reoperations, and prolonged and complex cardiac surgical procedures such as CABG with associated valve procedures<sup>(11)</sup>. The researchers' study observed no significant difference in CPB duration, CABG, or ASA-PS class incidence between patients with or without coagulopathy in Group 1 patients. However, the authors did find a significantly greater incidence of preoperative anticoagulant use, with or without antiplatelets, in patients with postoperative coagulopathy. This supports claims made by the previous studies<sup>(1,3,11)</sup> and recommended prohibitions prior to cardiac surgery with CPB.

# Intraoperative transfusions

High plasma-platelet ratios to red cell transfusions are required to prevent severe coagulopathy, maintain perfusion, and restore hemostasis<sup>(1)</sup>. Hemostasis is usually defined by PT, aPTT, PLT count, or fibrinogen level<sup>(3)</sup>. The complexity and multifactorial nature of CPB have led to a wide variability in transfusion and treatment practices based on defined PT/aPTT thresholds levels<sup>(2,5)</sup>.

While intra- and post-operative red cell product transfusions have decreased over time, FFP transfusions have increased<sup>(6,22)</sup>. CPB surgery is often accompanied by FFP transfusions, particularly in cyanotic patients<sup>(13)</sup>. The risk-benefit ratio it exhibits depends on whether it is administered prophylactically or as treatment for bleeding and coagulopathy<sup>(6)</sup>. Its procoagulant factors do reduce bleeding as treatment, but prophylactically FFP was not found to prevent bleeding or PLT aggregation<sup>(6,16,23)</sup>. No significant difference was observed in ICU stay, reoperation rates, or mortality<sup>(6)</sup>. Instead, FFP transfusion increased subsequent transfusion requirements<sup>(6,16)</sup> and was independently associated with numerous underdiagnosed and under-reported AEs<sup>(13)</sup>. Steinbicker et al.<sup>(13)</sup> even suggested improved patient outcomes with reduced FFP administration. The authors found postoperative coagulopathy to be more prevalent in groups that received FFP and/or cryo compared to groups that received no transfusions (4.8% versus 3.9%). This supports prohibiting prophylactic use of FFP, particularly in non-complicated cardiac surgeries without coagulopathy<sup>(24)</sup>.

Postoperative PLT transfusions rates are also high, reaching up to 51% depending on PLT counts<sup>(2,5,25)</sup>. A PLT count of 50×10<sup>9</sup> cells/L is recommended as a therapeutic target according to the American Association of Blood Banks (AABB)<sup>(26)</sup>, particularly for complex cardiac surgery cases<sup>(14)</sup> or thrombocytopenia<sup>(8)</sup>. Preoperative antiplatelet and anticoagulant use, preoperative liver disease, CABG and valve surgery, emergency surgery type, and CPB duration are factors associated with intraoperative PLT transfusion<sup>(27,28)</sup>. However, there is also no data to support prophylactic PLT transfusion according to Bolliger et al.<sup>(8)</sup>, with inferior results compared to standard care regimens and increased transfusion requirement<sup>(2)</sup>. Others found that PLT transfusions were associated with adverse outcomes like postoperative pneumonia, AKIs, stroke, acute myocardial infarction, prolonged readmission, and mortality<sup>(12,28)</sup>. Meanwhile, Shams Hakimi et al.<sup>(29)</sup> reported improved PLT function upon PLT transfusion as postoperative treatment. Restricted PLT transfusions for CABG patients did not increase postoperative bleeding or red cell transfusion requirements(30), nor increase serious adverse outcomes<sup>(2)</sup>. This may be due to a discrepancy in adjusting for confounding factors and different study parameters. The authors observed median PLT counts to be highest in patients that received PLT transfusions, and postoperative thrombocytopenia to be significantly more prevalent in groups that did not receive PLT transfusions. This supports previous literature that PLT transfusions may help minimize thrombocytopenia across non-complicated cardiac surgical procedures. Stringent transfusion thresholds must be established to prevent over-transfusion.

Cryo is typically administered in active bleeding cases due to its higher fibrinogen concentration compared to FFP and additional procoagulant factors<sup>(13)</sup>. Fibrinogen-rich products (cryo) or concentrates (PCC) can help reduce required FFP intraoperative cardiac surgery transfusions after CPB<sup>(3,8,31-33)</sup>, particularly for complex procedures<sup>(5)</sup>. Cryo transfusion may help also compensate for thrombocytopenia, as fibrinogen declines are strongest during CPB and transfusions have proven both effective and well-tolerated by patients<sup>(5)</sup>. The risks and adverse reactions differ according to the transfused component and individual patient<sup>(15)</sup>. The authors observed patients who received PLT, FFP, and/or cryo had significantly longer operative and CPB durations. Being on CPB for longer than two to three hours in hypothermic conditions severely imbalances coagulation cascades and promotes PLT dysfunction<sup>(4,34,35)</sup>. Additionally, lower PLT counts, enhanced aggregation, and hyperreactivity have been reported in older age groups<sup>(36,37)</sup>.

One study found 27% of transfusions in elective CABG surgeries were unnecessary, and 32% of plasma and 47% of PLT transfusions were inappropriate<sup>(38)</sup>. Zaffar et al. reported that surgery type and preoperative antiplatelet use were two factors that influenced physicians' decision to transfuse PLT<sup>(27)</sup>. The researchers' findings aligned with this. The authors found preoperative antithrombotic use as the main variable that affected physicians' decision to transfuse PLT and/or cryo, respectively. Nearly all Group 2 patients had a history of preoperative antiplatelet use. This increased the risk of physicians' over-transfusing during CABG procedures. In addition, Group 1 patients, with the

lowest PLT counts observed across groups (68,000 cells/mm<sup>3</sup>), continued to receive intraoperative transfusions despite PLT counts being above the AABB's recommended transfusion threshold.

# Limitation

There were limitations in the study. The first was bias associated with its unblinded nature during red cell and non-red cell blood product transfusions. The second regards the different thresholds used to define postoperative thrombocytopenia in the past literature, influencing interpreted incidence. However, the researchers' thresholds lie within those applied in previous analyses. The third was the descriptive, retrospective nature of the present study. The lack of risk factor analysis limits the ability to associate risk factors with thrombocytopenia and coagulopathy incidence. The fourth was its small sample size, with Group 3 being underpowered.

# Implications and future directions

Multimodal perioperative management and treatment approaches are required to minimize complications of cardiac surgery with CPB, including thrombocytopenia and coagulopathy<sup>(7)</sup>. Optimizing surgical techniques, managing heparin administration and neutralization, utilizing antifibrinolytic agents prophylactically such as TXA, and minimizing preoperative antithrombotic administration, all help minimize surgical and medical bleeding<sup>(6,8,39)</sup>. Such measures also reduce medical costs, required transfusions, adverse outcomes, reoperation, complications, morbidities, and mortality<sup>(1,6,8,40)</sup>. Implementing restrictive PLT thresholds, targeted coagulation algorithms, and individualized patient blood management (PBM) programs reduce transfusion requirements even further<sup>(13,24,41,42)</sup>. Prophylactic non-red cell transfusions can be particularly restricted across low-risk procedures to prevent unnecessary or inappropriate transfusion practices<sup>(14)</sup>. Recombinant and purified coagulation products such as activated factor VIIa, factor XIII, PCCs, or topical hemostatic agents, as alternatives to standard treatments for controlling bleeding and coagulopathy also warrants further research<sup>(7,9)</sup> across large, ethnically-diverse cohorts.

# Conclusion

Transfusion practices should be carefully considered with respect to individual patient laboratory results, clinical condition, and surgical factors beforehand. The researchers' study confirms that preoperative antithrombotic use prior to cardiac surgical procedures influences physicians' decision to transfuse and does not support prophylactic FFP and PLT administration. Implementing restrictive transfusion strategies that tolerate mild coagulopathy and treat underlying causes are recommended.

# What is already known on this topic?

CPB activates fibrinolytic and inflammatory pathways, potentially disrupting hemostasis. Red cell and non-red cell such as PLT, FFP and/or cryo blood product transfusions are often administered prophylactically as conventional methods of addressing complications like coagulopathy or thrombocytopenia. The decision to transfuse is often unstandardized, hence under- or overdosing.

# What this study adds?

Implementing PLT thresholds and individualized PBM programs, restricting routine non-red cell blood product transfusions during simple cardiac surgeries, and tolerating mild coagulopathy is recommended. Physicians are urged to address/treat underlying causes of bleeding.

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# **Conflicts of interest**

The authors declare no conflict of interest.

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