

Association between Postoperative Thrombocytopenia and Acute Kidney Injury in On-Pump versus Off-Pump Coronary Artery Bypass Grafting

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ABSTRACT

Objective: To assess the association between postoperative Thrombocytopenia and Acute Kidney Injury (AKI), in patients undergoing on-pump and off-pump coronary artery bypass grafting (CABG).

Study Design: Quasi Experimental Study.

Place and Duration of Study: Department of Cardiac Surgery, Armed Forces Institute of Cardiology/National Institute of Heart Diseases (AFIC/NIHD), Rawalpindi Pakistan, from Aug 2025 to Jan 2026.

Methodology: The study evaluated 136 patients over the age of 18, regardless of gender, who underwent isolated CABG with left ventricular function (LVEF >35%) and coronary artery disease (CAD) of single, double, or triple vessels. Patients were excluded if they had bleeding disorders, baseline hepatic or renal dysfunction. Patients with concomitant CABG and valvular surgery were also excluded. Platelet counts and serum creatinine were measured postoperatively at 12, 24, and 48 hours, and at discharge.

Results: Baseline platelet counts were almost similar between both groups. Postoperatively, Off-Pump patients experienced less reduction in platelet count compared to On-Pump and recovered by discharge (222.23 ± 75.78 vs. 178.02 ± 54.36 , p -value = 0.001) and had less creatinine increase (1.14 ± 0.48 mg/dL vs. 1.29 ± 0.44 mg/dL, p -value = 0.05) from baseline. The frequency of AKI was somewhat higher in the On-pump CABG group (26.0% vs. 20.0%), and in both groups, AKI was not significantly associated with postoperative thrombocytopenia (p -value >0.05).

Conclusion: Off-pump CABG is associated with milder platelet decline and reduced renal stress compared to on-pump CABG, suggesting that CPB contributes to increased postoperative morbidity, though thrombocytopenia did not significantly influence AKI in this cohort.

Keywords: Acute Kidney Injury, Coronary Artery Bypass, Platelet Count, Postoperative Complications, Thrombocytopenia.

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INTRODUCTION

Coronary artery bypass grafting (CABG) represents the most prevalent form of cardiac surgery, with around 400,000 operations performed annually in the United States.¹ CABG performed with cardiopulmonary bypass (CPB) initiates an inflammatory response with cellular, humoral, metabolic, and endocrine components, and where neutrophil-endothelium interactions and the crosstalk of coagulation and inflammation are integral.² The inflammation associated with post-CABG acute kidney injury (AKI) is multifactorial, from renal hemodynamic instability, ischemia-reperfusion injury, and inflammation, and may range from a mild elevation of creatinine to substantial renal impairment requiring intervention.³ After CABG, the incidence of

AKI can approach 30%, depending on the patient's demographics and diagnostic standards.

Patients at risk for AKI have been studied using a variety of different biomarkers, with platelets being one of them. Microthrombi, renal ischemia, and complications can occur with platelet drop, platelet dysfunction, and CPB aggravated thrombi.⁴⁻⁶ AKI after cardiac surgery has been correlated to high preoperative platelet-leukocyte aggregate and rapid postoperative plasminogen activation. The rate of AKI occurrence after CABG has been on the rise, in part, due to the refinements in detection and the recent criteria for AKI. Thus, the early detection of high-risk patients is of utmost importance. AKI occurs in 30-51% of patients' post-CABG and 3% of these patients end up requiring renal replacement therapy.⁷ Kertai *et al.*,⁸ found that the risk of postoperative AKI increased by 14% for every $30 \times 10^9/L$ decrease in platelet count (OR 1.14/ 95% CI 1.09-1.20). To

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minimize the negative effects of CPB, off-pump CABG (OPCAB) was introduced. Even though OPCAB addresses the CPB-induced platelet and inflammatory problems, the procedure has still not been adopted by many hospitals despite the growing use of minimally invasive and off-pump techniques.

AKI is a common and major post CABG complication and CPB impacts both platelets and kidney function. Postoperative thrombocytopenia and AKI have been researched independently but the linkage between platelets and AKI in on- pump CABG (ONCAB) versus OPCAB is still unknown. Clarifying this relationship may enable the earlier detection of patients at risk of developing AKI and optimize perioperative management. Thus, this study evaluated the association of thrombocytopenia and AKI in patients OPCAB and ONCAB, the results may enhance risk stratification and management of patients in cardiac surgery.

METHODOLOGY

This Quasi experimental study was conducted in the Cardiac Surgery Department of Armed Forces Institute of Cardiology/National institute of Heart Diseases, Rawalpindi Pakistan, from Aug 2025-Jan 2026, following the approval from Institutional Ethical Review Board, (IERB Itr # 9/2R&D/2025/376; Dated: 21st Aug 2025). Patients were recruited through non-probability consecutive sampling.

The required sample size of 73 was calculated using a 5% prevalence of AKI in CABG patients, a 5% margin of error, and a 95% confidence interval, based on the WHO sample size calculator. However, a total of 136 patients were ultimately recruited, with 68 patients in each of the on-pump and off-pump CABG groups.

Inclusion Criteria: All patients >18 years, irrespective of gender who underwent on-pump or off-pump CABG, left ventricular ejection fraction (LVEF >35%). Cases with single-vessel, double-vessel, or triple-vessel coronary artery disease (SVCAD, DVCAD, and TVCAD) were all included in the study.

Exclusion Criteria: Patients who had stopped aspirin intake less than three days prior to surgery were excluded. Those with known bleeding disorders, such as ITP, hemophilia, or von Willebrand disease, hepatic and renal dysfunction, including chronic kidney disease or chronic hepatic disease. Additionally, patients undergoing concomitant CABG and valvular surgery were excluded from the study.

After obtaining approval from IERB, written informed consent was received from all patients. Patients were selected who scheduled for isolated CABG via median sternotomy, with similar preoperative characteristics to minimize confounding effects on postoperative outcomes. Patient flow diagram is shown in Figure-1. Preoperatively, a detailed clinical history was obtained, including demographics, primary indication for surgery (SVCAD, DVCAD, or TVCAD), and comorbidities. Baseline investigations included LVEF, platelet count, and renal function tests (serum creatinine).

Patients were divided in to two groups as ONCAB-Group and OPCAB-Group. For on pump CABG, the standard CPB was established via an ascending aortic arterial cannula and a right atrial two-stage single venous cannula, followed by aortic cross clamping and cardioplegic arrest. For off-pump CABG, different stabilization devices were utilized for a motionless surgical field. The intraoperative variables included the durations of CPB and aortic cross-clamping. The need for inotropic support at CPB wean and in the ICU was also documented.

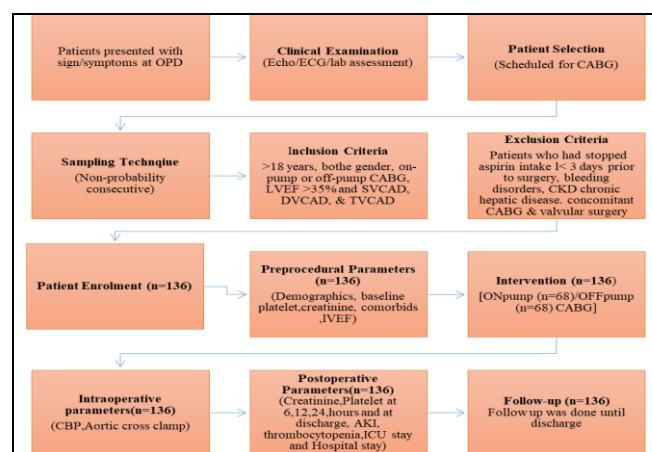


Figure: Patient flow Diagram

Creatinine and Platelet count was assessed at 12, 24, 48 hours after the operation, as well as at the time of patient discharge. Renal function, measured by serum creatinine levels, was also assessed at the same time intervals. The need for renal support, including hemodialysis, continuous renal replacement therapy, or medical management, was also documented. The number of blood transfusions, length of stay in the ICU, total length of hospital stay, and postoperative arrhythmias also comprised additional outcomes. In order to ease comparison, all outcome data were

divided by CABG type (on-pump and off-pump). Thrombocytopenia was defined as a platelet count less than 150,000 per microliter of blood.¹⁰ AKI was defined per the Acute Kidney Injury Network AKIN 9 criteria: Stage 1, an increase in serum creatinine of >0.3 mg/dL (>26 micromoles per liter) or 50%; Stage 2, a 100 to 200 percent increase; and Stage 3, greater than a 200 percent increase in serum creatinine levels preoperatively compared to preoperatively.

Data were analyzed with Statistical Package of Social Sciences (SPSS) version 23. Continuous variables were summarized as mean ± standard deviation (SD) while categorical variables were summarized as frequency and percentage (%). Normality was evaluated using Shapiro–Wilk test. All variables were normally distributed except EF, CBP time, Aortic Cross clamp time, hospital stay, ICU stay and decline in platelet therefore median (IQR) was reported. Variations of continuous variables (platelet counts and creatinine) from baseline to different point intervals postoperatively were analyzed by paired sample t-test. Between groups comparison (on pump vs. off pump CABG, AKI vs Non-AKI, and Thrombocytopenia vs. No Thrombocytopenia) were analyzed using independent t-test/Man Whitney test (for continuous variables) and chi-square/Fisher’s exact test (for categorical variables). Statistical significance was set at *p*-value ≤0.05.

RESULTS

The study included 136 participant patients. The gender distribution was approximately equal across both groups. Ejection fraction was significantly lower in the On-Pump CABG group (32.5 ± 12.83% vs. 48.5± 12.83%, *p*-value =0.001) while ICU and hospital length of stays did not statistically differ between CABG techniques. Overall, On-Pump CABG group had a slightly higher, AKI cases compared to on-pump CABG patients (26 vs. 20; *p*-value >0.05) . Complete details are mentioned in table-I.

Baseline platelet counts were almost similar between Off-Pump (235.97 ± 91.34 ×10³/μL) and On-Pump (227.25 ± 71.08 ×10³/μL, *p*-value =0.532). Postoperatively, Off-Pump patients experienced less reduction in platelet count compared to On-Pump and recovered by discharge (222.23 ± 75.78 vs. 178.02 ± 54.36, *p*=0.001). Off-Pump patients also had a lower maximum creatinine level (1.14 ± 0.48 mg/dL) than On-Pump (1.39 ± 0.44 mg/dL, *p*=0.002), indicating less renal stress and lower risk of AKI with Off-Pump CABG (Table-II).

Table-I: Baseline Characteristics, Comorbidities, and Perioperative Parameters of Study Participants (n=136)

Variable	OPCAB-Group (n=68)	ONCAB-Group (n=68)	<i>p</i> -value
	Mean±SD		
Demographics			
Age (years)	58.81±8.85	57.12±9.12	0.12
Gender			
Frequency(%)			
Female	23(33.8%)	25(36.8%)	0.68
Male	45(66.2%)	43(63.2%)	
Diagnosis			
Frequency(%)			
SVCAD	0(0.0%)	11(16.2%)	0.002
DVCAD	28(26.5%)	28(26.5%)	
TVCAD	50(73.5%)	39(57.4%)	
Comorbidities			
Frequency(%)			
HTN	24(35.3%)	10(14.7%)	<0.001
DM	25(36.8%)	13(19.1%)	
DM/HTN	15(22.1%)	17(25.0%)	
NIL	4(5.9%)	28(41.2%)	
Ejection Fraction (%)			
Median(IQR)			
	50.00(43.00-56.00)	45.00(46.00-50.00)	0.001
Intraoperative Parameters			
Median (IQR)			
CPB Time (min)		116.00(95.00-136.00)	-
Cross-clamp Time (min)		70.00(56.00-95.00)	-
Postoperative Parameters			
Median (IQR)			
ICU Stay (days)	1.00(1.00-2.00)	1.00(1.00-2.00)	0.14
Hospital Stay (days)	5.00(5.00-6.00)	5.00(4.00-5.00)	0.45
Frequency(%)			
SLED/HD	Yes	4(5.88%)	1.00
	No	64(94.1%)	
Transfusions	Yes	0	0.02
	No	68(100%)	
AKI	Yes	20(29.4%)	0.06
	No	48(70.6%)	
Stages of AKI	I	9(13.2%)	0.58
	II	10(14.7%)	
	III	1(1.5%)	
	None	48(70.6%)	

DM=Diabetes Mellitus; HTN=Hypertension; SVCAD =Single Vessel Coronary Artery Disease; DVCAD =Double Vessel Coronary Artery Disease; TVCAD =Triple Vessel Coronary Artery Disease; SLED/HD= Sustained Low-Efficiency Dialysis / Hemodialysis; AKI=Acute Kidney Injury; ONCAB=On pump Coronary artery bypass; OPCAB=Off pump Coronary Artery bypass; ICU stay=Intensive Care Unit; CBP=Cardiopulmonary Bypass time.

Table-II: Platelet and Creatinine changes after Coronary Artery Bypass Grafting (n=136)

Variable	OPCAB-Group (n=68)	ONCAB-Group (n=68)	<i>p</i> -value
	(Mean±SD)		
Baseline Platelets (×10 ³ /μL)	242.41±91.34	223.52±68.92	0.18
Platelets 12h	183.28±67.35	165.89±57.74	0.41
Platelets 24h	206.87±75.02	164.88±61.80	0.003
Platelets 48h	216.35±77.52	165.75±75.02	<0.001
Platelets at Discharge	227.88±75.78	175.02±56.36	<0.001
Nadir Platelets	197.29±74.72	148.19±53.69	<0.001
Baseline Creatinine (mg/dL)	0.91±0.37	1.03±0.22	0.09
Creatinine 12h	1.02±0.63	1.23±0.43	0.02
Creatinine 24h	1.09±0.52	1.35±0.42	0.03
Creatinine 48h	1.01±0.53	1.35±0.39	0.01
Creatinine at Discharge	0.94±0.51	1.17±0.37	0.005
Maximum increase in Creatinine	1.14±0.48	1.39±0.44	0.05

ONCAB=On pump Coronary artery bypass; OPCAB=off pump Coronary Artery bypass

Off-pump CABG was associated with a transient decrease in platelet count, reaching a nadir at 12 hours

postoperatively ($183.29 \pm 67.83 \times 10^3/\mu\text{L}$, p -value =0.03) and partially recovering by 24–48 hours, with levels nearly returning to baseline at discharge ($227.88 \pm 72.86 \times 10^3/\mu\text{L}$, p -value =0.215). In contrast, on-pump CABG caused a pronounced and sustained reduction in platelets at all postoperative time points (12h: $165.89 \pm 57.74 \times 10^3/\mu\text{L}$ and discharge: $175.24 \pm 56.70 \times 10^3/\mu\text{L}$, p -value <0.001). Similarly, serum creatinine showed only a mild and transient rise after off-pump CABG (12h: 1.02 ± 0.63 mg/dL p -value =0.03) and returned to baseline by discharge (0.94 ± 0.41 mg/dL, p -value =0.87), whereas on-pump CABG led to a significant and persistent increase in creatinine at all postoperative intervals from baseline (12h: 1.23 ± 0.37 and at discharge: 1.16 ± 0.38 mg/dL, p -value <0.001) (Table-III).

Table-III: Postoperative platelet count and serum creatinine changes within off-pump and on-pump CABG techniques (n=136)

Parameter	Baseline	12 hours	24 hours	48 hours	Discharge
OPCAB-Group					
Platelet count ($\times 10^3/\mu\text{L}$)	230.24±102.22	183.29±67.83	206.87±73.59	216.35±75.03	227.88±72.86
p -value*	-	0.03	0.002	0.02	0.21
Serum Creatinine (mg/dL)	0.86±0.40	1.02±0.33	1.09±0.42	1.01±0.44	0.94±0.41
p -value*	-	0.03	0.10	0.24	0.87
ONCAB-Group					
	Baseline	12 hours	24 hours	48 hours	Discharge
Platelet count ($\times 10^3/\mu\text{L}$)	225.95±68.44	165.89±57.74	164.88±61.81	165.75±59.24	175.24±56.70
p -value*	-	<0.001	<0.001	<0.001	<0.001
Serum Creatinine (mg/dL)	1.00±0.22	1.23±0.37	1.27±0.42	1.22±0.38	1.16±0.38
p -value*	-	<0.001	<0.001	<0.001	<0.001

* p value against baseline; ONCAB=on pump Coronary artery bypass; OPCAB=off pump Coronary Artery bypass

Table-IV: Postoperative platelet counts and thrombocytopenia with and without AKI after CABG (n=136)

CABG Type	Parameter	Acute Kidney Injury		p -value
		No (n=48)	Yes (n=20)	
OPCAB-Group		Mean±SD		
	Baseline Platelets ($\times 10^3/\mu\text{L}$)	240.42±70.05	248.88±147.34	0.75
	Platelets at 12 hours	199.26±70.34	147.07±45.68	0.01
	Platelets at 24 hours	223.08±70.92	154.19±56.68	<0.001
	Platelets at 48 hours	229.79±75.38	172.69±56.23	<0.03
	Platelets at Discharge	240.39±74.39	185.33±48.75	0.009
	Thrombocytopenia [Frequency (%)]	Yes	13(27.1%)	7(35.0%)
	No	35(72.9%)	13(65.0%)	
ONCAB-Group		Mean±SD		
	Baseline Platelets ($\times 10^3/\mu\text{L}$)	224.14±67.48	221.95±74.39	0.90
	Platelets at 12 hours	162.79±52.59	174.17±70.72	0.48
	Platelets at 24 hours	161.39±52.56	173.89±82.06	0.54
	Platelets at 48 hours	165.31±54.88	166.89±70.93	0.53
	Platelets at Discharge	172.49±50.38	181.88±71.01	0.92
	Thrombocytopenia [Frequency (%)]	Yes	23(54.8%)	15(57.7%)
	No	19(45.2%)	11(42.3%)	

ONCAB=On pump Coronary artery bypass; OPCAB=off pump Coronary Artery bypass

Among Off-pump CABG patients, those who developed AKI ($248.88 \pm 147.34 \times 10^3/\mu\text{L}$) and those who did not ($240.42 \pm 70.05 \times 10^3/\mu\text{L}$, p -value =0.75) had similar baseline platelet levels, although post op, AKI group had significantly lower platelets at 12 hours (147.07 ± 45.68 vs. $199.26 \pm 70.34 \times 10^3/\mu\text{L}$, p -value =0.01), at 24 hours (154.19 ± 56.68 vs. $223.08 \pm 70.92 \times 10^3/\mu\text{L}$, p -value <0.001), at 48 hours (172.69 ± 56.23 vs. $229.79 \pm 75.38 \times 10^3/\mu\text{L}$, p -value <0.03) and at discharge (185.33 ± 48.75 vs. $240.39 \pm 74.39 \times 10^3/\mu\text{L}$, p -value =0.009). The rate of thrombocytopenia was marginally elevated in the AKI group but not to a statistically significant degree in both techniques ($p>0.05$) [Table-IV].

DISCUSSION

Current study finding shows that trends in postoperative platelets and AKI formation varied between Off-pump and On-pump CABG patients. Off-pump CABG had a small and short-lived decrease in platelet count. In contrast, On-pump CABG had a slightly longer and more enduring decrease. In the On-pump group, AKI occurred slightly higher, suggesting that the pronounced decrease in platelets may be associated with a higher risk of postoperative renal failure. This explains the type of surgical method effects the relationship between platelets and acute kidney injury. These findings align with previous studies.¹¹⁻¹³

Rehan *et al.*,¹⁴ reported additional transfusions of blood and blood products were required for the on-pump group, and transfusions significantly differed between techniques. The reason for the decreased blood loss after surgery in the off-pump group is certainly multifactorial. Both CPB and off pump surgery lead to post-operative platelet dysfunction and thrombocytopenia, and while our results support this, but the difference was statistically insignificant, possibly due to the smaller sample size as well as effective perioperative hemostatic management in both cohorts.

Consistent with the findings, the previous studies by Ali *et al.*, and Yan *et al.*, pointed out the impact of exposure to extracorporeal circuits on the platelet count and function.^{15,16} Although the majority of platelet depletion after surgery is temporary, persistent thrombocytopenia particularly under the critical level of $100 \times 10^9/\text{L}$ has been reported to be associated with higher rates of complications or an adaptive inflammatory reaction. In the present study,

a limit of $<150 \times 10^9/L$ was used in accordance with the institutional protocol 16 which may represent some factors of the specific population or the institution. The use of this higher limit may attempt to clarify the absence of statistically significant association between thrombocytopenia and post-operative AKI, on the other hand, there was some suggestive association numerically. The potential mechanism in support of this association can be found in previous studies where it has been reported that activated platelet consumption in the microvasculature of the kidneys and the systemic circulation can be problematic.

Postoperative mean platelet counts reported by Waleed *et al.*,¹⁷ for CABG surgery were $184.36 \times 10^9/L \pm 54.26$ compared to $204.73 \times 10^9/L \pm 23.60$ preoperatively. Likewise, in this study, the platelet counts reduced from $232.97 \times 10^9/L \pm 80.13$ to $174.59 \times 10^9/L \pm 62.55$. This decrease in the counts is of clinical importance from the perspective of morbidity, as raises in inflammatory response, dysfunction of microvascular structures, and hemostatic mechanisms suggest greater the risks of adverse outcomes of prolonged recovery and renal function deterioration.

CPB is known to activate a complicated systemic inflammatory reaction, leading to numerous poor postoperative outcomes. Recently, off-pump coronary artery bypass grafting (OPCAB) has become popular as an alternative to conventional on-pump CABG. OPCAB, by avoiding CPB and the associated myocardial ischemia/reperfusion injury, not only diminishes the postoperative systemic inflammatory response and other physiological changes but also preserves platelet count and function, which may enhance renal function and improve overall clinical recovery.¹⁸

Prior studies have been limited in scope and have underspecified differences in platelet trends between types of CABG. For on-pump patients, we observed a consistent and marked decline in platelet count ($225.95 \times 10^3/\mu L \rightarrow 165.89 \times 10^3/\mu L$ at 12 h, p -value <0.001) whereas off-pump patients had a short-lived decline with recovery at discharge ($230.24 \times 10^3/\mu L \rightarrow 183.29 \times 10^3/\mu L$ at 12 h, p -value $=0.03$; $227.88 \times 10^3/\mu L$ at discharge, p -value $=0.215$). These findings align with the observations of Hoseinikhah *et al.*,¹⁹ where in the combined impact of hemodilution coupled with low Hct resulted in the most platelets on post-operative day 2, and with Lako *et al.*,²⁰ whom reported the most severe decline in platelets at the onset of CPB which persisted until post-operative day 3. The findings

reiterate the association between on-pump CABG and more severe and more enduring thrombocytopenia, on the grounds of CPB-induced platelet activation and consumption.

Ali *et al.*,²¹ noted the connection between thrombocytopenia and AKI; of 50 thrombocytopenic patients, 34 developed AKI, statistically significant compared to those without thrombocytopenia (p -value $=0.037$). This suggests that low platelet counts could worsen renal failure after CABG. Conversely, in our study, 22 out of 46 thrombocytopenic patients had AKI, which, however, was not statistically significant. Similar to our findings, Karhausen *et al.*, noted that 71.5% of AKI occurrences in the thrombocytopenic cohort after CABG was due to the statistically significant presence of 51%, 13%, and 7% in stages I, II, and III of kidney disease, respectively.²² This lack of significance may be attributed to several factors, including the relatively small sample size, which limits statistical power, and marginal thrombocytopenia threshold potentially capturing patients with only mild platelet reductions who are less likely to develop AKI. Additionally, population-specific variables, institutional perioperative management practices, and variability in the timing of platelet and creatinine measurements may have influenced postoperative outcomes, thereby diluting the observed effect.

In conclusion, platelet counts are reduced and are more persisting postoperatively in on-pump CABG as compared to off-pump CABG, which also shows a trend of more AKI frequency in the on-pump group. Due to the smaller sample size and the institutional cutoff for thrombocytopenia ($<150 \times 10^3/\mu L$), which is near normal values, the link between AKI and the resulting thrombocytopenia did not achieve the threshold of significance, although trends depicted are consistent with the CPB-related activation and consumption of platelets, systemic inflammation, and the associated renal consequences. These trends show off-pump CABG, is associated with less platelet consumption and may protect against the post-operative renal failure, thus emphasizing the adoption of off pump surgical technique. The combination of surgical technique, which is appropriate to the patient's risk profile, and post-operative vigilant monitoring of platelets and renal function, is most likely to provide the best post-operative result.

LIMITATIONS OF THE STUDY

This research has several limitations. It is a single-centered study with a small sample size which may

constrain statistical strength and the applicability of the study results. The authors did not consider the multiple aspects of platelet function or the activation of the platelets which may be more accurate in reflecting risks for complications such as AKI. In this study, thrombocytopenia was defined as $<150 \times 10^3 / \mu\text{L}$, which is quite closer to normal values. This may cause the inclusion of patients with less severe reductions and a lower likelihood of renal dysfunction. The results may also reflect the influence of various perioperative practices and patient specific factors and the timings of postoperative assessments may not have accounted for any transient changes in the platelet or creatinine level.

CONCLUSION

Postoperative platelet reduction is an important factor influencing outcomes after CABG, with more pronounced declines observed in on-pump procedures. Although a direct association with AKI was not statistically significant in this study, monitoring platelet decline trends and adopting surgical techniques that minimize platelet loss such as off-pump CABG may help reduce postoperative complications and improve patient outcomes.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

AR & FS: Data acquisition, data analysis, critical review, approval of the final version to be published.

AMJ & VIP: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

MN & MUA: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be 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.

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