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Preoperative platelet-related inflammatory burden is associated with delayed early hemodynamic recovery following minimally invasive cardiac surgery

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Abstract

Background Minimally invasive cardiac surgery (MICS) is associated with reduced surgical trauma and improved postoperative recovery; however, early hemodynamic recovery remains variable and may be influenced by patient-related biological factors. This study evaluated the association between preoperative inflammatory biomarkers and delayed early postoperative recovery following MICS.

Methods This retrospective observational study included 166 consecutive patients undergoing thoracotomy-based MICS at a single tertiary center between January 2020 and January 2026. Preoperative inflammatory indices, including platelet-to-lymphocyte ratio (PLR) and systemic immune-inflammation index (SII), were calculated from routine laboratory parameters. The primary endpoint was prolonged postoperative inotropic support (> 24 h); vasopressor-only therapy administered for vasoplegia or isolated blood pressure support was not counted. Multivariable complete-case logistic regression ($n = 154$), receiver operating characteristic (ROC) analysis, and sensitivity analyses were performed.

Results Prolonged inotropic support was needed in 41 patients (24.7%). Patients requiring prolonged support were older, had a higher prevalence of hypertension, and had longer cardiopulmonary bypass duration in univariable comparisons. LVEF was numerically lower but did not reach conventional statistical significance. PLR and SII were significantly higher in these patients ($p = 0.003$ and $p = 0.010$, respectively). In separate adjusted models, both $PLR \geq 142$ and $SII \geq 462$ were associated with prolonged support. In the combined complete-case model including both biomarkers, $PLR \geq 142$ remained independently associated with prolonged support (OR 4.18, 95% CI 1.30–13.40, $p = 0.016$), whereas $SII \geq 462$ did not (OR 1.66, 95% CI 0.52–5.31, $p = 0.391$). ROC analysis showed modest discrimination (PLR AUC 0.655, 95% CI 0.564–0.753, $p = 0.003$; SII AUC 0.634, 95% CI 0.538–0.729, $p = 0.010$). No significant associations were observed between inflammatory biomarkers and early mortality, acute kidney injury, or postoperative atrial fibrillation.

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Conclusion Preoperative platelet-related inflammatory burden, as reflected by PLR, was associated with delayed early postoperative hemodynamic recovery following MICS. However, the discriminatory performance of PLR was modest, and this biomarker should be interpreted as a complementary risk indicator rather than a stand-alone decision-making tool. These findings are exploratory and require prospective validation in independent cohorts.

Keywords Minimally invasive cardiac surgery, Inflammation, Platelet-to-lymphocyte ratio, Systemic immune-inflammation index, Cardiopulmonary bypass, Postoperative recovery

Introduction

Minimally invasive cardiac surgery (MICS) has gained increasing acceptance over the last two decades due to reduced surgical trauma, faster recovery, decreased bleeding complications, and improved postoperative outcomes compared with conventional sternotomy approaches [1, 2]. Advances in surgical techniques, myocardial protection strategies, and perioperative management have further expanded the indications for MICS in contemporary practice.

Many MICS procedures are performed under cardiopulmonary bypass (CPB), and CPB remains an important contributor to the perioperative inflammatory response. Contact of blood with artificial surfaces, ischemia–reperfusion injury, and surgical trauma may trigger systemic inflammatory activation, which may adversely affect early postoperative recovery and hemodynamic stability [3, 4]. Previous studies have demonstrated that inflammatory activation following cardiac surgery may contribute to postoperative morbidity including low cardiac output syndrome, acute kidney injury, and delayed recovery [5].

In recent years, simple inflammatory biomarkers derived from routine complete blood count parameters have attracted increasing interest as potential prognostic markers in cardiovascular disease and cardiac surgery [6–10]. Among these, neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), systemic immune-inflammation index (SII), and systemic inflammation response index (SIRI) have been evaluated because they reflect different aspects of inflammatory activation and immune regulation. Platelet-related indices may be particularly relevant in cardiac surgery populations because platelets participate not only in hemostasis but also in inflammatory signaling, endothelial dysfunction, and microvascular regulation [10]. Elevated PLR and SII may therefore reflect increased inflammatory susceptibility and impaired microcirculatory adaptation, potentially contributing to delayed postoperative myocardial recovery.

Although previous studies have demonstrated the prognostic value of inflammatory indices in conventional cardiac surgery, data focusing specifically on MICS remain limited [11]. Furthermore, most studies have focused on mortality or major complications, whereas early recovery parameters such as prolonged inotropic support have been less frequently investigated. Prolonged

postoperative inotropic requirement may reflect delayed myocardial recovery, inflammatory burden, and perioperative physiological stress. Identification of simple preoperative predictors of delayed hemodynamic recovery may therefore provide additional value for perioperative risk stratification.

To our knowledge, data specifically evaluating inflammatory predictors of delayed early hemodynamic recovery in MICS remain limited. The aim of this study was to investigate the association between preoperative inflammatory biomarkers and early postoperative recovery in patients undergoing MICS. We specifically aimed to evaluate whether platelet-related inflammatory indices such as PLR and SII are associated with prolonged postoperative inotropic support.

Methods

Study design and patient population

This retrospective observational study included consecutive adult patients who underwent thoracotomy-based MICS at a single tertiary cardiac surgery center between January 2020 and January 2026. Patients undergoing right anterior mini-thoracotomy MICS procedures including aortic valve replacement, mitral valve replacement or repair, tricuspid valve surgery, double valve procedures, and atrial septal defect closure were included. Patients undergoing emergency surgery, concomitant coronary artery bypass grafting, active infection, preoperative mechanical circulatory support, severe hepatic dysfunction, or those with missing key laboratory parameters were excluded from the analysis. During the study period, 207 patients were screened; 4 patients undergoing emergency surgery, 4 undergoing concomitant coronary artery bypass grafting, 12 with active infection, 4 with preoperative mechanical circulatory support, 2 with severe hepatic dysfunction, and 15 with missing laboratory data were excluded. A total of 166 patients were included in the descriptive analysis; complete-case multivariable analyses included 154 patients with available age, LVEF, CPB duration, PLR, SII, and primary-endpoint data.

The study was conducted in accordance with the Declaration of Helsinki and approved by the institutional ethics committee (Approval number: 1-26-2774). Due to the retrospective study design, the requirement for individual informed consent was waived.

Data collection

Demographic, clinical, echocardiographic, operative, and postoperative data were obtained from the institutional electronic medical record system.

Baseline variables included age, sex, hypertension, diabetes mellitus, chronic obstructive pulmonary disease, smoking status, and left ventricular ejection fraction. Operative variables included procedure type, cardiopulmonary bypass duration, aortic cross-clamp duration, cannulation strategy, and myocardial protection strategy when available. Postoperative outcomes included mechanical ventilation duration, intensive care unit stay, hospital length of stay, new-onset atrial fibrillation, acute kidney injury, reoperation for bleeding, mortality, and duration of inotropic support. Several potentially relevant variables, including renal function, hemoglobin, pulmonary hypertension, NYHA class, preoperative atrial fibrillation, EuroSCORE II/STS score, valve disease severity, and transfusion, were not consistently available in the final analysis dataset and were therefore not included in the primary models; this was considered when interpreting residual confounding.

Laboratory measurements and inflammatory indices

Preoperative laboratory measurements obtained within 24 h before surgery included neutrophil count, lymphocyte count, platelet count, monocyte count, C-reactive protein, albumin, total bilirubin, and high-density lipoprotein cholesterol levels.

Inflammatory indices were calculated using established formulas. Neutrophil-to-lymphocyte ratio (NLR) was calculated as neutrophil count divided by lymphocyte count. Platelet-to-lymphocyte ratio (PLR) was calculated as platelet count divided by lymphocyte count. Systemic immune-inflammation index (SII) was calculated as platelet count multiplied by neutrophil count divided by lymphocyte count. Systemic inflammation response index (SIRI) was calculated as neutrophil count multiplied by monocyte count divided by lymphocyte count. CRP-to-albumin ratio (CAR) was calculated as CRP divided by albumin. Albumin-to-total bilirubin ratio was calculated as albumin divided by total bilirubin. Monocyte-to-HDL ratio (MHR) was calculated as monocyte count divided by HDL cholesterol.

Study endpoints

The primary endpoint of the study was prolonged postoperative inotropic support, defined as the requirement for continuous intravenous inotropic therapy beyond 24 h after surgery despite adequate volume status and correction of reversible causes of hypotension. Inotropic agents counted for this endpoint included dobutamine, dopamine, epinephrine, milrinone, and levosimendan. Pure vasopressor therapy administered primarily for

vasoplegia or blood pressure support, including norepinephrine, vasopressin, and phenylephrine, was not counted as inotropic support unless it was used in combination with an inotropic agent; in patients receiving combined therapy, classification was based on the duration of the inotropic component. Short-term bolus therapy was not considered. No biomarker-guided weaning strategy was used. In general, inotropic support was tapered when the patient had stable mean arterial pressure, satisfactory urine output and peripheral perfusion, no escalating lactate trend, and no clinical or echocardiographic evidence of low cardiac output. Continuation or discontinuation of support was ultimately at the discretion of the attending intensive care and surgical team, which is acknowledged as a limitation of this surrogate endpoint.

Secondary endpoints included mechanical ventilation duration, ICU stay, hospital length of stay, postoperative atrial fibrillation, acute kidney injury, reoperation for bleeding, and early mortality.

Acute kidney injury was defined according to the Kidney Disease Improving Global Outcomes (KDIGO) criteria. New onset atrial fibrillation was defined as any postoperative episode requiring medical or electrical treatment during the index hospitalization.

Surgical technique

All procedures were performed through a right mini-thoracotomy approach. Cardiopulmonary bypass was established using femoral or axillary arterial and femoral venous cannulation. Venous drainage was achieved via femoral venous cannulation with additional superior vena cava cannulation when required.

Standard cardiopulmonary bypass management included non-pulsatile flow, mild systemic hypothermia (32 °C), and target mean arterial pressure between 60 and 80 mmHg. Activated clotting time was maintained above 480 s during CPB. Vacuum-assisted venous drainage was used when required to optimize exposure. Carbon dioxide insufflation was routinely used to reduce the risk of air embolism.

Myocardial protection was achieved using antegrade long-acting cardioplegia (Del Nido or Custodiol cardioplegia) following aortic cross-clamping. Procedures were performed under direct vision using long-shaft minimally invasive instruments. Because myocardial protection strategy may influence postoperative recovery, cardioplegia type was considered a potential confounder; however, complete adjustment was limited because cardioplegia strategy was not consistently coded across all cases in the final analysis dataset.

All patients were managed postoperatively according to standardized institutional intensive care protocols. Hemodynamic targets, volume optimization, and inotropic weaning were guided by routine clinical, biochemical,

and echocardiographic assessment rather than by inflammatory biomarker values.

Statistical analysis

Statistical analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA), R software version 3.6.3 (R Foundation for Statistical Computing, Vienna, Austria), and MedCalc version 19.1 (MedCalc Software, Ostend, Belgium). Normality of continuous variables was assessed using the Shapiro–Wilk test. Normally distributed variables were expressed as mean $\pm$ standard deviation, whereas non-normally distributed variables were expressed as median with interquartile range.

Continuous variables were compared using the independent samples t-test or Mann–Whitney U test as appropriate. Categorical variables were compared using the chi-square test or Fisher's exact test.

Table 1 Baseline clinical and operative characteristics according to prolonged inotropic support

Variable	Total (n = 166)	No prolonged (n = 125)	Prolonged (n = 41)	p value
Age (years; n = 157)	51.4 $\pm$ 14.8	48.3 $\pm$ 14.9	60.0 $\pm$ 10.4	< 0.001
Female sex (n = 155)	71/155 (45.8%)	47/114 (41.2%)	24/41 (58.5%)	0.056
LVEF (%; n = 156)	57.8 $\pm$ 6.6	58.5 $\pm$ 6.1	56.0 $\pm$ 7.7	0.064
Hypertension (n = 156)	51/156 (32.7%)	31/115 (27.0%)	20/41 (48.8%)	0.011
Diabetes mellitus (n = 156)	22/156 (14.1%)	13/115 (11.3%)	9/41 (22.0%)	0.093
COPD (n = 156)	17/156 (10.9%)	10/115 (8.7%)	7/41 (17.1%)	0.139
Smoking (n = 156)	54/156 (34.6%)	42/115 (36.5%)	12/41 (29.3%)	0.402
AVR	54 (32.5%)	42 (33.6%)	12 (29.3%)	0.031
MVR	52 (31.3%)	35 (28.0%)	17 (41.5%)	
MV repair	13 (7.8%)	7 (5.6%)	6 (14.6%)	
TVR	11 (6.6%)	8 (6.4%)	3 (7.3%)	
Double valve	7 (4.2%)	5 (4.0%)	2 (4.9%)	
ASD closure	29 (17.5%)	28 (22.4%)	1 (2.4%)	
CPB time (min; n = 154)	142.3 $\pm$ 53.9	128.4 $\pm$ 39.3	182.0 $\pm$ 68.9	< 0.001
Cross-clamp time (min; n = 138)	100.0 $\pm$ 45.4	89.0 $\pm$ 29.4	131.1 $\pm$ 64.9	< 0.001

Values are presented as mean $\pm$ standard deviation or number/available cases (percentage)

For variables with missing values, percentages and summary statistics were calculated using available data, as indicated in the variable labels

Continuous variables were compared using the independent samples t-test or Mann–Whitney U test, and categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate

The p value for procedure type represents the overall comparison across surgical categories; individual procedure rows are displayed descriptively

LVEF Left ventricular ejection fraction, COPD Chronic obstructive pulmonary disease, AVR aortic valve replacement, MVR Mitral valve replacement, MV repair Mitral valve repair, TVR Tricuspid valve replacement, ASD Atrial septal defect, CPB Cardiopulmonary bypass

Because the number of primary endpoint events was limited ($n = 41$), multivariable modelling was planned to avoid overfitting. Candidate variables were first screened by univariable analysis and clinical relevance. Instead of entering all variables with $p < 0.10$ into a single model, the final adjusted model was restricted to clinically relevant variables and to non-overlapping predictors. Variables reflecting the same construct were not entered simultaneously: CPB duration was preferred over aortic cross-clamp time in the primary model, and individual blood-cell components were not forced into the same model with composite inflammatory indices. Variables with $p < 0.10$ but not retained in the primary model were addressed by sensitivity analyses or discussed as potential residual confounders. Complete-case analysis was used for multivariable models.

Receiver operating characteristic analysis was performed to evaluate the discriminative performance of inflammatory markers. AUC values were reported with bootstrap 95% confidence intervals and p values derived from Mann–Whitney U statistics. Optimal cut-off values were determined using the Youden index and rounded to clinically usable thresholds. A two-sided p value < 0.05 was considered statistically significant.

Results

Study population

Among 166 included patients, the mean age was 51.4 ± 14.8 years, and 71 patients (42.8%) were female. The mean left ventricular ejection fraction (LVEF) was $57.8 \pm 6.6\%$. The mean cardiopulmonary bypass (CPB) duration was 142.3 ± 53.9 min, and the mean aortic cross-clamp time was 100.0 ± 45.4 min. Baseline clinical and operative characteristics are presented in Table 1.

Baseline and operative characteristics

Patients requiring prolonged inotropic support were significantly older (60.0 ± 10.4 vs. 48.3 ± 14.9 years, $p < 0.001$) and had a higher prevalence of hypertension (48.8% vs. 27.0%, $p = 0.011$). Female sex was more frequent in the prolonged-support group, but the difference did not reach conventional statistical significance (58.5% vs. 41.2%, $p = 0.056$). LVEF was numerically lower among patients with prolonged support ($56.0 \pm 7.7\%$ vs. $58.5 \pm 6.1\%$, $p = 0.064$). From an operative perspective, patients with prolonged inotropic support demonstrated significantly longer CPB duration (182.0 ± 68.9 vs. 128.4 ± 39.3 min, $p < 0.001$) and longer aortic cross-clamp time (131.1 ± 64.9 vs. 89.0 ± 29.4 min, $p < 0.001$) (Table 1).

Preoperative inflammatory biomarkers

Comparison of inflammatory biomarkers is summarized in Table 2. Patients requiring prolonged inotropic support demonstrated significantly higher platelet count

Table 2 Preoperative laboratory and inflammatory biomarkers according to prolonged inotropic support

Variable	Total (n = 166)	No prolonged (n = 125)	Prolonged (n = 41)	p value
Neutrophil ($\times 10^9/L$)	4.35 (3.56–5.53)	4.26 (3.52–5.49)	4.54 (3.73–5.54)	0.458
Lymphocyte ($\times 10^9/L$)	1.97 (1.60–2.42)	2.05 (1.65–2.39)	1.76 (1.43–2.46)	0.189
Platelet ($\times 10^9/L$)	238 (186–287)	230 (183–283)	251 (203–325)	0.019
CRP (mg/L; n = 143)	4.0 (1.0–10.0)	4.0 (1.0–9.6)	5.0 (1.0–12.1)	0.400
Albumin (g/L)	43 (41–46)	43 (41–46)	43 (41–45)	0.707
Total bilirubin (mg/dL)	0.64 (0.45–0.96)	0.61 (0.44–0.90)	0.80 (0.50–1.04)	0.102
NLR	2.27 (1.66–2.93)	2.24 (1.60–2.84)	2.38 (1.98–3.16)	0.140
PLR	121 (92–153)	118 (88–140)	143 (105–190)	0.003
SII	536 (346–759)	497 (330–724)	649 (469–948)	0.010
SIRI	1.01 (0.67–1.39)	0.93 (0.65–1.34)	1.18 (0.75–1.74)	0.099
CAR	0.07 (0.02–0.21)	0.07 (0.02–0.20)	0.07 (0.02–0.25)	0.464
Albumin/total bilirubin	66.7 (45.5–91.9)	68.1 (45.6–93.2)	52.5 (44.2–85.4)	0.117
MHR (n = 153)	0.011 (0.008–0.015)	0.011 (0.008–0.015)	0.010 (0.008–0.013)	0.132

For variables with missing values, summary statistics were calculated using available data, as indicated in the variable labels

Between-group comparisons were performed using the Mann–Whitney U test

Values are presented as median (interquartile range)

CRP C-reactive protein, NLR Neutrophil-to-lymphocyte ratio, PLR Platelet-to-lymphocyte ratio, SII Systemic immune-inflammation index, SIRI Systemic inflammation response index, CAR C-reactive protein-to-albumin ratio, MHR Monocyte-to-high-density lipoprotein ratio

Table 3 Postoperative clinical outcomes

Variable	Value
Ventilation time (hours)	8 (6–12)
ICU stay (days)	2 (1–3)
Hospital stay (days)	6 (5–8)
New onset atrial fibrillation	19 (11.4%)
Postoperative acute kidney injury	5 (3.0%)
Reoperation for bleeding	12 (7.2%)
Mortality	6 (3.6%)
Prolonged inotropic support (> 24 h)	41 (24.7%)

ICU Intensive care unit

Values are presented as median (interquartile range) or number (percentage)

(251 [203–325] vs. 230 [183–283] $\times 10^9/L$, $p = 0.019$), platelet-to-lymphocyte ratio (PLR) (143 [105–190] vs. 118 [88–140], $p = 0.003$), and systemic immune-inflammation index (SII) (649 [469–948] vs. 497 [330–724], $p = 0.010$). No significant differences were observed for neutrophil-to-lymphocyte ratio (NLR), CRP-to-albumin

Table 4 Multivariable logistic regression analysis for prolonged inotropic support

Variable	OR	95% CI	p
Age (per year)	1.09	1.04–1.14	< 0.001
LVEF (per %)	0.97	0.90–1.03	0.336
CPB duration (per 10 min)	1.33	1.17–1.51	< 0.001
PLR ≥ 142	4.18	1.30–13.40	0.016
SII ≥ 462	1.66	0.52–5.31	0.391

Model adjusted for age, LVEF, CPB duration, PLR ≥ 142 , and SII ≥ 462 ; model included 154 complete cases and 40 endpoint events

Variables were selected a priori to avoid overfitting and collinearity

OR Odds ratio, CI Confidence interval, LVEF Left ventricular ejection fraction, CPB Cardiopulmonary bypass, PLR Platelet-to-lymphocyte ratio, SII Systemic immune-inflammation index

ratio (CAR), albumin-to-total bilirubin ratio, or monocyte-to-HDL ratio (MHR). SIRI showed a borderline association but did not reach statistical significance.

Postoperative outcomes

Postoperative outcomes are summarized in Table 3. Prolonged inotropic support occurred in 41 patients (24.7%). New-onset atrial fibrillation was observed in 19 patients (11.4%), acute kidney injury in 5 patients (3.0%), and reoperation for bleeding in 12 patients (7.2%). Early mortality occurred in 6 patients (3.6%).

Multivariable analysis

In the primary parsimonious complete-case adjusted model ($n = 154$, 40 endpoint events), age (OR 1.09, 95% CI 1.04–1.14, $p < 0.001$) and CPB duration (OR 1.33 per 10 min, 95% CI 1.17–1.51, $p < 0.001$) were independently associated with prolonged inotropic support. LVEF did not retain statistical significance after adjustment (OR 0.97 per 1%, 95% CI 0.90–1.03, $p = 0.336$). PLR ≥ 142 remained independently associated with the primary endpoint (OR 4.18, 95% CI 1.30–13.40, $p = 0.016$), whereas SII ≥ 462 did not retain statistical significance when both biomarkers were included simultaneously (OR 1.66, 95% CI 0.52–5.31, $p = 0.391$) (Table 4). In separate adjusted models, both PLR ≥ 142 and SII ≥ 462 were associated with prolonged support (Supplementary Tables S1–S2).

During model construction, aortic cross-clamp time was not entered together with CPB duration in the primary model because both variables represent related measures of operative exposure. Similarly, PLR, SII, and individual cellular components were not forced into the same primary model because of shared platelet and lymphocyte components. PLR and SII showed a strong monotonic correlation (Spearman $\rho = 0.79$, $p < 0.001$; Pearson $r = 0.59$, $p < 0.001$). However, VIF values in the final cut-off-based model were low: age 1.13, LVEF 1.04, CPB duration 1.06, PLR ≥ 142 1.38, and SII ≥ 462 1.35. In the combined continuous biomarker model, VIF

values for PLR and SII were 1.88 and 1.84, respectively. Therefore, no conventional VIF threshold for problematic multicollinearity was exceeded, although attenuation of SII in the combined model likely reflects shared biological information.

As an exploratory assessment of model stability, bootstrap resampling was performed for the final $\text{PLR} \geq 142$ model. The bootstrap median odds ratio was 4.63, with a 95% percentile interval of 1.29–24.43, remaining directionally consistent with the primary analysis. Given the limited number of events, this analysis was intended only as an internal sensitivity assessment rather than formal model validation.

ROC analysis

Receiver operating characteristic analysis demonstrated modest discriminative ability for both PLR and SII (Fig. 1). The AUC was 0.655 for PLR (95% CI 0.564–0.753, $p=0.003$) and 0.634 for SII (95% CI 0.538–0.729, $p=0.010$). The rounded cut-off value for PLR was 142 (sensitivity 53.7%, specificity 75.2%), whereas the selected cut-off for SII was 462 (sensitivity 75.6%, specificity 44.0%). These results indicate that PLR and SII may provide supportive information but are not sufficiently discriminative to serve as stand-alone prediction tools.

Cut-off analysis

Patients with $\text{PLR} \geq 142$ demonstrated a significantly higher incidence of prolonged inotropic support compared with those with $\text{PLR} < 142$ (41.5% vs. 16.8%, $p=0.002$) (Table 5). A similar but less pronounced association was observed for SII. Patients with $\text{SII} \geq 462$ had a higher incidence of prolonged support compared with those with lower SII values (30.7% vs. 15.4%, $p=0.041$) (Supplementary Table S3). Because cut-offs were derived and tested in the same cohort, these threshold-based findings should be interpreted as exploratory.

Sensitivity analyses supported the direction of the primary findings. After additional adjustment for female sex and hypertension, $\text{PLR} \geq 142$ remained associated with prolonged support (OR 3.93, 95% CI 1.21–12.77, $p=0.023$), whereas $\text{SII} \geq 462$ did not (OR 1.59, 95% CI 0.49–5.14, $p=0.439$). In a model replacing CPB duration with aortic cross-clamp time, $\text{PLR} \geq 142$ also remained associated with prolonged support (OR 4.83, 95% CI 1.41–16.57, $p=0.012$). After excluding patients with atrial septal defect/PFO/PAPVD procedures identified in the operative description, $\text{PLR} \geq 142$ remained associated with prolonged support (OR 3.86, 95% CI 1.21–12.38, $p=0.023$). These sensitivity analyses were exploratory and were not intended to establish a validated prediction model.

Exploratory interpretation of operative exposure and inflammatory burden.

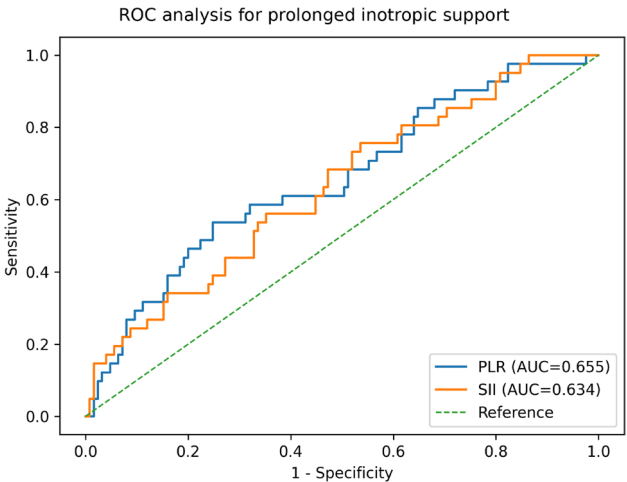


Fig. 1 ROC curves of PLR and SII for prolonged inotropic support. PLR demonstrated modest discrimination (AUC 0.655, 95% CI 0.564–0.753, $p=0.003$). SII also demonstrated modest discrimination (AUC 0.634, 95% CI 0.538–0.729, $p=0.010$)

Table 5 Association between PLR cut-off and prolonged inotropic support

PLR group	Patients (n)	Prolonged inotrope	p value
PLR < 142	113	19 (16.8%)	0.002
PLR ≥ 142	53	22 (41.5%)	

PLR Platelet-to-lymphocyte ratio

Because both preoperative inflammatory burden and operative exposure were associated with delayed recovery, the relationship between PLR and CPB duration was interpreted as potentially complementary rather than as a validated decision algorithm. The findings suggest that preoperative biological susceptibility and intraoperative stress may jointly contribute to postoperative hemodynamic recovery; however, no internally or externally validated risk score was developed in this study.

Clinical outcomes according to inflammatory markers

No significant differences were observed between PLR groups in terms of early mortality (7.5% vs. 1.8%, $p=0.083$), acute kidney injury (3.8% vs. 2.7%, $p=0.65$), or postoperative atrial fibrillation (15.1% vs. 9.7%, $p=0.31$). Similarly, no significant differences were identified between SII groups for mortality (5.0% vs. 1.5%, $p=0.40$), acute kidney injury (3.0% vs. 3.1%, $p=1.00$), or atrial fibrillation (10.0% vs. 13.8%, $p=0.46$) (Table 6).

Combined inflammatory risk analysis

Exploratory analyses of secondary clinical endpoints were limited by low event rates, particularly for mortality and acute kidney injury. Therefore, the absence of statistically significant associations with these outcomes should not be interpreted as evidence of no relationship.

Table 6 Postoperative outcomes according to PLR and SII cut-off values

Outcome	PLR < 142	PLR ≥ 142	P
Mortality	2 (1.8%)	4 (7.5%)	0.083
AKI	3 (2.7%)	2 (3.8%)	0.65
AF	11 (9.7%)	8 (15.1%)	0.31
Outcome	SII < 462	SII ≥ 462	P
Mortality	1 (1.5%)	5 (5.0%)	0.40
AKI	2 (3.1%)	3 (3.0%)	1.00
AF	9 (13.8%)	10 (10.0%)	0.46

PLR Platelet-to-lymphocyte ratio, SII Systemic immune-inflammation index, AKI Acute kidney injury, AF Atrial fibrillation

Discussion

This study evaluated the relationship between preoperative inflammatory biomarkers and early postoperative recovery following MICS. The principal finding is that platelet-related inflammatory burden, as reflected by PLR, was associated with delayed early postoperative hemodynamic recovery, defined by prolonged inotropic support. Three observations support this interpretation. First, patients requiring prolonged support had higher PLR and SII values. Second, both markers were associated with delayed recovery in separate adjusted models and when analyzed as continuous variables. Third, when PLR and SII were analyzed together, PLR retained statistical significance in the cut-off-based model whereas SII did not, suggesting that PLR may capture a simpler and more specific component of platelet-lymphocyte inflammatory burden. This interpretation should remain cautious because the study was retrospective and the marker-level discrimination was modest.

Systemic inflammation plays a central role in postoperative recovery after cardiac surgery. Cardiopulmonary bypass triggers a complex inflammatory cascade involving complement activation, cytokine release, endothelial dysfunction, and oxidative stress, all of which may impair myocardial performance and delay hemodynamic stabilization [5]. Patients with elevated preoperative inflammatory burden may be more susceptible to the perioperative inflammatory amplification. In this setting, prolonged inotropic requirement likely reflects delayed myocardial recovery rather than irreversible myocardial injury. This interpretation is supported by the relatively preserved ventricular function observed in many patients despite prolonged hemodynamic support.

From a pathophysiological perspective, inflammatory activation may lead to transient myocardial depression, microvascular dysfunction, and impaired ventricular-vascular coupling [5]. These mechanisms may delay early postoperative stabilization without necessarily translating into structural myocardial damage, which may explain the absence of association with hard clinical outcomes. Although vasopressor-only treatment for vasoplegia or

isolated blood pressure support was not counted in the primary endpoint, prolonged inotropic support remains influenced by ICU practice, institutional protocols, and physician-dependent weaning decisions; it should therefore be considered a clinically relevant but imperfect surrogate of delayed hemodynamic recovery rather than a definitive diagnosis of low cardiac output syndrome.

Platelets are increasingly recognized as active mediators of inflammation, beyond their role in hemostasis. Platelet activation promotes cytokine release, leukocyte recruitment, endothelial interaction, and microvascular dysregulation, all of which may impair myocardial perfusion and recovery [12]. In contrast, SII reflects a broader inflammatory profile by incorporating neutrophil, lymphocyte, and platelet components [13]. The attenuation of SII in the combined model may reflect shared biological information between SII and PLR rather than absence of inflammatory relevance. Therefore, PLR should not be interpreted as a definitive mechanistic marker; rather, it may be a simpler and more specific surrogate of platelet-related inflammatory burden within the limitations of this dataset.

Another important observation was the relationship between inflammatory status and operative variables. Longer CPB duration remained independently associated with prolonged postoperative inotropic support, supporting the concept that procedural complexity and operative stress contribute to delayed hemodynamic recovery. Prolonged CPB exposure may amplify systemic inflammatory activation, endothelial dysfunction, and myocardial stress, thereby impairing early postoperative stabilization [3, 4]. In this context, postoperative recovery following MICS appears to be influenced not only by surgical factors but also by individual inflammatory susceptibility. This interpretation remains hypothesis-generating and requires validation in larger datasets.

Importantly, the discriminatory performance of PLR was modest. Although PLR was statistically associated with prolonged support, an AUC of 0.66 indicates limited stand-alone predictive ability. Therefore, PLR should not be used in isolation for clinical decision-making. Its potential value is more appropriately considered as an adjunct to conventional clinical and operative risk factors, such as age, ventricular function, procedure type, CPB duration, and postoperative hemodynamic assessment.

Despite the association between inflammatory biomarkers and prolonged inotropic support, no significant relationship was observed with early mortality, acute kidney injury, or postoperative atrial fibrillation. This likely reflects the relatively low event rates inherent to MICS populations, limiting statistical power for secondary endpoints. These findings indicate that inflammatory biomarkers in this cohort were more closely related to

early functional recovery than to hard clinical endpoints, but larger studies are required before conclusions can be drawn regarding mortality or major morbidity.

MICS is associated with reduced surgical trauma and a lower inflammatory response compared with conventional approaches [1, 2]. Nevertheless, the present findings demonstrate that patient-related inflammatory burden remains an important determinant of recovery even in this setting. This highlights an important concept: reducing surgical invasiveness does not eliminate biological variability. Even after technically successful procedures, patients with elevated inflammatory burden may experience delayed recovery.

PLR is a simple, inexpensive, and readily available biomarker that can be derived from routine laboratory tests [14]. Recent cardiac surgery observations have also supported the prognostic relevance of routine blood-count-derived inflammatory markers; Bilgiç et al. reported an association between delta neutrophil index and mortality during cardiopulmonary bypass [15]. Identification of patients with elevated PLR may help clinicians recognize a subgroup with higher likelihood of delayed early hemodynamic recovery, but it should be interpreted together with established perioperative variables. In this cohort, complementary continuous-variable analyses supported the association of increasing PLR and SII with prolonged support in separate models, while simultaneous inclusion attenuated both estimates. Future prospective studies should evaluate whether integrating PLR into validated multiparametric risk models improves calibration, discrimination, and clinical usefulness.

Limitations

This study has several limitations. First, its retrospective single-center design may limit generalizability. Second, the primary endpoint, prolonged inotropic support beyond 24 h, is clinically relevant but partly dependent on institutional ICU protocols, physician preference, and local weaning practices; therefore, inter-center reproducibility may be limited. Although vasopressor-only therapy for vasoplegia or isolated blood pressure support was not counted, the endpoint remains a surrogate measure and should not be interpreted as a definitive diagnosis of low cardiac output syndrome. Third, the study population included heterogeneous MICS procedures with different operative complexity and expected recovery patterns. Although operative variables were considered, residual confounding by procedure type, cardioplegia strategy, perioperative transfusion, surgeon experience, and postoperative inotropic management cannot be excluded. Fourth, the number of primary endpoint events was limited, which constrained the number of variables that could be included in multivariable models and increased the risk of overfitting. Fifth, dichotomization of PLR and

SII using ROC-derived thresholds may have resulted in loss of information and overestimation of effect sizes, particularly because the same cohort was used to derive and test the thresholds. Sixth, the low number of secondary endpoint events, especially mortality and acute kidney injury, limited statistical power for these outcomes. Seventh, inflammatory biomarkers were assessed at a single preoperative time point, and dynamic perioperative changes were not evaluated. Finally, several potentially relevant baseline variables, including renal function, hemoglobin, pulmonary hypertension, NYHA class, preoperative atrial fibrillation, EuroSCORE II/STS score, and valve disease severity, were not consistently available in the final analysis dataset and may have contributed to residual confounding. The observational design precludes causal inference. Although an exploratory bootstrap sensitivity analysis yielded directionally consistent results, formal internal and external validation of the model was beyond the scope of the present study.

Conclusion

In conclusion, preoperative platelet-related inflammatory burden, as reflected by PLR, was associated with delayed early postoperative hemodynamic recovery following MICS. However, the predictive performance of PLR was modest, and it should be considered a complementary marker rather than a stand-alone clinical decision tool. Broader indices such as SII may provide supportive inflammatory context but did not retain independent significance when analyzed together with PLR. Prospective studies with standardized inotropic weaning protocols, broader adjustment for procedural and perioperative factors, and external validation are required.

Abbreviations

AKI	Acute kidney injury
AUC	Area under the curve
CAR	C-reactive protein-to-albumin ratio
CI	Confidence interval
COPD	Chronic obstructive pulmonary disease
CPB	Cardiopulmonary bypass
CRP	C-reactive protein
ICU	Intensive care unit
LVEF	Left ventricular ejection fraction
MHR	Monocyte-to-high-density lipoprotein ratio
MICS	Minimally invasive cardiac surgery
NLR	Neutrophil-to-lymphocyte ratio
OR	Odds ratio
PLR	Platelet-to-lymphocyte ratio
ROC	Receiver operating characteristic
SII	Systemic immune-inflammation index
SIRI	Systemic inflammation response index

Supplementary Information

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Supplementary Material 1.

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Not applicable.

Authors' contributions

BBA conceived and designed the study. EBG contributed to the study design, methodology, data collection, interpretation of the data, and drafted the manuscript. GL contributed to manuscript review and editing. AY performed data curation and visualization. MA contributed to statistical analysis and data validation. SK contributed to data interpretation and critically revised the manuscript. HLM supervised the study, contributed to the study design, and critically revised the manuscript. All authors read and approved the final manuscript.

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Data availability

The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request, subject to institutional and ethical restrictions.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Ethics Committee of Ankara Bilkent City Hospital (Approval No. 1-26-2774). Due to the retrospective nature of the study, the requirement for written informed consent was waived by the Ethics Committee.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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