Research Article

Preoperative Systemic Immune-Inflammation Index Is Associated With Postoperative Delirium After Cardiac Surgery

Ahmet Ozan Koyuncu[1], **Mehmet Ali Yesiltas**[2,*], **Faruk Gençoglu**[3], **Erman Süreyya Kiris**[4], **Kemal Sagir**[1]

[1] Department of Cardiovascular Surgery, Turkey
[2] Department of Cardiovascular Surgery, Sisli Kolan International Hospital, Turkey
[3] Department of Cardiovascular Surgery, Hisar Intercontinental Hospital, Turkey
[4] Department of Cardiovascular Surgery, Sisli Etfal Hospital, Turkey

Correspondence: dr.maliyes@gmail.com

Received: 21/12/2025: Accepted: 23/03/2026: Published: 20/04/2026

ABSTRACT:

Objective: Postoperative delirium (POD) is a frequent and serious complication following cardiac surgery and is closely linked to systemic inflammatory activation. The systemic immune-inflammation index (SII), derived from routine complete blood count parameters, integrates neutrophil, lymphocyte, and platelet counts and may reflect the perioperative inflammatory milieu. We aimed to evaluate the association between preoperative SII and POD in patients undergoing cardiac surgery.

Methods: This retrospective cohort study included 1,532 adult patients undergoing cardiac surgery. Preoperative SII was calculated as platelet count × neutrophil count / lymphocyte count. Postoperative delirium was assessed using the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) from the day of surgery through postoperative day 4. POD was defined as at least one positive CAM-ICU assessment. Multivariable logistic regression analysis was performed to evaluate the independent association between SII and POD after adjustment for clinically relevant covariates. Model discrimination was assessed using the area under the receiver operating characteristic curve (AUC). Quartile-based analyses were conducted to explore dose–response relationships.

Results: POD occurred in 365 patients (23.8%). Patients who developed POD had significantly higher preoperative SII values (median log-SII, 6.5 vs 6.3; $p < 0.001$). In multivariable analysis, higher preoperative SII remained independently associated with POD (adjusted OR 2.16, 95% CI 1.75–2.66, $p < 0.001$). Age (adjusted OR 1.02 per year, $p = 0.001$) and prolonged intubation (adjusted OR 1.52, $p = 0.020$) were also independent predictors. A graded increase in POD risk was observed across increasing SII quartiles, with the highest quartile demonstrating nearly a threefold increased risk compared with the lowest quartile. The model demonstrated moderate discrimination (AUC 0.654).

Conclusions: Elevated preoperative SII is independently associated with postoperative delirium after cardiac surgery. As an inexpensive and widely available biomarker, SII may provide practical value for preoperative risk stratification and for identifying patients at increased risk for delirium.

Keywords: postoperative delirium, cardiac surgery, systemic immune-inflammation index, inflammation, biomarkers

I. INTRODUCTION

Postoperative delirium (POD) is a common and serious complication following cardiac surgery, affecting a substantial proportion of patients and contributing to increased morbidity, mortality, and long-term cognitive decline [1, 2]. Despite advances in perioperative care, POD remains a persistent clinical challenge, particularly in high-risk surgical populations [3].

The pathophysiology of POD is multifactorial and incompletely understood. However, systemic inflammation has emerged as a central mechanistic pathway linking surgical stress to acute postoperative neurocognitive dysfunction [3, 4]. Cardiac surgery, characterized by extensive tissue injury, cardiopulmonary bypass, and pronounced inflammatory activation, represents a setting of heightened vulnerability to delirium [5].

Numerous biomarkers have been investigated to identify patients at increased risk of POD. While inflammatory mediators such as cytokines and acute-phase reactants have demonstrated associations with delirium, their routine clinical application is limited by cost, availability, and variability [3, 6, 7]. Consequently, there is growing interest in simple, reproducible, and widely accessible inflammatory indices derived from standard laboratory parameters.

The systemic immune-inflammation index (SII), calculated from neutrophil, lymphocyte, and platelet counts, integrates key components of inflammatory and thrombotic activity [7]. Unlike isolated leukocyte-based markers, SII may reflect more comprehensively the complex inflammatory milieu relevant to postoperative complications. Although SII has been associated with adverse outcomes in cardiovascular and oncologic settings, its relationship with postoperative delirium remains insufficiently explored, particularly in

cardiac surgical populations.

Therefore, the aim of this study was to evaluate the association between preoperative SII and postoperative delirium, assessed using structured CAM-ICU screening, in patients undergoing cardiac surgery.

II. METHODS

A. Study Design and Population

This retrospective cohort study included adult patients undergoing cardiac surgery. Patients with incomplete laboratory or delirium assessment data were excluded.

B. Inclusion/Exclusion Criteria

Adult patients undergoing cardiac surgery during the study period were eligible for inclusion. Patients were required to have available preoperative complete blood count (CBC) data sufficient for calculation of the systemic immune-inflammation index (SII), as well as postoperative delirium assessments using the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) during the predefined observation period. Patients were excluded if preoperative CBC parameters required for SII calculation were missing. Patients were also excluded in cases of missing or insufficient CAM-ICU assessments during postoperative days 0–4 (Figure 1).

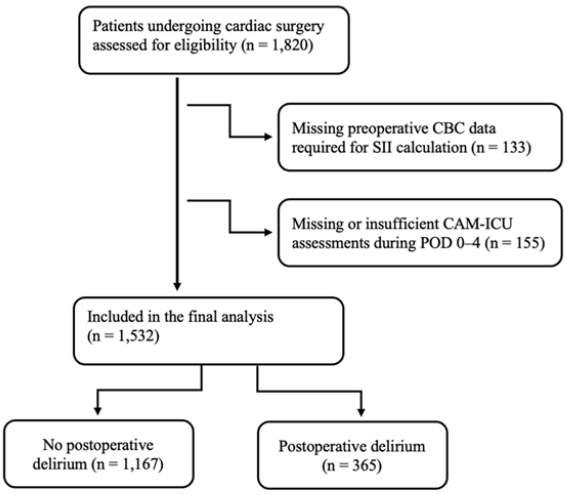

Figure 1. Flow Chart

C. Systemic Immune-Inflammation Index

Preoperative SII was calculated as [8]:

$$\text{SII} = \frac{\text{Platelet count} \times \text{Neutrophil count}}{\text{Lymphocyte count}}.$$

D. Postoperative Delirium Assessment

Postoperative delirium was assessed using the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) [9]. CAM-ICU evaluations were performed at least twice daily in both the ICU and surgical ward from the day of surgery through postoperative day 4. Patients were considered unable to be assessed during deep sedation or coma (RASS -4/-5). POD was defined as at least one positive CAM-ICU assessment.

E. Ethical Approval

The study was approved by the institutional ethics committee. The requirement for informed consent was waived because of the retrospective design of the study.

F. Statistical Analysis

Statistical analyses were performed using IBM SPSS version 21.0 software (IBM Corp., Armonk, NY, USA). Continuous variables were assessed for distributional characteristics and are presented as mean ± standard deviation or median (interquartile range), as appropriate. Normality was evaluated using visual methods and the Shapiro–Wilk test. Comparisons between groups were performed using Student's t-test or the Mann–Whitney U test for continuous variables and the chi-square test for categorical variables.

Variables considered clinically relevant to postoperative delirium were entered into the multivariable logistic regression model. Multicollinearity was assessed before model construction. Model discrimination was evaluated using the area under the receiver operating characteristic curve (AUC). Adjusted odds ratios (ORs) with 95% confidence intervals (CIs) are reported.

Analyses were conducted using complete-case data. For quartile-based analyses, SII quartiles were modeled as categorical variables with the lowest quartile serving as the reference. A p for trend across quartiles was assessed by modeling quartiles as an ordinal variable.

All statistical tests were two-tailed, and a p-value < 0.05 was considered statistically significant.

III. RESULTS

A. Patient Population

A total of 1,532 patients were included in the final analysis. Postoperative delirium (POD), defined as at least one positive CAM-ICU assessment between the day of surgery and postoperative day 4, occurred in 365 patients (23.8%).

B. Baseline and Perioperative Characteristics

Comparisons of baseline and perioperative variables according to POD status are presented in Table 1. Patients who developed POD were significantly older than those without POD (63 [57–71] vs 61 [54–67] years, $p < 0.001$). Cross-clamp duration was modestly but significantly longer in the POD group (87 [70–111] vs 84 [64.5–110] min, $p = 0.023$). Preoperative systemic immune-inflammation index (SII) values were significantly higher among patients who developed POD (log-SII 6.5 [6.2–6.9] vs 6.3 [6.0–6.6], $p < 0.001$). Prolonged intubation was more frequent in patients with POD (21.9% vs 11.5%, $p < 0.001$). No statistically significant differences were observed in ICU length of stay or hospital length of stay between the groups.

C. Multivariable Logistic Regression Analysis

Results of the multivariable logistic regression analysis are shown in Table 2. Higher preoperative SII remained independently associated with an increased risk of POD (adjusted OR 2.16, 95% CI 1.75–2.66, $p < 0.001$). Age was also independently associated with POD (adjusted OR 1.02 per year, 95% CI 1.01–1.03, $p = 0.001$). Prolonged intubation was associated with a higher likelihood of POD (adjusted OR 1.52, 95% CI 1.07–2.16, $p = 0.020$).

Other covariates, including sex, diabetes mellitus, hypertension, cross-clamp time, and EuroSCORE category, were not independently associated with POD. The discriminatory ability of the model

Table 1. Baseline and Perioperative Characteristics According to POD Status

Variable	No POD	POD	p-value
Age, years	61.0 (54.0-67.0)	63.0 (57.0-71.0)	<0.001
Cross-clamp time, min	84.0 (64.5-110.0)	87.0 (70.0-111.0)	0.023
Preoperative SII (log)	6.3 (6.0-6.6)	6.5 (6.2-6.9)	<0.001
ICU length of stay, days	2.0 (2.0-3.0)	2.0 (2.0-4.0)	0.080
Hospital length of stay, days	6.0 (5.0-8.0)	6.0 (5.0-8.0)	0.872
Female sex	275 (23.6%)	104 (28.5%)	0.067
Diabetes mellitus	737 (63.2%)	240 (65.8%)	0.401
Hypertension	975 (83.5%)	308 (84.4%)	0.767
Prolonged intubation	134 (11.5%)	80 (21.9%)	<0.001
EuroSCORE category 1	975 (83.5%)	269 (73.7%)	
EuroSCORE category 2	157 (13.5%)	70 (19.2%)	
EuroSCORE category 3	35 (3.0%)	26 (7.1%)	

Continuous variables are presented as median (interquartile range).

Table 2. Multivariable Logistic Regression Analysis for Postoperative Delirium

Variable	Adjusted OR (95% CI)	p-value
EuroSCORE category 2 vs 1	1.07 (0.75-1.52)	0.699
EuroSCORE category 3 vs 1	1.75 (0.98-3.12)	0.060
log(SII)	2.16 (1.75-2.66)	<0.001
Age (per year)	1.02 (1.01-1.03)	0.001
Female sex	1.09 (0.82-1.44)	0.553
Diabetes mellitus	1.11 (0.85-1.44)	0.448
Hypertension	1.00 (0.71-1.42)	0.999
Cross-clamp time (per min)	1.00 (1.00-1.00)	0.357
Prolonged intubation	1.52 (1.07-2.16)	0.020

OR: odds ratio; CI: confidence interval; SII: systemic immune-inflammation index.

was moderate (AUC 0.654). Given the multifactorial nature of postoperative delirium, the moderate discriminatory ability of the model is consistent with prior delirium prediction studies.

D. Dose–Response Relationship

A graded increase in POD incidence was observed across increasing SII quartiles. Compared with the lowest quartile (Q1), patients in Q3 and Q4 demonstrated significantly higher odds of POD, consistent with a dose–response pattern (Table 3).

Table 3. Association Between Preoperative SII Quartiles and Postoperative Delirium

SII Quartile	Adjusted OR (95% CI)	p-value
Quartile 1 (Reference)	—	—
Quartile 2	1.20 (0.81–1.76)	0.364
Quartile 3	1.87 (1.30–2.68)	<0.001
Quartile 4	2.97 (2.09–4.22)	<0.001

Adjusted for age, sex, diabetes mellitus, hypertension, cross-clamp time, prolonged intubation, and EuroSCORE category.

IV. DISCUSSION

Postoperative delirium (POD) remains a frequent and clinically significant complication following cardiac surgery. In the present study, POD occurred in nearly one quarter of patients, a rate consistent with prior investigations employing structured delirium screening protocols [1, 2, 3]. The principal finding of this study is that an elevated preoperative systemic immune-inflammation index (SII) was independently associated with POD, even after adjustment for established clinical and perioperative risk factors.

Accumulating evidence supports a central role for systemic inflammation in the pathogenesis of POD. Surgical trauma and cardiopulmonary bypass trigger a cascade of inflammatory mediators, endothelial activation, and microcirculatory disturbances, which may ultimately affect cerebral homeostasis [6, 10]. Neuroinflammatory mechanisms, including blood–brain barrier (BBB) disruption and microglial activation, are increasingly recognized as key contributors to acute postoperative neurocognitive dysfunction [5].

Within this framework, SII offers a biologically plausible marker. Unlike isolated leukocyte-based indices, SII integrates neutrophil-driven inflammation, lymphocyte-mediated immune regulation, and platelet-related thrombo-inflammatory activity. Platelets are particularly relevant in POD, given their involvement in endothelial signaling, microvascular integrity, and inflammatory amplification [7]. Thus, SII may better capture the composite inflammatory-thrombotic milieu characteristic of cardiac surgery.

Previous studies have explored associations between POD and conventional inflammatory markers such as CRP or cytokines; however, these biomarkers are not routinely available in daily clinical practice [5, 6]. In contrast, SII is derived from standard complete blood count parameters, making it inexpensive, universally accessible, and readily reproducible.

The observed dose–response relationship across SII quartiles further strengthens the validity of our findings. Patients in higher SII categories demonstrated a progressively increased risk of POD, suggesting that baseline inflammatory burden may modulate vulnerability to postoperative cerebral dysfunction. This pattern aligns with the broader perioperative literature linking inflammatory dysregulation to delirium susceptibility [10, 9]. The absence of a significant association in the lower SII quartiles, followed by a marked increase in POD risk in Q3 and Q4, suggests a potential threshold effect. This pattern supports the hypothesis that a critical inflammatory burden may be required to precipitate postoperative cerebral dysfunction.

Age remains one of the most consistent predictors of POD, reflecting age-related changes in cerebral reserve, neurovascular regulation, and inflammatory responsiveness [2, 9]. In our cohort, age retained an independent association with POD, while SII remained significant after adjustment, indicating that systemic inflammatory status provides additional risk information beyond chronological age alone.

Prolonged intubation was also independently associated with POD. This association likely reflects illness severity, sedation exposure, and postoperative complications rather than a direct causal pathway [11]. Importantly, the persistence of the SII effect after adjustment for prolonged intubation suggests that preoperative inflammation is not merely a surrogate for perioperative instability.

Contrary to several earlier reports, POD was not associated with significantly prolonged ICU or hospital length of stay in this study. This finding may reflect evolving perioperative and critical care practices, including early mobilization, sedation minimization, and systematic delirium monitoring [12]. Structured delirium screening is known to increase detection of transient and hypoactive phenotypes, which may not necessarily translate into prolonged hospitalization [3].

The clinical relevance of these findings lies in the potential role of SII as a simple preoperative risk stratification tool. Identification of patients with an elevated inflammatory burden may facilitate targeted preventive strategies, such as intensified delirium

surveillance, optimization of perioperative sedation, and early mobilization protocols. Given the multifactorial nature of POD, SII should not be interpreted as a standalone diagnostic marker but rather as part of a broader perioperative risk profile.

V. LIMITATIONS

Several limitations warrant consideration. First, the retrospective design precludes causal inference. Second, although CAM-ICU represents a validated delirium assessment tool, delirium remains a fluctuating syndrome subject to temporal variability [10]. Third, inflammatory indices were evaluated at a single preoperative time point, and dynamic perioperative changes were not analyzed. Finally, unmeasured confounders inherent to observational studies cannot be excluded.

VI. CONCLUSIONS

Elevated preoperative SII was independently associated with postoperative delirium following cardiac surgery. As a routinely available and biologically meaningful marker, SII may offer practical value in perioperative risk assessment. Prospective studies are warranted to validate these findings and clarify the mechanistic links between systemic inflammation and postoperative neurocognitive outcomes.

CONFLICTING INTERESTS

No conflict of interest was declared by the authors.

FUNDING

The authors have not declared financial support.

ETHICAL APPROVAL

The protocol was approved by the institutional Ethics Committee.

CONTRIBUTORSHIP

All authors contributed equally.

ACKNOWLEDGEMENTS

None

References

[1] Inouye, Sharon K., et al. "Delirium in elderly people–Authors' reply." The Lancet 383.9934 (2014): 2045.

[2] Smulter, Nina, et al. "Delirium after cardiac surgery: incidence and risk factors." Interactive Cardiovascular and Thoracic Surgery 17.5 (2013): 790-796.

[3] Aldecoa, César, et al. "European Society of Anaesthesiology evidence-based and consensus-based guideline on postoperative delirium." European Journal of Anaesthesiology| EJA 34.4 (2017): 192-214.

[4] Andrási, Terézia B., et al. "Risk factors for postoperative delirium after cardiac surgical procedures with cardioplegic arrest." European Journal of Cardio-Thoracic Surgery 62.1 (2022): ezab570.

[5] Gottesman, Rebecca F., et al. "Delirium after coronary artery bypass graft surgery and late mortality." Annals of Neurology 67.3 (2010): 338-344.

[6] Rudolph, James L., and Edward R. Marcantonio. "Postoperative delirium: acute change with long-term implications." Anesthesia & Analgesia 112.5 (2011): 1202-1211.

[7] Evered, Lis, et al. "Recommendations for the nomenclature of cognitive change associated with anaesthesia and surgery—2018." Journal of Alzheimer's Disease 66.1 (2018): 1-10.

[8] Hu, Bo, et al. "Systemic immune-inflammation index predicts prognosis of patients after curative resection for hepatocellular carcinoma." Clinical Cancer Research 20.23 (2014): 6212-6222.

[9] Pandharipande, Pratik P., et al. "The intensive care delirium research agenda: a multinational, interprofessional perspective." Intensive Care Medicine 43.9 (2017): 1329-1339.

[10] Maldonado JR. Neuropathogenesis of delirium: review of current etiologic theories and common pathways. Am J Geriatr Psychiatry. 2013;21(12):1190–222.

[11] Devlin, John W., et al. "Clinical practice guidelines for the prevention and management of pain, agitation/sedation, delirium, immobility, and sleep disruption in adult patients in the ICU." Critical Care Medicine 46.9 (2018): e825-e873.

[12] Chen, Haiyan, et al. "Risk factors of postoperative delirium after cardiac surgery: a meta-analysis." Journal of Cardiothoracic Surgery 16.1 (2021): 113.