



Article

Association Between Inflammatory Indices and Major Adverse Events After Coronary Artery Bypass Surgery: A Retrospective Cohort Study

Gürcan Güler^{1,*}, Buket Özyaprak¹, Mehmet Gamlı², Hüseyin Çetinkaya¹,
Damla Bozan Güler³, Ayşe Neslihan Balkaya¹, Serpil Ekin¹, Derful Gülen¹,
İlkay Ceylan¹, Nermin Kılıçarslan¹, Gönül Erkan⁴, Mesut Engin⁵

¹Department of Anesthesiology and Reanimation, University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital, 16100 Bursa, Türkiye

²Department of Anesthesiology and Reanimation, University of Health Sciences, Bursa City Hospital, 16100 Bursa, Türkiye

³Department of Anesthesiology and Reanimation, Suluova State Hospital, 05500 Amasya, Türkiye

⁴Department of Anesthesiology and Reanimation, Trabzon Ahi Evren Training and Research Hospital, University of Health Sciences, 61040 Trabzon, Türkiye

⁵Department of Cardiovascular Surgery, University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital, 16100 Bursa, Türkiye

*Correspondence: gurcanguler.45@gmail.com (Gürcan Güler)

Academic Editor: Haiyang Li

Submitted: 24 March 2026 Revised: 15 June 2026 Accepted: 23 June 2026 Published: 14 October 2026

Abstract

Background: Coronary artery bypass grafting (CABG) is associated with a significant risk of postoperative major adverse event (MAE), largely driven by systemic inflammatory responses. Easily accessible inflammatory indices such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), systemic immune-inflammation index (SII), and plateletcrit (PCT) have been proposed as potential predictors; however, the comparative performance and optimal timing of these indices remain unclear. Thus, this study aimed to evaluate the association between perioperative inflammatory indices measured at different time points and postoperative MAEs in patients undergoing elective on-pump CABG, and to compare the discriminatory performance of these indices. **Methods:** This single-center retrospective cohort study included 500 patients who underwent elective on-pump CABG between January 2022 and December 2023. Inflammatory indices (NLR, PLR, SII, and PCT) were calculated preoperatively and on postoperative days 0 (POD0), 1, and 3. The primary outcome was MAE, defined as mortality, stroke, sepsis, or acute kidney injury (AKI). Multivariable logistic regression and receiver operating characteristic curve analyses were performed to assess independent associations and discriminatory performance. **Results:** MAE occurred in 120 patients (24.0%) and were predominantly driven by AKI. Meanwhile, inflammatory indices measured on PODs0 and 1 showed limited discriminative ability. Conversely, NLR on POD3 was independently associated with MAE (odds ratio (OR): 1.16 per unit increase; 95% confidence interval (CI): 1.11–1.22; $p < 0.001$) and demonstrated the highest discriminatory performance (area under the curve (AUC): 0.733), followed by SII and PLR, whereas PCT showed poor performance. A cut-off value of $\text{NLR} \geq 10$ on POD3 was associated with a significantly increased risk of MAE (OR: 3.98, 95% CI: 2.49–6.37; $p < 0.001$) and AKI (OR: 3.44, 95% CI: 2.09–5.66; $p < 0.001$). **Conclusions:** The prognostic value of inflammatory markers after CABG is time-dependent. NLR measured on POD3 showed the strongest and most consistent association with adverse outcomes and may serve as a practical tool for postoperative risk stratification, particularly for AKI. However, given the potential influence of reverse causality, these findings should be confirmed in prospective, multicenter studies.

Keywords: acute kidney injury; coronary artery bypass; inflammation; lymphocytes; neutrophils; postoperative complications

1. Introduction

Coronary artery bypass grafting (CABG) is one of the most important surgical interventions that improves survival in patients with advanced coronary artery disease. However, despite advances in surgical techniques and perioperative care, major adverse event (MAE) occurring in the postoperative period remain a significant cause of morbidity and mortality [1].

The pathophysiology of complications following CABG is primarily driven by a complex inflammatory process triggered by surgical trauma, cardiopulmonary bypass, and the neuroendocrine response. This inflammatory re-

sponse is closely associated with adverse outcomes such as acute kidney injury (AKI), sepsis, and mortality [2,3]. Therefore, evaluating inflammatory markers at appropriate time points is of great importance for identifying high-risk patients.

In recent years, parameters such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and systemic immune-inflammation index (SII), which can be easily obtained from routine blood tests, have gained attention as practical and cost-effective markers of systemic inflammation [4]. While an increased neutrophil count reflects heightened inflammatory activity, a



decreased lymphocyte count is associated with physiological stress and immunosuppression. The NLR, which represents a combination of these two parameters, is strongly associated with cardiovascular diseases and postoperative outcomes [5].

In the literature, particularly elevated preoperative or postoperative NLR values are associated with early mortality and complications following CABG [6,7]. Additionally, perioperative changes in NLR have been shown to be associated with AKI and other complications [8]. By contrast, evidence regarding the relationship between other inflammatory indices, such as PLR and SII, and clinical outcomes remains more limited [4,9].

On the other hand, although numerous studies have evaluated inflammatory markers at different time points during the perioperative period, there is no clear consensus regarding their relative performance or superiority in discriminating clinical outcomes. The associations of parameters such as NLR, PLR, and SII with clinical outcomes have shown variable results across different studies [4,8,9]. Furthermore, studies that comparatively evaluate these inflammatory indices within the same patient population are limited. Therefore, clinical practice still lacks a clear consensus on which parameter is more reliable.

Although platelet parameters such as platelet count and mean platelet volume (MPV) are associated with clinical outcomes in cardiac patients in several studies, data on plateletcrit (PCT), which reflects total platelet mass, remain quite limited [10]. In particular, the prognostic value of PCT in the CABG population has not been sufficiently investigated, representing an important gap in the literature.

Therefore, the aim of this study was to evaluate the association between NLR, PLR, SII, and PCT values measured at different perioperative time points and postoperative MAE in patients undergoing elective on-pump CABG. Although inflammatory markers after cardiac surgery have been investigated previously, the distinctive aspect of the present study is the comparative evaluation of multiple inflammatory indices within the same homogeneous CABG cohort across serial perioperative time points, together with formal comparison of discriminatory performance and component-level assessment of the composite endpoint, particularly AKI.

2. Materials and Methods

This study was designed as a single-center, retrospective cohort study. Patients who underwent elective on-pump CABG between January 1, 2022 and December 31, 2023, at our institution were included. Ethical approval was obtained from the Medical Sciences Ethics Committee of University of Health Sciences Bursa Yuksek Ihtisas Training and Research Hospital on February 7, 2024 (Protocol No. 2024/02-03).

Patients aged between 40 and 75 years were included in the study. Patients who underwent emergency surgery,

or concomitant cardiac valve procedures alongside their CABG were excluded. Individuals on routine hemodialysis or with a history of active malignancies or chronic inflammatory diseases were also excluded. A total of 500 eligible patients were included in the final analysis.

Patient data were retrospectively obtained from the hospital information management system and medical records. The following variables were recorded: age, sex, diabetes mellitus, hypertension, chronic obstructive pulmonary disease, chronic kidney disease, previously documented coronary artery disease, ejection fraction, EuroSCORE II, cardiopulmonary bypass duration, aortic cross-clamp time, duration of mechanical ventilation, length of intensive care unit stay, length of hospital stay, and mortality status. Previously documented coronary artery disease was defined as a documented diagnosis of coronary artery disease before the index CABG admission, including prior myocardial infarction, previous coronary angiography demonstrating coronary artery disease, or previous coronary revascularization.

Chronic kidney disease was defined as a documented preoperative diagnosis of chronic kidney disease or an estimated glomerular filtration rate <60 mL/min/1.73 m² for at least 3 months [11]. Patients receiving routine hemodialysis were excluded. Sepsis was diagnosed retrospectively through a review of postoperative medical records and consultations with infectious diseases or intensive care specialists.

Laboratory parameters were recorded at the following time points: preoperative period, postoperative day 0 (POD0), POD1, and POD3. The analyzed parameters included white blood cell count, neutrophil count, lymphocyte count, platelet count, urea, and creatinine levels.

Inflammatory indices were calculated as follows [4,12,13]:

$NLR = \text{neutrophil/lymphocyte}$

$PLR = \text{platelet/lymphocyte}$

$SII = \text{platelet} \times \text{neutrophil/lymphocyte}$

$PCT = \text{platelet count} \times MPV/10,000$

The primary outcome of the study was the development of MAE, was defined as the occurrence of at least one of the following: mortality, stroke, sepsis, or AKI. AKI was evaluated according to the Kidney Disease: Improving Global Outcomes criteria [14].

Statistical Analyses

Statistical analyses were performed using IBM SPSS Statistics 27.0 (IBM Corp., Armonk, NY, USA). The normality of continuous variables was assessed using the Kolmogorov–Smirnov test and visual inspection methods. Data not conforming to a normal distribution are presented as the median and interquartile range (IQR). Comparisons of continuous variables between two independent groups were performed using the Mann–Whitney U test, as the data were not normally distributed. Categorical variables are ex-

Patient Flow Diagram

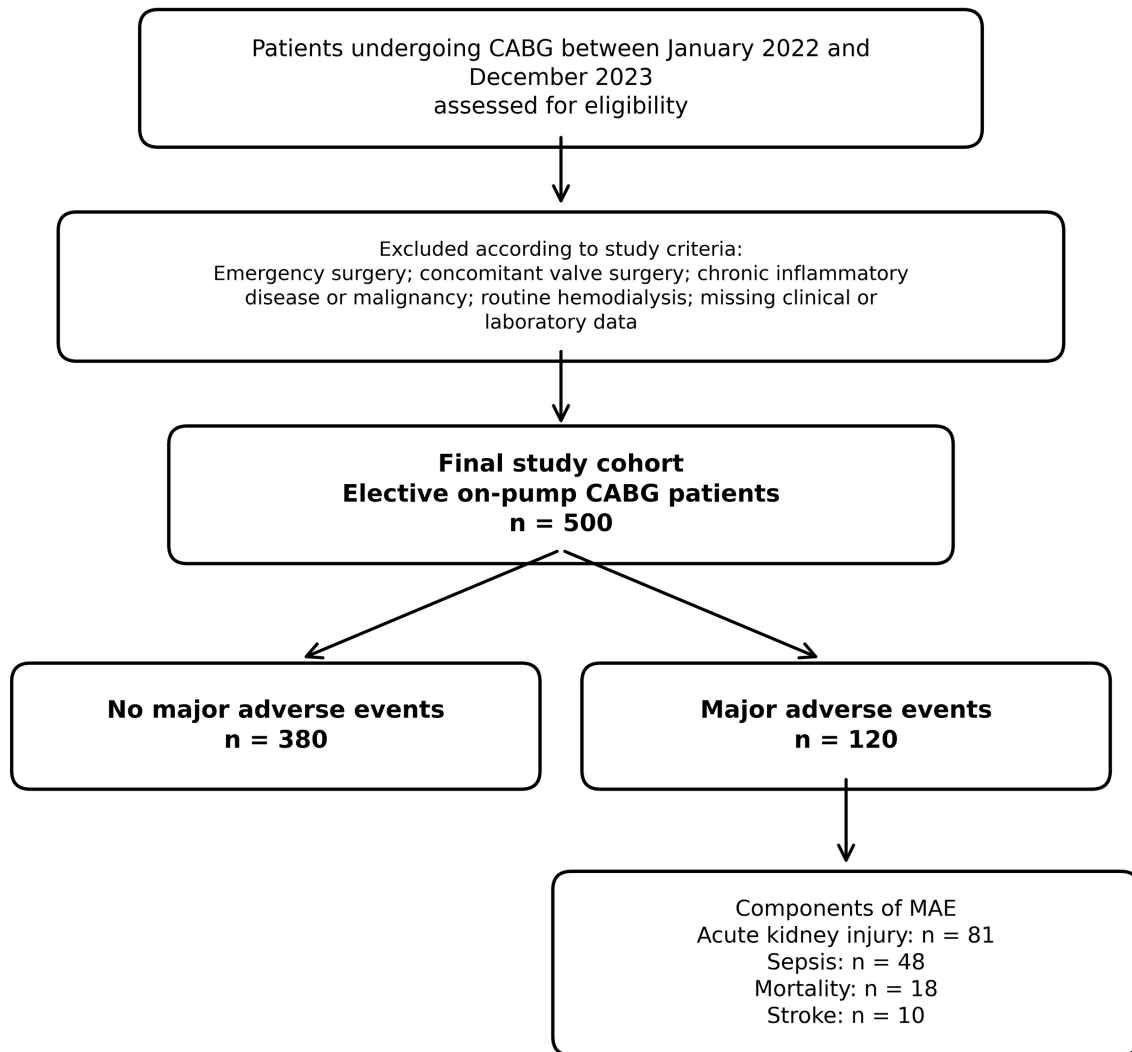


Fig. 1. Flow diagram. Acute kidney injury (81) was the most common complication, followed by sepsis (48), mortality (18), and stroke (10). n, number; CABG, coronary artery bypass grafting; MAE, major adverse event.

pressed as counts and percentages (%). The Pearson chi-square test was used for comparisons of categorical variables, and Fisher's exact test was applied when expected cell counts were low.

Because NLR, PLR, SII, and PCT were compared between the MAE and non-MAE groups at four predefined perioperative time points, the Holm–Bonferroni procedure was applied across the resulting 16 comparisons to control the family-wise error rate. Both unadjusted and Holm-adjusted p values were reported, and statistical significance after correction was defined as an adjusted p value < 0.05 .

To identify independent predictors of postoperative MAE, multivariable logistic regression analysis was performed. Variables considered clinically relevant were included in the model. Results were reported as odds ratios (ORs) with 95% confidence intervals (CIs). Model calibration was assessed using the Hosmer–Lemeshow test, and

model explanatory power was evaluated using the Nagelkerke R^2 coefficient.

The discriminatory performance of inflammatory markers for MAE and AKI was evaluated using receiver operating characteristic (ROC) analysis. The area under the curve (AUC) was calculated, and optimal cut-off values were determined using the Youden index. Pairwise comparisons of AUC values were performed using the DeLong test.

All statistical analyses were two-tailed, and $p < 0.05$ was considered statistically significant.

3. Results

A total of 500 patients were included in the study. MAE developed in 120 patients (24.0%). The most frequent complication was AKI, observed in 81 patients (16.2%), followed by sepsis in 48 patients (9.6%), mortality

Table 1. Baseline demographic, clinical characteristics, and postoperative outcomes according to MAE.

Variable	No MAE (n = 380)	MAE (n = 120)	<i>p</i> -value
Age (years), median (IQR)	62 (56–69)	61 (55.25–66)	0.337
Sex (Male, n, %)	305 (80.2)	89 (74.1)	0.154
Diabetes mellitus (n, %)	175 (46.1)	63 (52.5)	0.218
Hypertension (n, %)	205 (53.9)	88 (73.3)	<0.001
Prior coronary artery disease (n, %)	146 (38.4)	31 (25.8)	0.012
Chronic obstructive pulmonary disease (n, %)	20 (5.3)	9 (7.5)	0.361
Chronic kidney disease (n, %)	5 (1.3)	3 (2.5)	0.405
EuroSCORE II, median (IQR)	3 (2–5)	4 (2–6)	0.011
Ejection fraction (%), median (IQR)	55 (50–60)	55 (45–60)	0.005
Cardiopulmonary bypass time (min), median (IQR)	99 (93–108.75)	98 (91–115)	1
Aortic cross-clamp time (min), median (IQR)	75 (71–85)	75.5 (70–88)	0.667
Duration of mechanical ventilation (hours), median (IQR)	8 (7–8)	8 (8–24)	<0.001
ICU length of stay (days), median (IQR)	3 (2–3)	4 (3–7)	<0.001
Hospital length of stay (days), median (IQR)	7 (6–8)	10 (7–14)	<0.001

Data are presented as the median (IQR) or n (%). ICU, Intensive care unit; IQR, Interquartile range; MAE, Major adverse event; n, number.

Table 2. Preoperative laboratory parameters and inflammatory indices.

Variable	No MAE	MAE	<i>p</i> -value	Holm-adjusted <i>p</i> -value
White blood cell count ($10^3/\mu\text{L}$), median (IQR)	8.06 (6.73–9.48)	8.11 (6.82–9.22)	0.816	–
Urea (mg/dL), median (IQR)	16 (13–19)	18 (14–22)	0.008	–
Creatinine (mg/dL), median (IQR)	0.91 (0.80–1.04)	0.92 (0.80–1.13)	0.341	–
NLR, median (IQR)	2.25 (1.73–2.91)	2.35 (1.83–3.17)	0.224	1.000
PLR, median (IQR)	112.1 (88.1–142.8)	120.8 (87.8–173.6)	0.052	0.518
SII, median (IQR)	537.9 (400–751.9)	558.5 (421.8–907.7)	0.167	1.000
PCT, median (IQR)	0.25 (0.21–0.29)	0.26 (0.22–0.30)	0.223	1.000

Data are presented as the median (IQR). IQR, Interquartile range; MAE, Major adverse event; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, systemic immune-inflammation index; PCT, plateletcrit. Holm adjustment was applied to the 16 prespecified comparisons involving NLR, PLR, SII, and PCT across four perioperative time points. Other laboratory variables were not included in the multiplicity-adjustment family.

in 18 patients (3.6%), and stroke in 10 patients (2.0%) (Fig. 1). Among the components of the composite endpoint, AKI was the most frequently observed event, occurring in 81 patients (16.2%). Because MAE was defined as a composite endpoint, individual components were not mutually exclusive.

The demographic, clinical, intraoperative, and postoperative characteristics of the patients according to MAE status are presented in Table 1. Regarding demographic and clinical characteristics, hypertension was more frequent in the MAE group than in the non-MAE group (73.3% vs. 53.9%; $p < 0.001$), whereas previously documented coronary artery disease before the index CABG surgery was less frequent in patients who developed MAE than in those without MAE (25.8% vs. 38.4%; $p = 0.012$). EuroSCORE II values significantly differed between the groups ($p = 0.011$). Although ejection fraction also showed a statistically significant difference ($p = 0.005$), the median values were comparable between the groups. Regarding intraoperative variables, cardiopulmonary bypass time and aortic cross-clamp time did not significantly differ between the

groups (both $p > 0.05$). Regarding postoperative outcomes, patients who developed MAE showed statistically longer mechanical ventilation duration, intensive care unit stay, and hospital stay than those without MAE (all $p < 0.001$).

Preoperative laboratory parameters and inflammatory indices are presented in Table 2. There were no significant differences between the groups in terms of white blood cell count, NLR, PLR, SII, and PCT after Holm–Bonferroni correction (all $p > 0.05$). Only preoperative urea levels were significantly higher in the MAE group ($p = 0.008$). There was no significant difference between the groups with respect to creatinine levels.

POD0 laboratory parameters are presented in Table 3. When evaluated in terms of inflammatory indices, no significant differences were observed between the groups with respect to NLR, PLR, SII and PCT values ($p > 0.05$). Conversely, white blood cell count ($p = 0.003$), urea ($p < 0.001$), and creatinine ($p < 0.001$) levels were significantly higher in the MAE group.

POD1 and POD3 laboratory parameters are presented in Table 4. On POD1, white blood cell count, urea, creati-

Table 3. Postoperative day 0 laboratory parameters and inflammatory indices.

Variable	No MAE	MAE	<i>p</i> -value	Holm-adjusted <i>p</i> -value
White blood cell count ($10^3/\mu\text{L}$), median (IQR)	11 (8.9–13.2)	12.3 (9.6–15)	0.003	–
Urea (mg/dL), median (IQR)	13.2 (11–16)	16.9 (13.6–21)	<0.001	–
Creatinine (mg/dL), median (IQR)	0.85 (0.75–1)	1.10 (0.85–1.37)	<0.001	–
NLR, median (IQR)	15.1 (11.3–20.5)	16.9 (11.3–24.9)	0.113	0.906
PLR, median (IQR)	288.4 (211.7–382.5)	262.4 (202.2–392.9)	0.348	1.000
SII, median (IQR)	2775.9 (1997.8–3948.9)	3036.7 (1936.9–4411.7)	0.438	1.000
PCT, median (IQR)	0.19 (0.16–0.23)	0.19 (0.15–0.24)	0.310	1.000

Data are presented as median (IQR). IQR, Interquartile range; MAE, Major adverse event; NLR, Neutrophil-to-lymphocyte ratio; PCT, Plateletcrit; PLR, Platelet-to-lymphocyte ratio; SII, Systemic immune-inflammation index. Holm adjustment was applied to the 16 prespecified comparisons involving NLR, PLR, SII, and PCT across four perioperative time points. Other laboratory variables were not included in the multiplicity-adjustment family.

nine, NLR, and SII values were significantly higher in the MAE group ($p < 0.05$). NLR and SII remained significantly higher in the MAE group after Holm–Bonferroni correction (adjusted $p = 0.002$ and adjusted $p = 0.007$, respectively). However, no significant difference was observed in terms of PLR.

On POD3, the differences between the groups became more pronounced. White blood cell count, urea, creatinine, NLR, PLR, and SII values were all significantly higher in the MAE group (all $p < 0.001$). NLR, PLR, and SII were significantly higher in the MAE group after correction (adjusted $p < 0.001$, adjusted $p = 0.007$, and adjusted $p < 0.001$, respectively). By contrast, PCT was significantly lower in the MAE group (adjusted $p = 0.001$).

Multivariable logistic regression analysis is presented in Table 5. Hypertension (OR: 2.11, 95% CI: 1.26–3.52; $p = 0.005$) and NLR measured on POD3 (OR: 1.16 per unit increase, 95% CI: 1.11–1.22; $p < 0.001$) were found to be independently associated with the development of MAE. Age, diabetes mellitus, prior history of coronary artery disease, preoperative creatinine level, aortic cross-clamp time, and cardiopulmonary bypass duration were not significant in the multivariable model. The model demonstrated good calibration (Hosmer–Lemeshow $p = 0.783$) and moderate explanatory power (Nagelkerke R^2 : 0.273).

The discriminatory performance of NLR across perioperative time points was evaluated using ROC analysis. POD3 NLR showed the highest AUC for MAE discrimination compared with preoperative NLR, POD0 NLR, and POD1 NLR. Pairwise comparison of AUC values using the DeLong test showed that POD3 NLR had significantly higher discriminatory performance than preoperative NLR (AUC: 0.733 vs. 0.533; $p < 0.001$), POD0 NLR (AUC: 0.733 vs. 0.544; $p < 0.001$), and POD1 NLR (AUC: 0.733 vs. 0.619; $p < 0.001$).

Among the evaluated POD3 inflammatory indices, NLR demonstrated the highest discriminatory power for MAE, with an AUC of 0.733 (95% CI: 0.680–0.787; $p < 0.001$), followed by SII (AUC: 0.668, 95% CI: 0.610–0.727; $p < 0.001$) and PLR (AUC: 0.605, 95% CI: 0.544–

0.667; $p = 0.001$). PCT showed an AUC below 0.5 (AUC: 0.379, 95% CI: 0.321–0.438; $p < 0.001$), indicating poor discriminatory performance in the expected direction. The ROC curve of POD3 NLR for MAE is shown in Fig. 2.

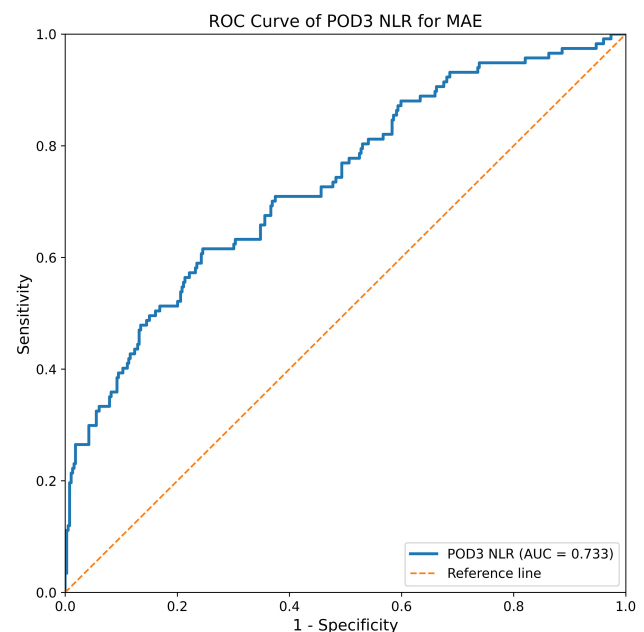


Fig. 2. Receiver operating characteristic (ROC) curve of postoperative day 3 neutrophil-to-lymphocyte ratio (POD3 NLR) for discrimination of major adverse event (MAE) (area under the curve [AUC]: 0.733).

Based on ROC analysis, the optimal cut-off value for NLR on POD3 was determined as 10 using the Youden index (sensitivity: 51.3%; specificity: 80.7%). This threshold was used only for clinically interpretable risk stratification and was not intended to imply improved discriminatory ability compared with the continuous NLR variable. In the threshold-based analysis, patients with $\text{NLR} \geq 10$ on POD3 were linked to an increased risk of MAE (OR: 3.98, 95% CI: 2.49–6.37; $p < 0.001$).

Table 4. Postoperative day 1 and Postoperative day 3 laboratory parameters according to MAE Status.

Variable	POD1	POD1	<i>p</i> -value	Holm-adjusted <i>p</i> -value	POD3	POD3	<i>p</i> -value	Holm-adjusted <i>p</i> -value
	No MAE	MAE			No MAE	MAE		
White blood cell count ($10^3/\mu\text{L}$), median (IQR)	13 (10.8–15.7)	14.1 (11.9–17.9)	0.003	–	12 (9.7–14.5)	13.2 (10.6–16.7)	<0.001	–
Urea (mg/dL), median (IQR)	15.4 (12.1–19)	22.5 (18.3–29)	<0.001	–	18 (14–22.2)	28.2 (20.9–37)	<0.001	–
Creatinine (mg/dL), median (IQR)	0.8 (0.7–1)	1.2 (0.9–1.6)	<0.001	–	0.87 (0.7–1)	1.21 (0.8–1.5)	<0.001	–
NLR, median (IQR)	8.4 (6.6–11.6)	10.3 (7.4–16.4)	<0.001	0.002	6.1 (3.8–9)	10.3 (6.2–17.2)	<0.001	<0.001
PLR, median (IQR)	138.3 (100.9–186.7)	151.6 (109.3–204.6)	0.054	0.518	126 (93.2–170.6)	148 (108.2–220.3)	<0.001	0.007
SII, median (IQR)	1477.8 (1045.1–2160.7)	1863.1 (1180.6–2726.4)	<0.001	0.007	1183.6 (785.8–1757.2)	1655 (1128.4–2640.8)	<0.001	<0.001
PCT, median (IQR)	0.18 (0.16–0.22)	0.18 (0.15–0.23)	0.782	1.000	0.21 (0.17–0.26)	0.19 (0.15–0.22)	<0.001	<0.001

Data are presented as the median (IQR). IQR, Interquartile range; MAE, Major adverse event; POD, postoperative day. Holm adjustment was applied to the 16 prespecified comparisons involving NLR, PLR, SII, and PCT across four perioperative time points. Other laboratory variables were not included in the multiplicity-adjustment family.

Table 5. Multivariable logistic regression analysis for MAE.

Variable	OR	95% CI	<i>p</i> -value
Age (per year)	1.024	0.998–1.051	0.071
Diabetes mellitus	1.143	0.708–1.845	0.585
Hypertension	2.105	1.257–3.524	0.005
Coronary artery disease	0.706	0.423–1.179	0.183
NLR at POD3 (per unit increase)	1.164	1.113–1.217	<0.001
Preoperative creatinine	1.155	0.637–2.095	0.636
Cross-clamp time (min)	0.999	0.975–1.023	0.915
Cardiopulmonary bypass time (min)	1.010	0.992–1.029	0.272

Data are presented as odds ratios (ORs) with 95% confidence intervals (CIs). Continuous variables are expressed per unit increase. MAE, Major adverse event; NLR, Neutrophil-to-lymphocyte ratio; POD3, Postoperative day 3.

In addition, multivariable analysis for AKI demonstrated that POD3 NLR was independently associated with the development of AKI (OR: 1.099, 95% CI: 1.057–1.142; $p < 0.001$). In this model, POD3 NLR was evaluated together with age, hypertension, and preoperative creatinine levels. The incidence of AKI was significantly higher in patients with NLR ≥ 10 on POD3 (29.3% vs. 10.8%; $p < 0.001$). Based on this threshold, patients with NLR ≥ 10 had approximately a 3.4-fold increased risk of developing AKI (OR: 3.436; 95% CI: 2.085–5.664).

The performance of inflammatory indices in discriminating AKI was evaluated using ROC analysis. POD3 NLR demonstrated the highest discriminatory power for AKI (AUC: 0.718, 95% CI: 0.656–0.780; $p < 0.001$), followed by SII (AUC: 0.652, 95% CI: 0.585–0.719; $p < 0.001$) and PLR (AUC: 0.609, 95% CI: 0.538–0.680; $p = 0.002$). PCT showed an AUC below 0.5 (AUC: 0.405, 95% CI: 0.335–0.475; $p = 0.008$), indicating poor discriminatory performance in the expected direction.

4. Discussion

In this study, the relationship between perioperative inflammatory markers and postoperative MAE was evaluated in patients undergoing elective CABG. The findings indicate that the association between inflammatory markers and clinical outcomes is markedly time-dependent, and that the NLR measured on POD3 is independently associated with MAE. By contrast, inflammatory indices measured in the preoperative and early postoperative periods demonstrated limited performance in discriminating clinical outcomes. Thus, rather than simply confirming that postoperative inflammation is associated with adverse outcomes, this study clarifies the relative performance and timing of routinely available inflammatory indices and suggests that POD3 NLR provides the most informative discrimination for postoperative MAE in this cohort.

Although the dynamic behavior of inflammatory markers after cardiac surgery has been previously investigated, the present study adds to the literature by directly

comparing NLR, PLR, SII, and PCT across multiple perioperative time points in the same elective on-pump CABG cohort. Our findings suggest that the clinical relevance of these markers is not uniform over time and that POD3 NLR provides the most consistent discriminatory performance. In addition, the component-level evaluation showed that the association between POD3 NLR and the composite MAE outcome was largely driven by AKI, which provides a more nuanced interpretation of the prognostic value of postoperative inflammatory markers.

In our study, the prevalence of hypertension was also found to be higher in patients who developed MAE. Hypertension is associated with chronic inflammation, endothelial dysfunction, and vascular stiffness, all of which may contribute to an increased risk of postoperative complications [15]. By contrast, the lower prevalence of a prior history of coronary artery disease in the MAE group is noteworthy. This finding may be related to closer clinical follow-up or more optimal medical management in these patients [16]. Furthermore, although mechanical ventilation duration, intensive care unit stay, and hospital stay were statistically longer in patients with MAE, the clinical magnitude of these differences should be interpreted cautiously. Therefore, these findings should be considered supportive indicators of the postoperative course rather than definitive evidence of a large clinical impact. In this regard, our findings are consistent with the existing literature [17].

The absence of significant differences in inflammatory markers in the preoperative period suggests that these parameters may have limited utility in risk stratification when used alone at baseline. Although previous studies have reported an association between preoperative NLR and adverse clinical outcomes, this relationship appears to be variable across different patient populations and methodological approaches [2,3].

It is well established that the inflammatory response following cardiac surgery is triggered by multifactorial mechanisms, including surgical trauma, cardiopulmonary bypass, and ischemia–reperfusion injury [18,19]. The inflammatory response observed in the early postoperative period is generally considered to be physiological, and therefore may have limited value in discriminating clinical outcomes [19]. The absence of significant differences in inflammatory indices at POD0 in our study supports this notion.

Although differences between the groups in certain inflammatory markers began to emerge on POD1, one of the most notable findings of our study is that the dynamic changes in inflammatory markers over time play a decisive role in their association with clinical outcomes. Conversely, on POD3, inflammatory markers were markedly higher in patients who developed MAE, providing a clear separation between the groups. Importantly, POD3 reflects a phase of persistent inflammatory response rather than the early surgical stress response. Therefore, NLR values mea-

sured at this time point appear to demonstrate greater utility for clinical risk stratification, which is consistent with the underlying biological processes. It is well established that the systemic inflammatory response following cardiac surgery is triggered by ischemia–reperfusion injury, cardiopulmonary bypass, and neuroendocrine activation, and that persistence of this response is associated with organ dysfunction [18,19]. Importantly, the between-group differences in POD3 NLR, PLR, SII, and PCT remained statistically significant after Holm–Bonferroni correction, supporting the robustness of the observed late postoperative associations.

In our study, the comparative evaluation of different inflammatory indices within the same patient population demonstrated that only NLR yielded consistent and significant results, both as a continuous variable and when analyzed using the predefined threshold (≥ 10). The higher discriminatory power of NLR compared to other inflammatory indices in ROC analysis may be explained by its ability to simultaneously reflect systemic inflammation through both neutrophil activation and lymphocyte suppression [5,20]. From a clinical perspective, the observed effect sizes—particularly for POD3 NLR—suggest a clinically meaningful association. However, these effects should be interpreted in light of the limitations of the study design. In addition to statistical significance, consideration of effect sizes is important for the clinical interpretation of findings. In daily practice, POD3 NLR may serve as a simple adjunctive marker to identify patients who may benefit from closer postoperative surveillance, renal function monitoring, and careful evaluation for infectious or inflammatory complications. However, it should not be used as a standalone predictor, and clinical decisions should be based on the overall clinical context.

By contrast, the weaker and more variable performance of more complex indices such as SII and PLR in the present study suggests that these parameters may provide limited incremental prognostic value compared with NLR, although previous studies have reported associations between these indices and postoperative outcomes after CABG [4]. Although PCT is associated with saphenous vein graft disease after CABG and with cardiopulmonary bypass-related hematological changes in open-heart surgery, these associations do not necessarily translate into reliable discrimination of early postoperative adverse outcomes [21,22]. In our cohort, PCT demonstrated poor discriminatory ability, suggesting a limited prognostic value for the outcome assessed in this patient group.

The relatively high frequency of MAE in the present cohort should be interpreted in the context of the composite endpoint definition. MAE included mortality, stroke, sepsis, and AKI, and these components were not mutually exclusive. In addition, AKI was the most frequent component and was defined according to KDIGO criteria, which may include mild postoperative renal dysfunction. There-

fore, the overall MAE rate mainly reflects the cumulative burden of postoperative complications rather than the incidence of a single severe event.

In this study, the association between NLR and MAE appeared to be closely related to the AKI component, which was the most frequently observed event within the composite outcome. The higher risk of AKI associated with a POD3 NLR ≥ 10 , coupled with comparable ROC findings for AKI and MAE, suggests that inflammatory indices are primarily capturing postoperative renal complications within the composite endpoint. The relationship between systemic inflammation and AKI following CABG has also been demonstrated in previous studies [8]. This association may be explained by the close relationship between inflammatory activation, impaired renal perfusion, and microcirculatory dysfunction [23].

However, the threshold-based analysis should be interpreted cautiously. The NLR ≥ 10 cut-off was used to provide a clinically interpretable risk stratification threshold and should not be considered evidence of improved discriminatory ability compared with the continuous NLR variable. Categorizing a continuous biomarker may amplify apparent group differences without increasing the marker's intrinsic discriminatory performance. Therefore, the continuous NLR analysis and ROC-based discriminatory performance remain the primary basis for interpreting the prognostic value of POD3 NLR.

These findings highlight the importance of analyzing individual components when interpreting composite endpoints. Because AKI was the most frequent component of MAE, the observed associations should not be generalized equally to all components of the composite outcome.

However, the measurement of inflammatory markers at specific time points constitutes an important methodological limitation. In particular, it cannot be excluded that NLR values measured on POD3 may have been obtained after the development of MAE in some patients. This raises the possibility that the observed association may reflect the inflammatory response accompanying existing complications rather than a causal relationship. Therefore, POD3 NLR may be more appropriately interpreted not as a true predictor, but rather as a biomarker or risk stratification tool reflecting early postoperative complications.

This study had several notable strengths. First, it was conducted in a relatively large and homogeneous patient population, which enhances the robustness of the findings. Second, the evaluation of inflammatory markers at multiple preoperative and postoperative time points (POD0, POD1, and POD3) allowed for assessment of the temporal dynamics of the inflammatory response. Third, the comparative analysis of different inflammatory indices, including NLR, SII, PLR, and PCT, within the same patient population contributed to identifying the most clinically reliable parameter among them.

Moreover, the use of both continuous variable analysis and a clinically applicable threshold value ($\text{NLR} \geq 10$) improves the practical applicability of the findings. Finally, additional analyses focusing on AKI enabled a more detailed evaluation of the components of the composite endpoint, allowing for a more in-depth interpretation of the results.

Limitations

This study had several important limitations. First, the retrospective, single-center design of this study may lead to selection bias and limit the generalizability of the findings. Inflammatory markers can be influenced by multiple factors, including surgical trauma, infection, blood transfusions, and medications, and these variables cannot be fully controlled. Although patients receiving routine hemodialysis were excluded and the prevalence of chronic kidney disease was low, pre-existing renal dysfunction may still have influenced postoperative AKI and MAE risk. Therefore, residual confounding related to baseline renal function cannot be completely excluded.

Second, because inflammatory markers were measured at specific time points, some may have been taken after complications had already developed. This creates a risk of reverse causality, meaning it is unclear if the NLR is a true predictor of complications or simply an early indicator of them. Moreover, due to the lack of detailed data regarding the timing of MAE, the temporal relationship between inflammatory marker measurements and clinical events could not be definitively established. This further increases the likelihood of reverse causality and necessitates cautious interpretation of the findings.

The heterogeneous nature of the composite endpoint (MAE), and particularly the predominance of the AKI component in this study, suggests that the results may mainly reflect a specific complication. Therefore, the findings should not be generalized equally across all components of MAE. In addition, sepsis was identified retrospectively based on consultation records and clinical documentation, which may have introduced classification variability. The evaluation of inflammatory markers only at predefined time points may have limited the assessment of dynamic changes over time. Longitudinal trajectory analyses, such as repeated-measures correlation or linear mixed-effects models, were not performed because the primary objective of this study was to compare the association and discriminatory performance of inflammatory indices at predefined perioperative time points rather than to model within-patient temporal changes. Therefore, the within-patient evolution of inflammatory indices over time could not be fully characterized.

5. Conclusions

The prognostic value of inflammatory indices after elective on-pump CABG appears to be time-dependent. Among the evaluated markers, POD3 NLR showed the

strongest and most consistent association with postoperative MAE, largely reflecting AKI-related AEs. However, given the retrospective design and the possibility of reverse causality, POD3 NLR should be interpreted as a practical postoperative risk stratification biomarker rather than a definitive predictor. Prospective multicenter studies are needed to validate these findings.

Availability of Data and Materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

GG: Conceptualization, Methodology, Formal analysis, Data curation, Writing—original draft. BÖ: Data curation, Investigation, Validation, Writing—review & editing. MG: Supervision, Methodology, Writing—review & editing. HÇ: Data curation, Investigation, Formal analysis, Writing—review & editing. DBG: Data curation, Investigation, and Writing—review & editing. ANB: Investigation, Data curation, Writing—review & editing. SE: Investigation, Resources, Writing—review & editing. DG: Investigation, Data curation, Writing—review & editing. İC: Investigation, Validation, Writing—review & editing. NK: Investigation, Data curation, Writing—review & editing. GE: Interpretation of the data, Validation, Writing—review & editing. ME: Methodology, Supervision, Writing—review & editing. All authors contributed to the final version, approved the manuscript, and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was approved by the Medical Sciences Ethics Committee of University of Health Sciences Bursa Yüksek İhtisas Training and Research Hospital (Approval date: 07 February 2024; Approval number: 2024/02-03). The study was conducted in accordance with the Declaration of Helsinki. The requirement for informed consent was waived by the Ethics Committee due to the retrospective nature of the study.

Acknowledgment

Not applicable.

Funding

This research received no external funding.

Conflicts of Interest

The authors declare no conflicts of interest.

References

- [1] Garganeeva A, Kuzheleva E, Tukish O, Kondratiev M, Vitt K, Andreev S, et al. Predictors of Adverse Cardiovascular

- Events After CABG in Patients with Previous Heart Failure. *Life* (Basel, Switzerland). 2025; 15: 387. <https://doi.org/10.3390/life15030387>
- [2] Bae MI, Shim JK, Song JW, Ko SH, Choi YS, Kwak YL. Predictive Value of the Changes in Neutrophil-Lymphocyte Ratio for Outcomes After Off-Pump Coronary Surgery. *Journal of Inflammation Research*. 2023; 16: 2375–2385. <https://doi.org/10.2147/JIR.S411057>
 - [3] Perry LA, Liu Z, Loth J, Penny-Dimri JC, Plummer M, Segal R, et al. Perioperative Neutrophil-Lymphocyte Ratio Predicts Mortality After Cardiac Surgery: Systematic Review and Meta-Analysis. *Journal of Cardiothoracic and Vascular Anesthesia*. 2022; 36: 1296–1303. <https://doi.org/10.1053/j.jvca.2021.07.001>
 - [4] Önder R, Özçobanoğlu S, Gündoğdu BP, Taçkın VB, Kakilioglu İ. Association of preoperative and postoperative systemic inflammatory markers with early mortality and morbidity after CABG surgery. *Journal of Cardiothoracic Surgery*. 2026; 21: 186. <https://doi.org/10.1186/s13019-026-03928-x>
 - [5] Gosav EM, Tanase DM, Buliga-Finis ON, Rezuş II, Morariu PC, Floria M, et al. The Prognostic Role of the Neutrophil-to-Lymphocytes Ratio in the Most Frequent Cardiovascular Diseases: An Update. *Life* (Basel, Switzerland). 2024; 14: 985. <https://doi.org/10.3390/life14080985>
 - [6] Lim HA, Kang JK, Kim HW, Song H, Lim JY. The Neutrophil-to-Lymphocyte Ratio as a Predictor of Postoperative Outcomes in Patients Undergoing Coronary Artery Bypass Grafting. *Journal of Chest Surgery*. 2023; 56: 99–107. <https://doi.org/10.5090/jcs.22.082>
 - [7] Şahin A, Sisli E. Retrospective Evaluation of the Pre- and Postoperative Neutrophil-Lymphocyte Ratio as a Predictor of Mortality in Patients Who Underwent Coronary Artery Bypass Grafting. *The Heart Surgery Forum*. 2021; 24: E814–E820. <https://doi.org/10.1532/hcf.4099>
 - [8] Yu R, Song H, Bi Y, Meng X. Predictive role of the neutrophil: lymphocyte ratio in acute kidney injury associated with off-pump coronary artery bypass grafting. *Frontiers in Surgery*. 2022; 9: 1047050. <https://doi.org/10.3389/fsurg.2022.1047050>
 - [9] Yu H, Li S, Wu Y, Ren X. Prognostic Value of Platelet to Lymphocyte Ratio for Myocardial Infarction: A Systematic Review and Meta-Analysis. *Clinical Cardiology*. 2025; 48: e70215. <https://doi.org/10.1002/clc.70215>
 - [10] Gul M, Uyarel H, Akgul O, Akkaya E, Surgit O, Cakmak HA, et al. Long-term prognostic significance of admission plateletcrit values in patients with non-ST elevation myocardial infarction. *Blood Coagulation & Fibrinolysis*. 2016; 27: 696–701. <https://doi.org/10.1097/MBC.0000000000000484>
 - [11] Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney International*. 2024; 105: S117–S314. <https://doi.org/10.1016/j.kint.2023.10.018>
 - [12] Mohamed AAB, Elnady HM, Alhewaig HK, Moslem Hefny H, Khodery A. The mean platelet volume and plateletcrit as predictors of short-term outcome of acute ischemic stroke. *The Egyptian Journal of Neurology, Psychiatry and Neurosurgery*. 2019; 55: 4. <https://doi.org/10.1186/s41983-018-0035-x>
 - [13] Budak YU, Polat M, Huysal K. The use of platelet indices, plateletcrit, mean platelet volume and platelet distribution width in emergency non-traumatic abdominal surgery: a systematic review. *Biochemia Medica*. 2016; 26: 178–193. <https://doi.org/10.11613/BM.2016.020>
 - [14] Kellum JA. Diagnostic Criteria for Acute Kidney Injury: Present and Future. *Critical Care Clinics*. 2015; 31: 621–632. <https://doi.org/10.1016/j.ccc.2015.06.001>
 - [15] Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension. *European Heart Journal*. 2018; 39: 3021–3104. <https://doi.org/10.1093/eurheartj/ehy339>
 - [16] Neumann FJ, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U, et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. *European Heart Journal*. 2019; 40: 87–165. <https://doi.org/10.1093/eurheartj/ehy394>
 - [17] Jawitz OK, Gulack BC, Brennan JM, Thibault DP, Wang A, O'Brien SM, et al. Association of postoperative complications and outcomes following coronary artery bypass grafting. *American Heart Journal*. 2020; 222: 220–228. <https://doi.org/10.1016/j.ahj.2020.02.002>
 - [18] Squicciarino E, Labriola C, Malvindi PG, Margari V, Guida P, Visicchio G, et al. Prevalence and Clinical Impact of Systemic Inflammatory Reaction After Cardiac Surgery. *Journal of Cardiothoracic and Vascular Anesthesia*. 2019; 33: 1682–1690. <https://doi.org/10.1053/j.jvca.2019.01.043>
 - [19] Landis RC, Brown JR, Fitzgerald D, Likosky DS, Shore-Lesserson L, Baker RA, et al. Attenuating the Systemic Inflammatory Response to Adult Cardiopulmonary Bypass: A Critical Review of the Evidence Base. *The Journal of Extra-Corporeal Technology*. 2014; 46: 197–211.
 - [20] Ruta VM, Man AM, Alexescu TG, Motoc NS, Tarmure S, Ungur RA, et al. Neutrophil-To-Lymphocyte Ratio and Systemic Immune-Inflammation Index-Biomarkers in Interstitial Lung Disease. *Medicina* (Kaunas, Lithuania). 2020; 56: 381. <https://doi.org/10.3390/medicina56080381>
 - [21] Akpınar I, Sayin MR, Gursoy YC, Karabag T, Kucuk E, Buyukuysal MC, et al. Plateletcrit. A platelet marker associated with saphenous vein graft disease. *Herz*. 2014; 39: 142–148. <https://doi.org/10.1007/s00059-013-3798-y>
 - [22] Hatamighouschi E, Kaya A, Ademoğlu E. The effects of changes in thrombocyte indices, on-on-pump time on prognosis in open heart surgery. *Perfusion*. 2025; 40: 1622–1632. <https://doi.org/10.1177/02676591251316436>
 - [23] Scurt FG, Bose K, Mertens PR, Chatzikyrkou C, Herzog C. Cardiac Surgery-Associated Acute Kidney Injury. *Kidney360*. 2024; 5: 909–926. <https://doi.org/10.34067/KID.0000000000000466>