# Predictors of Total Occlusion of the Culprit Epicardial Coronary Artery in Low-to-Intermediate Risk NSTEMI: A Retrospective Study

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## Abstract

**Aim:** In patients with low-to-intermediate risk acute non-ST-elevation myocardial infarction–acute coronary syndrome (NSTEMI-ACS), non-invasive treatments have gained importance. However, these patients may present with a wide spectrum, ranging from microvascular involvement to partial or complete epicardial artery occlusion. Patients with total occlusion of the culprit artery have higher morbidity and mortality rates. Early invasive treatment may reduce these rates. Therefore, early identification of such patients is important. Nonetheless, no specific clinical or laboratory distinguishing factors have been identified. This study aimed to investigate the role of inflammatory markers in identifying patients with total occlusion of the culprit artery among those with low-to-intermediate risk NSTEMI-ACS.

**Methods:** This retrospective cohort study included patients diagnosed with NSTEMI-ACS who underwent coronary angiography in a tertiary cardiology clinic between January 2018 and December 2019. A total of 276 patients were enrolled, while 32 meeting exclusion criteria were excluded. The remaining patients were classified as those with total occlusion of the culprit artery (n=47) and those without (n=229). Inflammatory markers were compared between groups.

**Results:** Statistically significant differences were found between the groups in terms of neutrophil-to-lymphocyte ratio (NLR) (p=0.01), systemic immune-inflammation index (SII) (p=0.016), and mean platelet volume (MPV) (p=0.028).

**Conclusions:** According to the findings of this study, NLR, SII, and MPV may be useful in determining the presence of total occlusion of the culprit artery in NSTEMI-ACS patients. However, the causal relationship between these parameters and total occlusion remains unclear. Larger, multicenter studies are required to confirm their predictive value and determine the ideal cutoff points.

***Keywords****: Non-ST-elevation myocardial infarction; total occlusion; neutrophil-to-lymphocyte ratio; systemic immune-inflammation index; mean platelet volume*

## 1. Introduction

Despite significant advances in the diagnosis and management of low-to-intermediate risk non–ST-segment elevation myocardial infarction–acute coronary syndrome (NSTEMI-ACS)—including the development of high-sensitivity biomarkers, advanced imaging techniques, and updated invasive treatment strategies—risk stratification within this clinically heterogeneous patient population remains challenging. The persistence of suboptimal morbidity and mortality rates in low-to-intermediate risk NSTEMI-ACS underscores the importance of optimizing diagnostic and therapeutic approaches, particularly in the early phase of care. Current guidelines recommend performing coronary angiography within the first 24 hours to assess coronary anatomy in these patients.[1] Coronary angiography enables the detection of total occlusion and high-risk plaque morphology, thereby exerting a direct influence on clinical decision-making. Accordingly, the early and accurate identification of the subset of patients who initially appear to have a low-to-intermediate risk profile yet actually harbor total occlusion of the culprit epicardial coronary artery and consequently carry a substantially higher risk of morbidity and mortality has the potential to guide timely invasive intervention and ultimately improve clinical outcomes.

Numerous clinical studies have investigated the relationship between coronary artery disease and inflammatory markers such as leukocyte count, neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), systemic immune-inflammation index (SII), and mean platelet volume (MPV).[2-6] Studies have reported that

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patients with severe atherosclerotic cardiovascular disease, such as diffuse vessel involvement and complete occlusion, can be predicted by blood inflammatory markers.[7,8]

In this study, we aimed to investigate the role of hematologic inflammatory markers in distinguishing patients with total occlusion among low-to-intermediate risk NSTEMI-ACS patients, according to the Global Registry of Acute Coronary Events (GRACE) risk classification.[9]

## 2. Materials and Methods

This study was designed as a retrospective cohort study. Data were obtained from hospital records. Patients diagnosed with NSTEMI-ACS between January 2018 and December 2019 were included.

NSTEMI-ACS was defined as ischemic chest pain without ST-segment elevation on a 12-lead electrocardiogram (ECG) and elevated troponin-I levels >0.01 ng/mL.

Inclusion criteria: Patients aged ≥18 years, diagnosed with low-to-intermediate risk NSTEMI-ACS, and undergoing coronary angiography.

Exclusion criteria: Age <18 years, persistent chest pain despite medication, hemodynamic instability, fatal ventricular arrhythmias, dynamic ST-T changes, heart failure (ejection fraction <40%), severe anemia, malignancy, sepsis, obesity [body mass index (BMI) >30 kg/m$^2$], renal failure (glomerular filtration rate <60 mL/min/1.73 m$^2$), chronic hematologic disease, collagen vascular disease, moderate-to-severe liver failure, severe valvular heart disease, electrolyte imbalance, chronic use of anti-inflammatory drugs, history of chronic inflammatory disease, or severe infection within the last month.

A total of 276 consecutive patients were screened, and after applying exclusion criteria (n=32), 244 patients were analyzed. They were divided into two groups: patients with total occlusion (n=47) and those without (n=229).

BMI was calculated as weight in kilograms divided by the square of height in meters. GRACE risk scores were calculated online (http://www.outcomes-umassmed.org/grace). Complete blood counts were obtained from peripheral venous blood samples collected into calcium-EDTA tubes within the first 30 minutes of admission. Hemogram parameters, including hemoglobin, RDW, PDW, MPV, platelet count (P), neutrophil (N), and lymphocyte (L) counts, were recorded. PLR was calculated as platelet count divided by lymphocyte count, while NLR was calculated as neutrophil count divided by lymphocyte count. SII was calculated using the formula P × NLR[10].

Routine biochemical tests including glucose, creatinine, total cholesterol, high-density lipoprotein cholesterol (HDL), and low-density lipoprotein cholesterol (LDL) were performed after 12 hours of fasting, the morning after hospital admission.

Gensini scores were calculated from angiographic images by two blinded cardiologists[11]. TIMI 0–1 flow was defined as total occlusion. Echocardiographic evaluations were performed according to current American Heart Association guidelines[12].

Statistical analysis: Continuous variables were tested for normal distribution using the Shapiro–Wilk test and histograms. Normally distributed variables were expressed as mean ± SD, and non-normally distributed variables as median (25th–75th percentiles). Student's t-test was used for normally distributed data, while the Mann–Whitney U test was used otherwise. Categorical variables were compared using chi-square or Fisher's exact test. The predictive value of parameters for total occlusion was assessed by receiver operating characteristic (ROC) curve analysis. A p-value <0.05 was considered statistically significant. Analyses were performed with SPSS v.23.

**Table 1**

Comparison of demographic and clinical data of study patients between groups

| Continuous variables | Groups by occlusion | | *p* |
|---|---|---|---|
| | Total occlusion (-) (n=229) | Total occlusion (+) (n=47) | |
| Age (years) | 67.1±13.0 (n=229) | 68.3±14.0 (n=47) | 0.574 |
| Male (Gender) | %66,4 (n=151) | %66,0 (n=32) | 0.956 |
| BMI (kg/m2) | 27,3±1,2 (n=) | 27,5±1,2 (n=47) | 0.364 |
| Systolic TA (mmHg)) | 129,2±6,5 (n=229) | 129,6±5,1 (n=47) | 0.649 |
| Diastolic TA (mmHg) | 73,3±3,6 (n=229) | 73,3±3,6 (n=47) | 0.300 |
| Hypertension | %65,9 (n=151) | %70,2 (n=33) | 0.571 |
| Dyslipidema | %47,6 (n=109) | %48,9 (n=23) | 0.867 |
| DM | %32,3 (n=74) | 31,9 (n=14) | 0.957 |
| GRACE score | 121,20±21,09 (n=229) | 123,51±24,04 (n=47) | 0.505 |
| GENSINI score | 24 (2-130) ( n=229) | 36 (8-80) (n=47) | 0.017* |
| ACE/ARBs | %54,1 (n=124) | %51,1 (n=24) | 0.699 |
| Beta-blockers | %42,4,0 (n=97) | %42,6 (n=20) | 0.980 |
| HCT (Master's Degree) | %36,4 (n=79) | %27,1 (n=16) | 0.183 |
| CCB | %25,3 (n=82) | %23,4 (n=14) | 0.782 |
| Statins | %51,1 (n=117) | %46,8 (n=22) | 0.593 |
| OAD | %29,3 (n=67) | %31,9 (n=15) | 0.717 |
| Insulin | %12,7 (n=29) | %12,8 (n=6) | 0,985 |
| EF | 52,56±9,11 (n=138) | 51,17±7,27 (n=30) | 0.370 |
| RDW | 14,27±2,55 (n=229) | 14,12±1,31 (n=47) | 0.694 |
| MPV | 10,33±1,18 (n=228) | 10,70±0,76 (n=47) | 0.028* |
| CONTINUE | 794,6 (0,3-11911,9) (n=229) | 1042,1 (328,4-17490,2) (n=47) | 0.016* |
| NLR | 3,23 (0,97-77,35) (n=229) | 4,40 (1,41-48,05) (n=47) | 0.010* |
| PLR | 127,6 (0,1-957,1) (n=229) | 146,5 (54,2-1058,1) (n=47) | 0.437 |

*TA; Blood pressure, arterial, BMI; body mass index, ACE/ARBs; Angiotensin-converting enzyme inhibitors/Angiotensin receptor blockers, HCT; hydrochlorothiazide, CCB;,Calcium channel blockers, OAD; Oral antidiabetics, EF; Ejection fraction, RDW; Red cell distribution width relationship, MPV; Mean platelet volume, SII; Systemic immune inflammation index, NLR; Neutrophil/Lymphocyte ratio, PLR; Platelet to lymphocyte ratio. *The difference is statistically significant*

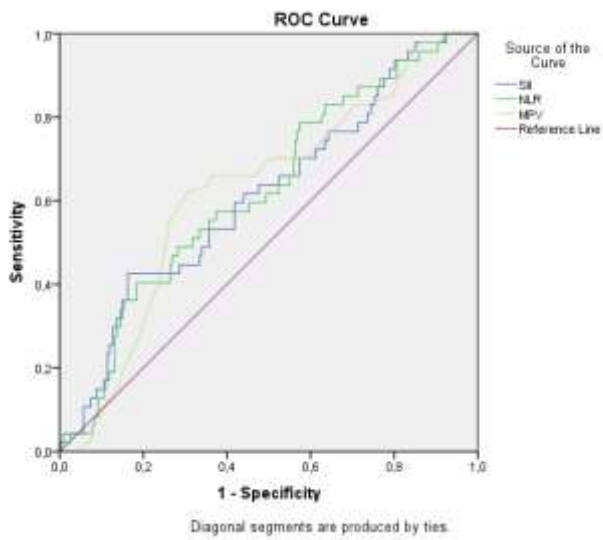
## 3. Results

Based on coronary angiography, patients were divided into two groups: those with total occlusion and those without. Demographic characteristics such as age, height, weight, and BMI were compared between groups (Table 1).

The primary aim of this study was to compare inflammatory markers between groups. Significant differences were observed in Gensini score (p=0.017), MPV (p=0.028), SII (p=0.016), and NLR (p=0.010) (Table 1). ROC analysis demonstrated that MPV, NLR, and SII predicted total occlusion (Figure 1).

**Figure 1**

The relationship between MPV, SII, and NLR levels and total occlusion of the culprit artery in NSTEMI-ACS




## 4. Discussion

This study demonstrated that higher MPV, SII, and NLR levels can be used to predict total occlusion of the culprit coronary artery in patients with low-to-intermediate risk NSTEMI-ACS.

Despite advances in technology and healthcare, cardiovascular disease remains the leading cause of death worldwide[13]. The incidence of ST-elevation myocardial infarction (STEMI) has declined with these advances, while the incidence of NSTEMI-ACS has increased[14,15]. Guidelines recommend coronary angiography within 2 hours for high-risk NSTEMI-ACS patients, while for low-to-intermediate risk patients, angiography within 24 hours is suggested[1]. However, some patients with low-to-intermediate risk NSTEMI-ACS are found to have total occlusion of the culprit artery. One study reported total occlusion in one-third of NSTEMI-ACS patients[16], and total occlusion has been associated with poor prognosis[17,18]. Early identification of such patients is therefore essential. Delay in intervention may increase mortality and morbidity rates in these patients with complete cessation of blood flow.

Inflammation plays a central role in plaque development, disruption, and erosion, which underlie NSTEMI-ACS. Inflammatory processes not only promote plaque formation but also destabilize plaques, making them more prone to rupture. Previous studies have shown that leukocyte and erythrocyte counts are associated with disease severity and prognosis in coronary artery disease[19,20]. Elevated SII values have been identified as good predictors of major cardiovascular events[10]. In our study, higher SII levels were observed in patients with total occlusion of the culprit artery.

MPV, a marker of platelet activation, has been shown to correlate with disease severity in ACS[21,22]. Similarly, in our study, MPV was significantly higher in patients with total occlusion compared to those without.

Neutrophils, by causing endothelial injury and promoting platelet activation, play a key role in ACS. High leukocyte and neutrophil counts combined with low lymphocyte counts are associated with poor prognosis in CAD[23,24]. The NLR has been shown to predict atherosclerotic processes with high sensitivity and specificity[25]. Consistent with previous findings, we observed higher NLR values in patients with total occlusion of the culprit artery.

To our knowledge, this is the first study investigating the role of inflammatory markers in predicting total occlusion of the culprit coronary artery in low-to-intermediate risk NSTEMI-ACS patients. Early detection and treatment of total occlusion in such patients may improve quality of life and reduce morbidity and mortality. Our results demonstrate that elevated SII, NLR, and MPV may help identify patients with total occlusion.

Limitations: The retrospective design and relatively small sample size are the main limitations. In addition, the absence of other commonly used biomarkers is another limitation.

## 5. Conclusion

The causal relationship between SII, NLR, MPV, and total occlusion remains unclear. However, elevated values of these parameters may be associated with total occlusion of the culprit coronary artery in low-to-intermediate risk NSTEMI-ACS patients and may aid in their identification. These findings also highlight the need for larger studies to further investigate the relationship between inflammatory markers and total occlusion in this patient group.

### Statement of ethics

The study protocol was approved by the Kahramanmaras Sutcu Imam University, Faculty of Medicine ethical committee (Date: 05.08.2020 - Approval number: 10). All participants were informed in detail about the study's purpose and procedures, and written informed consent was obtained from each participant in accordance with the Declaration of Helsinki.

### genAI

No artificial intelligence-based tools or generative AI technologies were used in this study. The entire content of the manuscript was originally prepared, reviewed, and approved by both authors.

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### Conflict of interest statement

The authors declare that they have no conflict of interest.

### Availability of data and materials

The datasets used and/or analyzed during the current study are

available from the corresponding author upon reasonable request.

## Author contributions

EA and MK made the most significant contributions to the writing of the manuscript. EA, MK participated in the design, data collection, critical review and analysis of the study. EA and MK participated in supervision, literature review, data collection and analysis. All authors read and approved the final version of the manuscript.

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