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# Neutrophil-to-albumin ratio: a promising tool for CAD assessment in non-ST elevation AMI

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**Abstract. – OBJECTIVE: In the context of coronary artery disease (CAD) pathogenesis, inflammation has emerged as a critical player. This study investigates the potential of the Neutrophil-to-Albumin Ratio (NAR) as a novel biomarker for assessing CAD severity and extension in patients suffering from acute myocardial infarction (AMI) without ST-segment elevation.**

**PATIENTS AND METHODS: We conducted a comprehensive analysis of consecutive patient records (n = 211) from a single center, focusing on individuals diagnosed with non-ST elevation AMI. To gauge CAD severity, we employed Syntax Scores (SS) and examined their correlation with NAR, C-reactive protein-albumin ratio (CRPALB), and the systemic immune inflammation index (SII). Statistical analyses were conducted to establish associations and predictive capabilities.**

**RESULTS: Our analysis revealed a significant correlation between NAR and Syntax Scores (r: .416, $p<0.01$). Notably, patients with intermediate-high SS exhibited significantly elevated NAR values compared to those in the low SS group [20.86+5.38 *vs.* 16.41+6.30 ($p<0.001$)]. Furthermore, NAR outperformed CRPALB, SII, and Neutrophil Percent-to-Albumin Ratio (NPAR) in discriminating CAD severity, as demonstrated by the Receiver Operating Characteristic (ROC) curve analysis (NAR AUC: 0.736; CRPALB AUC: 0.673; SII AUC: 0.660; NPAR AUC: 0.717).**

**CONCLUSIONS: This study underscores the potential of NAR as a robust predictor of CAD severity and extension in non-ST elevation AMI patients. While previous markers, such as CRPALB and SII, are advantageous, NAR's superior predictive capabilities are a valuable addition to the clinician's toolkit, offering enhanced risk assessment for this specific patient subgroup.**

*Key Words:*
Neutrophil-to-albumin ratio, Non-ST elevated myocardial infarction, SYNTAX score.

## Introduction

Coronary artery disease (CAD) is a complex condition influenced by many factors, including inflammation. Inflammation has been recognized as a pivotal player in the entire spectrum of CAD, from the initiation of atherosclerotic plaque formation to its subsequent destabilization, leading to acute coronary syndromes[1]. Such events encompass plaque rupture, intravascular thrombus formation, and neointimal proliferation, culminating in severe coronary stenosis.

Central to CAD management is the assessment of plaque burden and extent within the coronary arteries, as these factors distinctly contribute to the severity of the disease. While the syntax score has proven to be effective in evaluating CAD severity post-coronary intervention, its application necessitates prior knowledge of disease severity[2]. Predicting disease severity before interventional procedures would undoubtedly advance pre-procedural preparation, underscoring the importance of identifying reliable predictors.

Past investigations have illuminated the role of acute phase reactants and inflammatory markers, such as neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), Systemic immune inflammation index (SII), C-reactive protein (CRP), and albumin in the context of CAD[3-6]. Recent developments have unveiled the C-reactive protein-albumin ratio (CRPALB) as a potential indicator of CAD severity[7]. However, a demand persists for novel, robust predictors that can aptly gauge both the severity and extent of CAD.

Enter the neutrophil-to-albumin ratio (NAR), an amalgamation of neutrophil and albumin levels readily attainable through routine blood testing. The NAR has garnered attention for its prognostic significance in cancer outcomes, stroke prognosis, subarachnoid hemorrhage prognosis[8-10], and even as a predictor of Behçet's disease activity[11]. Furthermore, elevated NAR has been linked to intra-stent restenosis following carotid angioplasty and stenting[12]. Despite these promising associations, a critical gap remains: a comparative stu-

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dy between NAR and established inflammatory markers for predicting atherosclerotic burden in myocardial infarction without ST elevation.

Consequently, our study aims to elucidate the correlation between NAR and the Syntax (Synergy Between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery) score – a recognized measure of CAD severity – and juxtapose this association against other inflammatory markers, such as SII and CRPALB. By scrutinizing the performance of NAR within this framework, we endeavor to uncover a potential new avenue for assessing CAD severity and extend our understanding of inflammatory markers in this clinical context.

## Patients and Methods

### Study Design and Population

This study was approved by the Fırat University Ethics Committee (Ethics Committee acceptance number: 16817) in accordance with the International Code of Ethics and the Declaration of Helsinki. This retrospective study examined the medical records of 354 consecutive patients who were admitted to the Cardiology Department at Fethi Sekin City Hospital in Elazığ, Turkey, during the period from October 2022 to April 2023. The study exclusively focused on patients who had previously received a diagnosis of non-ST segment elevation myocardial infarction (NSTEMI) and subsequently underwent coronary angiography. Only the patients who were referred to the emergency department within the first 12 hours of the onset of symptoms were included in the study to minimize the effect of time on acute-phase reactants. Detailed baseline clinical data and demographic characteristics were extracted from the medical records. Exclusion criteria were applied, leading to the removal of 143 patients with active infectious diseases, active carcinoma, hematological proliferative diseases, chronic inflammatory conditions, active hepatobiliary disorders, autoimmune disease under steroid therapy, or a lack of recorded admission laboratory parameters. Ultimately, the retrospective analysis was conducted on a cohort of 211 eligible patients who met the predefined inclusion criteria. A flowchart of our retrospective study design is given in Figure 1.

### Data Collection

The data collection process involved a comprehensive review of electronic medical records, including admission notes, laboratory reports, angiography images, and clinical assessments. Data were collected in accordance with ethical and privacy guidelines, ensuring patient confidentiality and anonymity.

### Angiography Evaluation

The angiographic images from the eligible patient records were assessed by two experienced interventional cardiologists. These evaluators were blinded to the patients' clinical conditions to minimize bias. In cases where discrepancies arose during visual assessments, a third independent observer was consulted to achieve consensus.

### Coronary Artery Stenosis Assessment

Lesions causing over 50% of luminal occlusion in vessels larger than 1.5 mm contributed to the overall Syntax Score (SS). The cumulative SS was computed utilizing online calculator version 2.11 (www.syntaxscore.com). Patients were categorized into two groups based on SS: low (<22) and intermediate-high (>22)[2].

### Diagnostic Criteria

The diagnosis of non-ST segment elevation myocardial infarction (NSTEMI) followed the established guidelines of the European Society of Cardiology (ESC)[10]. These guidelines provided a standardized diagnostic framework to ensure consistency in the patient cohort.

### Laboratory Measurements

The results of the blood analysis included complete blood count, plasma blood glucose, urea, creatinine, high-sensitive troponin (hs-troponin), serum

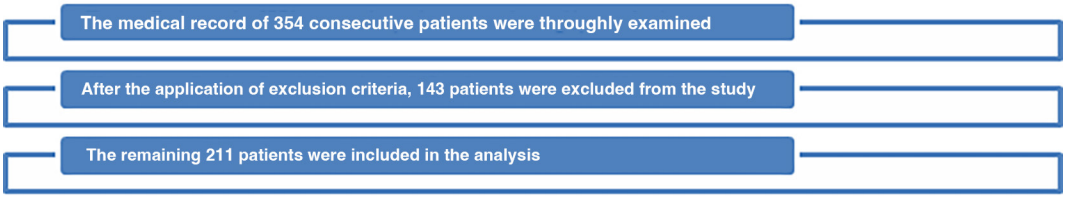


**Figure 1.** A flowchart of our retrospective study.

albumin, and C-reactive protein (CRP) levels, total cholesterol, triglycerides, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol levels taken before the PCI in the emergency room and coronary ICU were analyzed. The estimated glomerular filtration rate (eGFR) was calculated using the Cockcroft-Gault formula[14].

### Calculation of Inflammatory Markers

Inflammatory markers, such as the neutrophil-to-albumin ratio (NAR), neutrophil percent-to-albumin ratio (NPAR), C-reactive protein-albumin ratio (CRPALB), and systemic immune inflammation index (SII), were calculated using the relevant formulas. These markers provided valuable insights into the inflammatory status of the patients[12,15-20].

### Left Ventricular Ejection Fraction (LVEF) Measurement

LVEF was determined using the modified Simpson's method on both end-diastolic and end-systolic apical two and four-chamber views.

### Statistical Analysis

Statistical analyses were performed using SPSS 22.0 (IBM Corp, Armonk, NY, USA). The Kolmogorov-Smirnov test assessed the normal distribution of variables. Normally distributed data were presented as mean ± standard deviation (SD) and analyzed using Student's *t*-test. Non-normally distributed data were presented as medians (interquartile range) and analyzed using the Mann-Whitney U test. Binary variables were expressed as percentages and analyzed using the Chi-square test. Pearson's coefficient described parameter correlations among themselves and with SS. Univariate analysis and multivariate logistic regression identified intermediate-high SS risk factors. The Receiver Operating Characteristic (ROC) curve and Area Under the Curve (AUC) assessed NAR's discrimination performance. The optimal cutoff value was determined from the point of maximal sensitivity plus specificity. Results were evaluated within a 95% confidence interval (CI), with statistical significance set at $p < 0.05$.

## Results

The study cohort consisted of 211 patients diagnosed with non-ST segment elevation myocardial infarction (NSTEMI), with a mean age of 64.5 ± 11.2 years. Among these individuals, 77 (36.5%) were female, 117 (55.5%) had hypertension (HT), 93 (44.1%) had diabetes mellitus (DM), 75 (35.5%) had dyslipidemia, and 88 (41.7%) were active smokers. The mean Syntax Score (SS) for the entire cohort was 15.22 ± 10.45, with 44 (20.8%) patients categorized as having intermediate-high SS (SS>22).

Patients with intermediate-high SS were notably older [70.18+8.58 *vs.* 63.02+11.38 ($p$<0.01)] and exhibited a higher number of DM patients compared to those with low SS (SS<22) [59.1% *vs.* 40.1% ($p$ = 0.027)]. An overview of the clinical, demographic, and angiographic characteristics of the study cohort is shown in Table I.

The intermediate-high SS group demonstrated elevated serum C-reactive protein (CRP) levels ($p$<0.001) and neutrophil counts ($p$<0.001). Moreover, patients with intermediate-high SS had significantly higher NAR [20.86±5.38 *vs.* 16.41±6.30 ($p$<0.001)], NPAR [188.71±28.84 *vs.* 163.07±33.08 ($p$<0.001)], SII [1160.00±576.35 *vs.* 911.77±619.41 ($p$ = 0.017)], and CRPALB [21.30+9.54 *vs.* 15.90±7.62 ($p$<0.001)] values when contrasted with the low SS group (Table II).

Correlation analysis unveiled a significant correlation between NAR and SS (r: .416, $p$<0.01) (Figure 2).

To determine the independent predictors of intermediate high SS, we performed multivariable logistic regression analysis by using variables that showed statistically significant associations in the univariate analysis, except for the angiographic parameters. As we found a perfect correlation between NAR and NPAR, we developed two separate multivariate analysis models that included NAR (model 1) and NPAR (model 2) separately. Model 1 multivariate analysis demon-

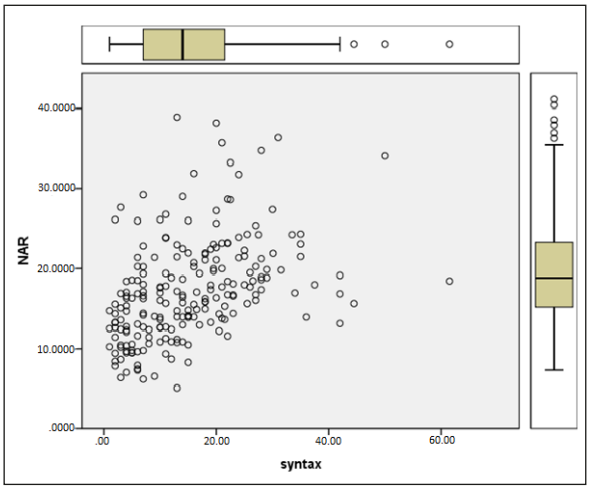


**Figure 2.** Correlation analysis of NAR with the SS.

**Table I.** Demographic, clinical, and angiographic parameters of the study population grouped by synergy between percutaneous coronary intervention with taxus and cardiac surgery score.

| Parameters | Low Syntax (<22) (167) | Intermediate-High Syntax (>22) (44) | *p*-value |
|---|---|---|---|
| **Clinical Characteristics** | | | |
| LVEF (%) | 54.60 ± 6.57 | 53.14 ± 6.82 | 0.194 |
| GFR (mL/min/1.73 m²) | 89.34 ± 14.69 | 85.98 ± 13.60 | 0.171 |
| Age (years) | 63.02 ± 11.38 | 70.18 ± 8.58 | <0.001 |
| Sex (female) [n (%)] | 59 (35.3%) | 18 (40.9%) | 0.488 |
| BMI (kg/m²) | 25.80 ± 3.37 | 25.42 ± 4.19 | 0.535 |
| Hypertension [n (%)] | 89 (53.3%) | 28 (63.6%) | 0.237 |
| Diabetes Mellitus [n (%)] | 67 (40.1%) | 26 (59.1%) | 0.027 |
| Dyslipidemia [n (%)] | 58 (34.9%) | 17 (38.6%) | 0.724 |
| Smoking [n (%)] | 75 (44.9%) | 13 (29.5%) | 0.085 |
| **Angiographic Characteristics** | | | |
| LMCA Disease [n (%)] | 2 (1.2%) | 9 (20.5%) | <0.001 |
| TVD [n (%)] | 35 (21.0%) | 32 (72.7%) | <0.001 |
| Bifurcation [n (%)] | 36 (21.6%) | 33 (75.0%) | <0.001 |
| CTO [n (%)] | 16 (9.6%) | 23 (52.3%) | <0.001 |
| Lesion Length >20 mm [n (%)] | 104 (62.3%) | 40 (90.9%) | <0.001 |
| Severe Tortuosity [n (%)] | 32 (19.2%) | 31 (70.5%) | <0.001 |
| Heavy Calcification [n (%)] | 63 (37.7%) | 39 (88.6%) | <0.001 |
| Thrombus [n (%)] | 81 (48.8%) | 27 (61.4%) | 0.175 |
| SS | 11.13 ± 6.39 | 30.74 ± 7.98 | <0.001 |

CTO, Chronic Total Occlusion; GFR, Glomerular Filtration Rate; BMI, Body Mass Index; LMCA, left main coronary artery; LVEF, left ventricular ejection fraction; SS, Synergy Between Percutaneous Coronary Intervention with Taxus and cardiac surgery score; TVD, three-vessel disease.

**Table II.** Laboratory parameters of study population grouped by synergy between percutaneous coronary intervention with taxus and cardiac surgery score.

| Parameters | Low Syntax (<22) (167) | Intermediate-High Syntax (>22) (44) | *p*-value |
|---|---|---|---|
| Urea (mg/dL) | 37.52 ± 23.77 | 38.25 ± 12.70 | 0.843 |
| Creatinine (mg/dL) | 0.82 ± 0.17 | 0.78 ± 0.16 | 0.165 |
| Glucose (mg/dL) | 151.90 ± 66.69 | 168.05 ± 69.14 | 0.158 |
| Troponin (ng/L) | 267.52 ± 160.58 | 257.20 ± 142.31 | 0.698 |
| TC (mg/dL) | 190.23 ± 44.95 | 186.61 ± 37.48 | 0.624 |
| LDL-C (mg/dL) | 118.85 ± 40.50 | 122.61 ± 34.77 | 0.573 |
| HDL-C (mg/dL) | 43.50 ± 9.89 | 45.92 ± 12.38 | 0.175 |
| Triglycerides (mg/dL) | 172.50 ± 94.49 | 144.64 ± 72.50 | 0.070 |
| Albumin (g/L) | 40.84 ± 3.65 | 40.36 ± 4.30 | 0.455 |
| CRP (mg/L) | 6.41 ± 2.96 | 8.54 ± 3.80 | <0.001 |
| WBC ($10^9$/L) | 9.85 ± 2.57 | 11.08 ± 2.23 | 0.004 |
| Neutrophil ($10^9$/L) | 6.65 ± 2.49 | 8.34 ± 1.98 | <0.001 |
| Neutrophil percent (%) | 66.03 ± 11.79 | 75.29 ± 7.58 | <0.001 |
| Monocyte ($10^9$/L) | 0.79 ± 0.50 | 0.76 ± 0.26 | 0.656 |
| Lymphocyte ($10^9$/L) | 2.27 ± 1.10 | 1.79 ± 0.77 | 0.007 |
| Lymphocyte percent (%) | 23.12 ± 9.73 | 16.12 ± 6.38 | <0.001 |
| Platelet ($10^9$/L) | 253.81 ± 64.78 | 208.98 ± 53.63 | <0.001 |
| Hemoglobin (g/dL) | 14.07 ± 1.56 | 13.80 ± 1.26 | 0.290 |
| NAR | 16.41 ± 6.30 | 20.86 ± 5.38 | <0.001 |
| NPAR | 163.07 ± 33.08 | 188.71 ± 28.84 | <0.001 |
| SII | 911.77 ± 619.41 | 1160.00 ± 576.35 | 0.017 |
| CRPALB | 15.90 ± 7.62 | 21.30 ± 9.54 | <0.001 |

CRPALB: C-reactive protein-to-albumin ratio, CRP: C-reactive protein, HDL-C: High-density lipoprotein cholesterol, LDL-C: Low-density lipoprotein cholesterol, NAR: Neutrophil-to-albumin ratio, TC: Total cholesterol, SII: Systemic immune inflammatory index, NPAR: Neutrophil percent-to-albumin ratio.

strated that higher NAR values [odds ratio (OR): 1.108; 95% CI: 1.035-1.186; $p$=0.003], elevated CRPALB values (OR: 1.071; 95% CI: 1.023-1.122; $p$ = 0.004), and advanced age (OR: 1.067; 95% CI: 1.027-1.109; $p$ = 0.001) were independent predictors of intermediate-high SS. Elsewhere, model 2 multivariate analysis revealed that higher NPAR values (OR: 1.022; 95% CI: 1.006-1.038; $p$=0.006), elevated CRPALB values (OR: 1.070; 95% CI: 1.022-1.120; $p$ = 0.004), and advanced age (OR: 1.053; 95% CI: 1.014-1.095; $p$ = 0.008) were independent predictors of intermediate-high SS (Table III). Owing to multicollinearity, CRP, WBC, lenfosit, and neutrophil counts were not included in the regression analysis.

Comparing the Receiver Operating Characteristic (ROC) curves, the area under the curve (AUC) for NAR [AUC: .736 (CI; .668-.805)] demonstrated significant differentiation from both CRPALB [AUC: .673 (CI; .582-.765)]; $p$<0.001) and SII [AUC: .660 (CI; .577-.743)] as well as NPAR [AUC: .717 (CI; .641-.793)]; $p$<0.001) (Figure 3). To assess the additional predictive capabilities of NAR for CAD severity, a ROC analysis was performed, yielding a NAR cutoff value of 16.58 with 84% sensitivity and 59% specificity.

## Discussion

This study shows that NAR is superior to CRPALB and SII in predicting the extent and severity of Coronary Artery Disease (CAD) in patients diagnosed with NSTEMI.

The well-documented role of neutrophils in atherosclerosis development and their contribution to acute coronary syndromes and heart failure pathogenesis underscore the significance of our investigation[21]. Neutrophils, as integral components of the white blood cell population, play a pivotal role in orchestrating inflammatory responses[22-24]. While platelets' involvement in CAD development is recognized, several inflammatory markers, such as Neutrophil-Lymphocyte Ratio (NLR), Platelet-Lymphocyte Ratio (PLR), SII, and CRPALB, have been proposed to correlate with CAD[3,4,7,19,24,25].

Recent research[18] has suggested that SII may be a more robust predictor of inflammatory events than single- or dual-component markers. It has demonstrated enhanced predictive value over other markers for cardiovascular events[19]. For instance, Candemir et al[20] found SII to be associated with atherosclerosis and possibly superior to NLR and PLR in predicting coronary artery lesion severity. In line with these findings,

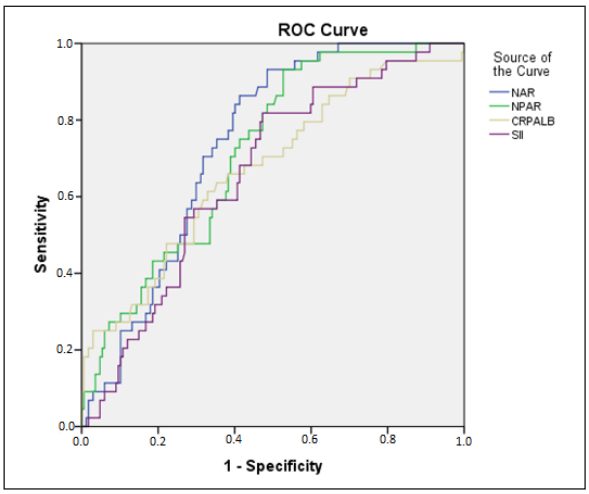


**Figure 3.** Receiver operating characteristic (ROC) curves of the C-reactive protein-to-Albumin ratio (CRPALB), SII, Neutrophil percent -to-Albumin ratio (NPAR) and Neutrophil-to-Albumin ratio (NAR) for prediction the intermediate-high Synergy Between Percutaneous Coronary Intervention with Taxus and cardiac surgery score. CI, confidence interval.

**Table III.** Factors independently associated with intermediate-high SS score in univariate and multivariate logistic regression analysis models.

| | Univariate | | Model 1 Multivariate | | Model 2 Multivariate | |
|---|---|---|---|---|---|---|
| Variables | OR (95% CI) | $p$-value | OR (95% CI) | $p$-value | OR (95% CI) | $p$-value |
| CRPALB | 1.082 (1.038-1.129) | <0.001 | 1.071 (1.023-1.122) | 0.004 | 1.070 (1.022-1.120) | 0.004 |
| AGE | 1.063 (1.029-1.099) | <0.001 | 1.067 (1.027-1.109) | 0.001 | 1.053 (1.014-1.095) | 0.008 |
| DM | 0.464 (0.236-0.912) | 0.026 | 0.570 (0.264-1.230) | 0.152 | 0.607 (0.281-1.311) | 0.204 |
| NAR | 1.110 (1.053-1.171) | <0.001 | 1.108 (1.035-1.186) | 0.003 | - | - |
| NPAR | 1.026 (1.014-1.039) | <0.001 | - | - | 1.022 (1.006-1.038) | 0.006 |
| SII | 1.001 (1.000-1.001) | 0.020 | 1.000 (0.999-1.001) | 0.604 | 1.000 (0.999-1.001) | 0.960 |

CRPALB: C-reactive protein to albumin ratio, NAR: Neutrophil-to-albumin ratio, NPAR: Neutrophil percent-to-albumin ratio, SII: Systemic immune inflammatory index, DM: Diabetes Mellitus.

our study demonstrated a significant correlation between SII and a higher Syntax Score.

Existing evidence[26-28] links reduced plasma albumin levels with atherosclerosis, as low serum albumin levels have been associated with CAD development and adverse clinical outcomes. C-Reactive Protein (CRP), a systemic inflammation component, actively participates in atherogenesis[29]. CRP levels have been independently associated with CAD extent in acute coronary syndrome (ACS) patients[30]. Moreover, the novel inflammatory marker CRPALB has exhibited enhanced sensitivity and specificity in predicting various non-cardiac conditions compared to individual CRP and albumin values[15-17]. Previous research[7] has also demonstrated CRPALB's superior predictive value for CAD severity in NSTEMI patients compared to CRP and albumin alone. Consistent with these findings, our study highlighted a significant association between elevated CRPALB values and CAD severity as determined by the Syntax Score in NSTEMI patients.

Cui et al[31] found that NPAR was independently correlated with in-hospital mortality in patients with STEMI. Dai et al[32] showed that NPAR is a good indicator for predicting free wall rupture. Similar to the above studies, in our study, NPAR was higher in moderate-to-high SS patients, indicating a higher likelihood of complications. Also, Yu et al[33], Sun et al[34], Lin et al[35], and Hu et al[36] have independently established the significance of NPAR in predicting mortality in various critical and cardiac patient populations. In our study, NPAR was higher in moderate-high SS patients, consistent with the aforementioned studies.

Basyigit and Coteli[37] showed that a higher neutrophil/HDL-C ratio was associated with moderate or severe coronary artery stenosis. However, our investigation represents the first exploration of the relationship between CAD severity and NAR. We uncovered a significant correlation between elevated NAR values and CAD severity, as determined by the Syntax Score in NSTEMI patients. NAR emerged as an independent indicator of CAD severity. Remarkably, among the variables displaying significant correlations with CAD severity, namely CRPALB, Diabetes Mellitus (DM), age, NAR, and SII, only NAR, NPAR, CRPALB, and age remained as independent predictors. However, ROC curve analysis showed NAR as superior to NPAR, CRPALB, SII, and age in prognosticating CAD severity as determined by the Syntax Score in NSTEMI patients.

In summary, our findings emphasize the enhanced predictive value of NAR over CRPALB and SII in assessing the extent and severity of CAD in NSTEMI patients. Predicting the severity of coronary artery disease before coronary intervention in patients presenting with NSTEMI is of tremendous importance for the operator. This aids in procedure planning and may contribute to lower mortality rates in NSTEMI patients, as it enables the operator to predict potential complications and take necessary precautions beforehand. By revealing NAR's robust association and independent predictive capability for CAD severity, this study introduces a potentially valuable biomarker that can aid in clinical decision-making for this patient population.

### Limitations

Our study, while contributing meaningful insights, bears certain limitations that warrant consideration. Firstly, it is essential to acknowledge the retrospective and single-center nature of our investigation, which might introduce bias and limit the generalizability of our findings. Furthermore, the study's sample size, although informative, is not extensive, potentially affecting the robustness of our conclusions. Additionally, it is worth noting that factors, such as stress and nutritional status, could potentially impact acute phase reactant levels, yet these aspects were not assessed within our study framework.

Future studies conducted with larger, multicenter cohorts and prospective designs could provide a more comprehensive understanding of NAR's utility as a predictor of atherosclerosis severity. Exploring potential confounding factors and considering a broader range of clinical parameters would offer a more nuanced interpretation of NAR's significance in cardiovascular risk assessment.

## Conclusions

In this investigation, we have demonstrated a significant association between the neutrophil-to-albumin ratio (NAR) and intermediate to high Syntax Scores, suggesting its potential as a parameter for predicting the severity and extent of atherosclerosis in patients with non-ST segment elevation myocardial infarction (NSTEMI). This finding underscores the

potential role of NAR in cardiovascular assessment, offering a means to identify individuals who could benefit from more aggressive therapeutic strategies and closer clinical monitoring. The incorporation of NAR into the cardiovascular evaluation toolkit may be promising in enhancing patient care and risk management.

### Ethics Approval
This study was approved by the Fırat University Ethics Committee (Ethics Committee acceptance date and number: 16.06.2023-16817) in accordance with the International Code of Ethics and the Declaration of Helsinki.

### Informed Consent
Not applicable.

### Availability of Data and Materials
All necessary data can be obtained from the corresponding author.

### Conflict of Interest
The authors declare no potential conflicts of interest regarding the research, authorship, and/or publication of this article.

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