

Relationship Between SYNTAX Score and New Inflammatory Marker (The Aggregate Index of Systemic Inflammation) in Patients Diagnosed with Non-ST-Segment Elevation Myocardial Infarction

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ABSTRACT

Introduction: Coronary artery disease is a growing global concern, and inflammation plays a significant role in its development. Inflammation is associated with plaque formation, rupture, endothelial dysfunction, platelet aggregation, and thrombus formation. Non-ST-segment elevation myocardial infarction (NSTEMI) accounts for 75% of acute coronary syndrome cases. The inflammatory response tends to increase prior to acute myocardial infarction (AMI) and becomes highly active after AMI. The Aggregate Index of Systemic Inflammation (AISI), a composite of multiple inflammatory markers, is a significant predictor of adverse outcomes in NSTEMI patients and underscores the role of inflammation in AMI. However, existing data do not indicate a correlation between the SYNTAX score (SXscore) and AISI in patients with NSTEMI.

Methods: This study included 226 NSTEMI patients who underwent coronary angiography between January 2022 and December 2023. The SXscore is categorized into low (≤ 22) and intermediate-high (> 22) groups. The AISI was used to assess systemic inflammation in whole blood.

Results: The study included 153 participants with an SXscore ≤ 22 and 73 with an SXscore > 22 . Laboratory analysis indicated significantly higher AISI levels in the cohort with an SXscore > 22 ($p=0.027$). Multivariable logistic regression showed that age ($p=0.010$) and AISI levels ($p=0.017$) independently predicted the intermediate-high SXscore and the group with SXscore > 22 , respectively.

Conclusion: The AISI, a biomarker, can identify patients with intermediate-to-high SXscore, aiding early risk assessment and triage decisions. Patients with high values require aggressive treatment.

Keywords: Non-ST-segment elevation myocardial infarction, the Aggregate Index of Systemic Inflammation, SYNTAX score

Introduction

Coronary artery disease (CAD) is a major cause of morbidity and mortality worldwide, and its prevalence is steadily rising, making it an increasingly common cardiovascular condition (1,2). Although atherosclerotic plaques in the coronary arteries are primarily linked to lipid accumulation (1), recent studies highlight the importance of inflammation, as evidenced by markers such as the systemic immune-inflammation index (SII) and the neutrophil-lymphocyte ratio (NLR). This study underscores the central role of inflammation in the initiation and progression of CAD (3-5). Inflammatory responses are deeply linked not only to plaque formation but also to endothelial dysfunction and thrombus formation (6). Non-ST-segment elevation myocardial infarction (NSTEMI) is a form of acute coronary syndrome (ACS), representing about 75% of ACS cases (1).

Despite medical advances, ACS remains a leading cause of illness and death worldwide. An inflammatory response begins before the onset of acute myocardial infarction (AMI) and becomes excessively active afterward. This highlights, to some extent, the inflammatory aspect of the condition (7). Early detection of high-risk individuals in this patient group is essential to improve prognosis. Recent efforts have focused on identifying new markers to better distinguish high-risk patients. Numerous scientific studies have demonstrated that inflammatory processes influence the mechanisms involved in the development and complications of atherosclerotic plaques, ultimately contributing to the onset of ACS. Consequently, novel indices, such as the Aggregate Index of Systemic Inflammation (AISI), SII, and the Systemic Inflammatory Response Index, have been developed to quantify the equilibrium between systemic inflammation and the immune response and to serve



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as objective markers (8). There is a broad consensus that composite inflammation indices, which integrate multiple markers, offer a more comprehensive perspective on inflammation than single indicators.

In this context, AISI was introduced in 2018 (9). Many NSTEMI patients have multivessel disease, and the SYNTAX score (SXscore) is crucial in selecting the optimal revascularization strategy (10).

Currently, no data demonstrate a link between AISI and CAD severity in NSTEMI patients. It is hypothesized that in these patients AISI correlates with more advanced stages of CAD, as reflected by the SXscore.

Methods

Study Population

This retrospective study calculated the minimum sample size required to detect an effect size of 0.2 with 90% statistical power. The sample size of the study, n=226, corresponds to the number of consecutively enrolled patients diagnosed with NSTEMI according to the European Society of Cardiology (ESC) Guidelines (11) who provided informed consent and underwent coronary angiography between January 2022 and December 2023. Specifically, the SYNTAX ≤22 group had a mean age of 62.4±10.2 years and 69.9% were male, while the SYNTAX >22 group had a mean

age of 66.6±12.2 years and 72.6% were male. The Non-Interventional Clinical Research Ethics Committee of Zonguldak Bülent Ecevit University approved the study (approval number: 2025/14, date: 09.07.2025), and the study was conducted in accordance with the Declaration of Helsinki. Patients were excluded if they had conditions that could influence systemic inflammatory markers, including chronic inflammatory or autoimmune diseases; active infection or sepsis; hematologic disorders (such as anemia or leukopenia); active or prior malignancy; severe renal dysfunction; liver dysfunction; recent major surgery or trauma; recent vaccination (within one month); recent blood transfusion or antibiotic use (within three months); glucocorticoid therapy (within two months); myocardial infarction with non-obstructive coronary arteries; or missing laboratory data. Figure 1 presents the flowchart of the study’s exclusion criteria.

Clinical and Laboratory Data

The patient demographic data, as well as the clinical, laboratory, and angiographic data, were retrieved from the institutional database.

The NSTEMI diagnosis was made according to the ESC guidelines for the treatment of ACS. For this diagnosis, at least one of the following criteria must be present, particularly when accompanied by elevated troponin

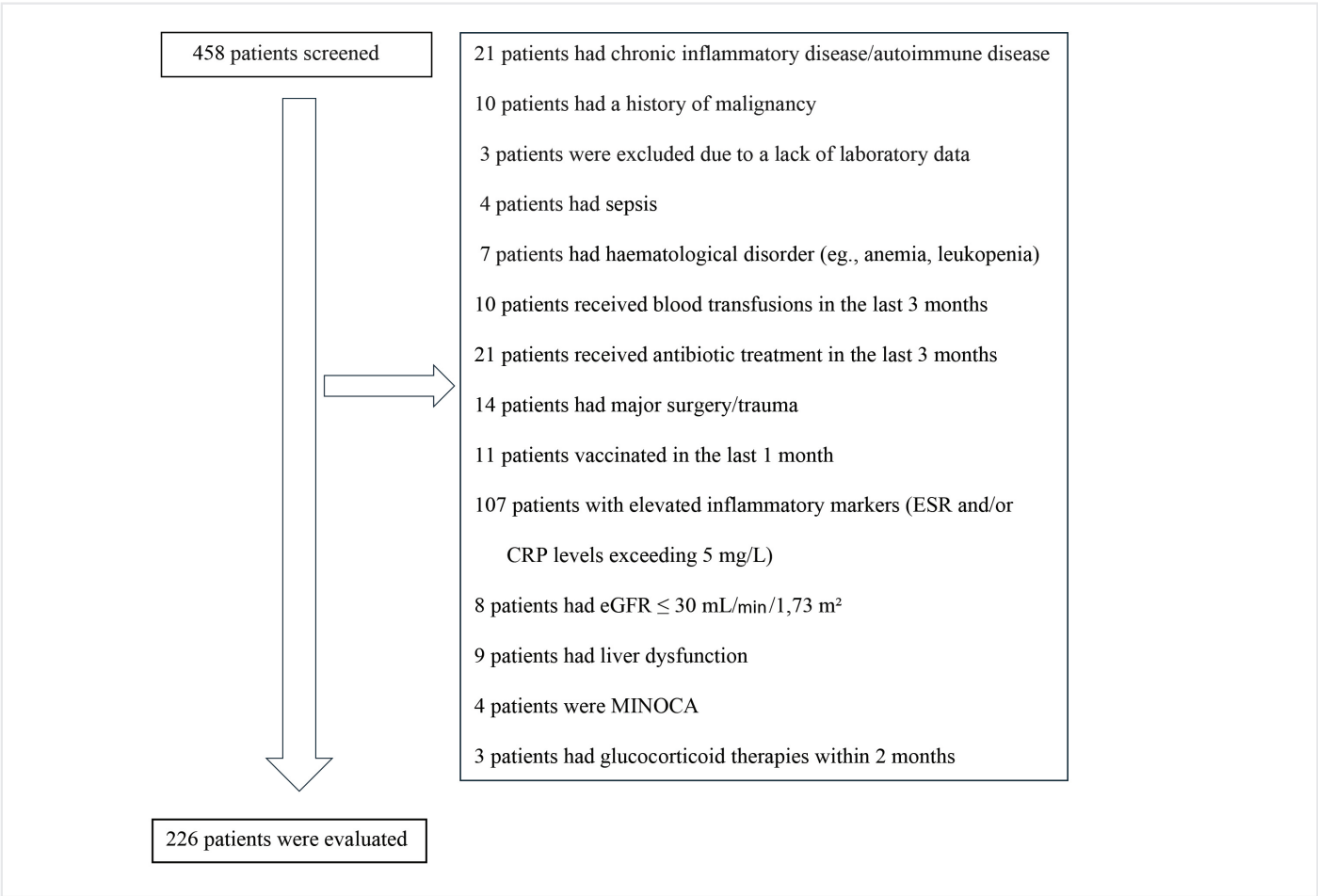


Figure 1. The exclusion criteria for the study population
ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, eGFR: estimated glomerular filtration rate, MINOCA: Myocardial infarction with non-obstructive coronary arteries

levels: symptoms suggestive of ischemia, particularly of recent onset, presence of pathological Q waves on electrocardiogram, evidence of new loss of viable myocardium on imaging studies, detection of segmental abnormalities in cardiac wall motion, or detection of coronary artery thrombus during angiography (11).

Smokers are people who have been smoking regularly for the past six months. Hypertension (HT) is defined as a systolic blood pressure of at least 140 mmHg and/or a diastolic blood pressure of at least 90 mmHg, or a prior diagnosis of HT requiring treatment (12). Diabetes mellitus (DM) was defined as a fasting plasma glucose level ≥ 126 mg/dL or the use of antidiabetic medication in individuals with a history of DM (13). Hyperlipidemia is characterized by a total cholesterol level exceeding 200 mg/dL, a low-density lipoprotein cholesterol level exceeding 130 mg/dL, or a documented history of hypercholesterolemia that was diagnosed and managed (14). Peripheral arterial disease is characterized by occlusion of one or more peripheral arteries, typically due to atherosclerosis, thrombosis, embolism, scoliosis, or fibromuscular dysplasia (15).

All metabolic and basic blood parameters were evaluated, and a complete blood count was measured in peripheral venous blood samples obtained at the time of NSTEMI diagnosis. The lipid panel and fasting plasma glucose levels were determined from the first blood samples obtained after at least 12 hours of fasting during hospitalization. Laboratory parameters, including routine blood tests, were analyzed at our hospital.

AISI was determined by multiplying the neutrophil, platelet, and monocyte counts and dividing the product by the lymphocyte count, using laboratory data (9).

Assessment of Coronary Angiography and Calculation of SYNTAX Score

Patients diagnosed with NSTEMI underwent coronary angiography, performed by experienced interventional cardiologists using the Seldinger technique, within the first 24 hours of hospital admission, and the angiographic results were evaluated. Images of the left anterior descending, left circumflex, and right coronary arteries were assessed from various angiographic angles.

Decisions on revascularization strategies and medical follow-up were left to physicians' discretion. When percutaneous coronary intervention (PCI) was indicated, it was performed using conventional techniques during the same session. Before angiography, all patients received a 300 mg loading dose of acetylsalicylic acid, a P2Y₁₂ inhibitor, and a standard dose of unfractionated heparin (50-70 U/kg).

An independent cardiologist, unaware of the patients' clinical characteristics, determined the SXscore. The SXscore was used to assess the anatomical severity of coronary narrowing, focusing on coronary vessels with diameters exceeding 1.5 mm and on segments with over 50% narrowing (<http://www.SYNTAXscore.com>) (16,17). The variability within observers in defining the SXscore was 1%, while the variability between observers was 2%. In our study, the SXscore was categorized into two groups-low (≤ 22) and intermediate-high (>22)- and subsequently analyzed.

Statistical Analysis

Statistical analyses were conducted using SPSS software version 21.0 for Windows (SPSS Inc., Chicago, Illinois, USA). Categorical variables are expressed as percentages, and continuous variables are shown as mean \pm standard deviation. The independent samples t-test or the Mann-Whitney U test, as appropriate, was used to analyze continuous variables, and the χ^2 test was applied to categorical variables. Variables with significant univariable regression coefficients for an intermediate-to-high SXscore were included in a multivariable regression analysis to identify independent predictors of an intermediate-to-high SXscore. Receiver operating characteristic (ROC) analysis was used to determine the cut-off levels of AISI for predicting an intermediate-to-high SXscore. The statistical significance level was set at $p < 0.05$, and 95% confidence intervals (CIs) were calculated.

Results

Baseline Characteristics

All study participants were included: 153 (67.70%) had SXscore ≤ 22 and 73 (32.30%) had SXscore >22 . No statistically significant differences were observed between the two groups with respect to sex, body mass index (BMI), comorbidities, or laboratory values (all $p > 0.05$). However, the prevalence of DM was higher in the SXscore >22 group than in the SXscore ≤ 22 group [47 (64.3%) vs. 72 (47.1%); $p = 0.037$]. Similarly, the mean age was higher in the SXscore >22 group (66.6 ± 12.2 years vs. 62.4 ± 10.2 years, $p = 0.020$). Patients with a SXscore >22 had significantly higher AISI values than those with a SXscore ≤ 22 (482.9 ± 233.8 vs. 416.0 ± 198.6 ; $p = 0.027$) (Table 1).

Predictors of SYNTAX Score >22 Group

Multivariable logistic regression analysis was conducted to identify independent predictors of SXscore in NSTEMI patients. Logistic regression analysis identified age ($p = 0.010$) as an independent predictor of an intermediate-high SXscore. Additionally, AISI levels were found to be independent predictors of membership in the SXscore >22 group [odds ratio (OR): 1.002; 95% CI: 1.000-1.003; $p = 0.017$]. In the multifaceted model, The probability ratio for AISI indicated that each one-unit increase in AISI was associated with a greater probability of an intermediate-to-high SXscore. This finding supports the independent prognostic value of AISI beyond traditional cardiovascular risk factors and established inflammatory markers (Table 2).

ROC Analysis for AISI

ROC curve analysis was performed to evaluate AISI's ability to predict which patients have an SXscore >22 . The study demonstrated that AISI had significant discriminative ability, with an area under the curve (AUC) that indicated good predictive performance in identifying complex coronary anatomy in NSTEMI patients. The AUC of the AISI for predicting the occurrence of the SXscore in patients was 0.578 (95% CI: 0.497–0.659; $p = 0.047$). The cut-off value of the AISI for predicting the SXscore was 398.6, with sensitivity and specificity of 0.534 and 0.536, respectively (Figure 2).

Table 1. Demographic features and laboratory findings of patients by SYNTAX score groups

Variables	SYNTAX score ≤22 (n=153)	SYNTAX score >22 (n=73)	p value
Age, years	62.4±10.2	66.6±12.2	0.020
Male, gender	107 (69.9)	53 (72.6)	0.690
BMI (kg/m ²)	29.30±3.36	29.36±3.41	0.902
Systolic BP (mmHg)	135±16.9	133±15.9	0.377
Diastolic BP (mmHg)	79.4±10.9	79.2±9.3	0.844
Previous history			
Smoking	89 (58.2)	35 (47.9)	0.149
Hypertension	100 (65.4)	48 (65.8)	0.954
Diabetes mellitus	72 (47.1)	47 (64.3)	0.037
Hyperlipidemia	74 (48.4)	37 (50.6)	0.744
PAD	27 (17.6)	11 (15.1)	0.628
Laboratory values			
White blood cell count (10 ⁹ /L)	9.0±2.5	8.8±2.3	0.591
Hemoglobin (g/L)	13.5±1.9	13.2±1.5	0.176
Creatinine (mg/dL)	0.90±0.20	0.95±0.24	0.130
LDL-C (mg/dL)	117.8±40.9	116.6±40.1	0.816
HDL-C (mg/dL)	40.3±10.8	38.7±9.7	0.202
Total cholesterol (mg/dL)	191.4±50.2	186.4±43.9	0.401
Triglyceride (mg/dL)	167.2±90.1	163.7±90.9	0.789
Glucose (mg/dL)	140.3±66.2	151.3±70.0	0.297
AISI	416±198.6	482.9±233.8	0.027

Data presented as mean ± standard deviation or number (%). BMI: Body mass index, BP: Blood pressure, PAD: Peripheral arterial disease, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, AISI: Aggregate Index of Systemic Inflammation

Table 2. Univariate and multivariate logistic regression analysis identifying the independent predictors of the presence of a SYNTAX score ≤22

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p	OR (95% CI)	p
Diabetes mellitus	1.156 (0.542-2.020)	0.618		
Age	1.032 (1.008-1.056)	0.016	1.035 (1.008-1.066)	0.010
AISI	1.001 (1.000-1.003)	0.028	1.002 (1.000-1.003)	0.017

OR: Odds ratio, CI: Confidence interval, AISI: Aggregate Index of Systemic Inflammation

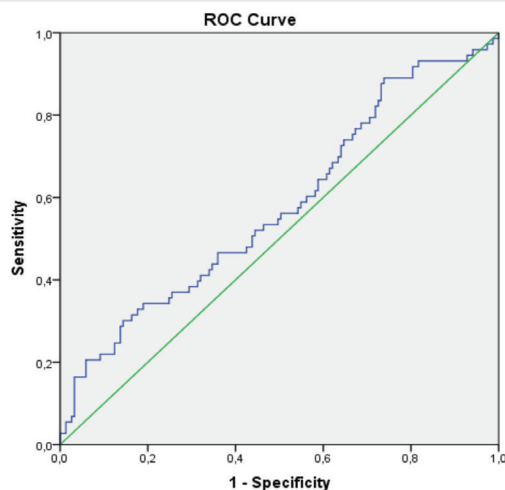


Figure 2. ROC curve for AISI value as a predictor of SYNTAX score >22
ROC: Receiver operating characteristic, AISI: Aggregate Index of Systemic Inflammation

Discussion

In our cohort, patients with NSTEMI were divided into two groups based on their Sxscore: those with scores >22 were considered high-risk according to clinical guidelines (16). Patients with medium-high Sxscore had high AISI values, suggesting a possible link between systemic inflammation and CAD complexity. This finding is consistent with previous studies suggesting that systemic inflammation plays a significant role in the initiation, progression, and destabilisation of atherosclerotic plaques, which can lead to ACS (18). AISI has demonstrated clinically meaningful sensitivity and specificity for predicting moderate-to-high Sxscore, highlighting its potential as a screening tool in clinical practice. Methods for assessing NSTEMI risk include clinical and angiographic data, as well as cardiac biomarkers. NSTEMI is associated with complex mechanisms involving systemic and local inflammatory processes that contribute to the progression of atherosclerosis and increase the risk of complications by triggering acute coronary thrombosis (19). Risk assessment tools such as Myocardial Infarction Triage and Intervention and Global Registry of Acute Coronary Events do not include inflammatory markers (20).

Current evidence suggests that inflammatory indices may enhance the prognostic value of these validated risk scores (21). In recent years, interest in inflammation and related markers has increased significantly, making it a fundamental topic in the field (22). Several studies emphasize the significance of inflammatory markers and indicators such as NLR and SII, highlighting the vital role of inflammation in the progression of CAD (23-25). The newly developed combined index, AISI, is a measure of systemic inflammation that evaluates neutrophils, lymphocytes, monocytes, and platelets (21). In patients presenting with ACS or AISI, and in those undergoing PCI, these factors have also been recognized as independent predictors of adverse clinical outcomes (23). Jiang et al. (19) have shown that elevated AISI levels in AMI patients are strongly associated with higher risks of major adverse cardiovascular and cerebrovascular events, including all-cause mortality. The study involving more than 1,044 patients showed that those in the highest AISI quartile had a 4.64-fold higher risk of all-cause mortality than those in the lowest quartile (10). Wang et al. (26) examined the link between AISI and the slow coronary flow phenomenon (SCFP) in patients with ischemia but no obstructive CAD. They found that AISI independently predicts SCFP; an optimal cut-off of 264.1 yielded sensitivity and specificity of 64.4% each. This study demonstrates the effectiveness of AISI in detecting coronary microvascular dysfunction in patients, which may represent an early stage of CAD (26). AISI offers various advantages as an additional risk classification tool. It can be obtained from standard complete blood count parameters, which are readily available in most clinical settings and do not incur additional costs or require specialized equipment. It can be detected immediately upon hospital admission, facilitating early risk assessment and triage decisions. The combined structure of AISI provides a more comprehensive assessment of inflammatory status than do individual blood cell counts or traditional inflammatory markers. The SXscore is an essential tool for evaluating coronary anatomical complexity, guiding treatment decisions, and directing revascularization strategies, but it requires invasive coronary angiography (11). The relationship between inflammatory markers and the SXscore was also examined using other composite indices. Cetinkaya et al. (21) examined the association between the pan-immuno-inflammatory value (PIV) and the severity of CAD in patients with NSTEMI. Their findings indicated that a high PIV independently predicted a higher SXscore (OR: 1.003) and correlated strongly with it (r : 0.68). Although PIV shows promise, the AISI might be advantageous because of its ease of calculation and broader applicability across different cardiovascular conditions (21). Konuş et al. (27) evaluated the advanced lung cancer inflammation index (ALI) in patients with NSTEMI and its relationship with the SXscore. Interestingly, they found an inverse relationship: lower ALI values are associated with higher SXscore. The ALI calculation incorporates the neutrophil-to-lymphocyte ratio, BMI, and serum albumin, which may explain its differing relationship with AISI (27). This underscores the importance of understanding how inflammatory indices are constructed and calculated when evaluating their clinical relevance. Specifically, inflammatory pathways are triggered by neutrophils, monocytes, platelets, and the key cytokines they produce. Additionally, circulating lymphocytes are believed to participate in certain inflammatory pathways.

The findings indicate that patients with more extensive and complex coronary atherosclerosis experience higher systemic inflammatory activation, which can accelerate disease progression and increase the risk of adverse events. AISI encompasses various cellular components of the inflammatory process and provides a more comprehensive assessment of inflammatory burden than individual biomarkers. The development of integrated risk assessment tools that combine clinical variables, traditional biomarkers, and new inflammatory indices, such as AISI, may enable more precise risk stratification and personalized treatment strategies. These tools can help identify patients who are most likely to benefit from aggressive medical treatment, early invasive procedures, or specific interventions. The AISI has been recognized as a promising biomarker for assessing CAD complexity in NSTEMI patients. Its strong correlation with the SXscore, together with its accessibility and cost-effectiveness, supports its potential for use in clinical settings. As our understanding of the inflammatory basis of CAD advances, biomarkers like AISI may become increasingly critical to personalized cardiovascular medicine and to improving patient outcomes.

Our results support recent studies showing a relationship between inflammatory markers and CAD severity. An advantage of this study is that the use of routine laboratory parameters to calculate the AISI enhances the clinical relevance of our results.

Study Limitations

The study's cross-sectional design prevents us from establishing a causal relationship between AISI and SXscore. Prospective studies are necessary to determine whether high AISI values indicate the development of complex coronary anatomy prior to, or as a consequence of, advanced atherosclerotic disease. In this study, the AISI parameters were not measured again, and the calculations were not redone. Our population might not include all NSTEMI patients, so validation in different cohorts is necessary to determine widely applicable cut-off values. The optimal cut-off for AISI may differ depending on population characteristics (age, gender, and ethnicity) and clinical context, including comorbidity levels. Although AISI's SXscore classification shows good predictive ability, its practical use ultimately relies on how well it predicts meaningful clinical outcomes. Future research should examine whether risk classification using AISI guidance leads to better patient outcomes, such as lower mortality rates, fewer recurrent cardiovascular events, and more efficient use of resources.

Conclusion

AISI, an advanced biomarker, has shown significant clinical potential for identifying patients with intermediate- to high SXscore. It can be calculated from routine blood count parameters at hospital admission, enabling early risk assessment and triage decisions without incurring additional costs or requiring specialized tests. Patients with high AISI values may benefit from aggressive medical treatment, closer monitoring, and potentially earlier invasive procedures. Conversely, those with lower AISI values may be suitable for conservative treatment. Identifying high-risk inflammatory phenotypes may enable personalized treatment strategies targeting both atherothrombotic and inflammatory factors

of CAD. AISI can also evaluate the effectiveness of anti-inflammatory therapy in patients. However, further validation is needed through prospective studies. Artificial intelligence methods can help create more comprehensive risk assessment tools.

Ethics

Ethics Committee Approval: The Non-Interventional Clinical Research Ethics Committee of Zonguldak Bülent Ecevit University approved the study (approval number: 2025/14, date: 09.07.2025).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions: Concept - N.E.G., İ.E.; Design - N.E.G., İ.E., U.K.; Data Collection or Processing - N.E.G., M.B.K., U.K.; Analysis or Interpretation - İ.E., M.B.K., U.K.; Literature Search - N.E.G., M.B.K., U.K.; Writing - N.E.G., M.B.K., U.K.

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