

The Atherogenic Index of Plasma as a Novel Marker of Critical Multivessel Disease in Non-ST-Elevation Myocardial Infarction

Non-ST Yükselmeli Miyokard Enfarktüsünde Kritik Çok Damar Hastalığının Yeni Bir Belirteci Olarak Plazma Aterojenik İndeksi

ABSTRACT

Objective: This study aimed to determine whether the atherogenic index of plasma (AIP) can predict critical multivessel coronary artery disease (MVD) in patients presenting with non-ST-segment elevation myocardial infarction (NSTEMI).

Method: In this retrospective analysis, patients diagnosed with NSTEMI who underwent coronary angiography between January and December 2024 were evaluated. Based on angiographic findings, patients were classified according to the number of major epicardial vessels with significant stenosis, and MVD was defined as critical involvement of all three major vessels. The AIP was calculated as log (triglyceride/high-density lipoprotein [HDL]-cholesterol). Multivariable logistic regression analysis was used to identify independent predictors of MVD, and receiver operating characteristic (ROC) curve analysis was performed to assess diagnostic accuracy.

Results: Of the 1,216 patients included in the study, 302 (24.8%) had MVD. Those with critical MVD had significantly higher AIP values than those without MVD (0.74 ± 0.28 vs. 0.59 ± 0.26 , $P < 0.001$). In multivariable analysis, AIP remained an independent determinant of MVD (odds ratio: 3.132, 95% confidence interval: 1.626–6.030, $P = 0.001$). Diabetes mellitus, higher hemoglobin A1c (HbA1c), and elevated low-density lipoprotein (LDL)-cholesterol levels were also independently associated with MVD. AIP demonstrated moderate discriminative ability for predicting MVD, with an area under the curve (AUC) of 0.689 and sensitivity and specificity of 65.6%.

Conclusion: AIP was independently associated with the presence of critical MVD in patients with NSTEMI. Given its simplicity, affordability, and accessibility, AIP may serve as a practical indicator of atherogenic burden and help identify patients who are more likely to have multivessel coronary involvement.

Keywords: Acute coronary syndrome, atherogenic index of plasma, multivessel coronary artery disease, non-ST-segment elevation myocardial infarction, predictors

ÖZET

Amaç: Bu çalışma, plazma aterojenik indeksi (AIP)'nin, non-ST-segment yükselmeli miyokard enfarktüsü (NSTEMI) tanısı alan hastalarda kritik çok damarlı koroner arter hastalığı (ÇDH) varlığını öngörmeye bir belirteç olarak kullanılıp kullanılamayacağını değerlendirmeyi amaçladı.

Yöntem: Bu retrospektif analizde, Ocak 2024 ile Aralık 2024 tarihleri arasında NSTEMI tanısı konulan ve koroner anjiyografi yapılan hastalar incelendi. Anjiyografik bulgulara göre hastalar, anlamlı darlık saptanan majör epikardiyal damar sayısına göre sınıflandırıldı ve ÇDH, üç ana epikardiyal damarın tamamında kritik darlık bulunması olarak tanımlandı. AIP, log (trigliserid/HDL-kolesterol) formülüyle hesaplandı. Çok değişkenli lojistik regresyon analizi, ÇDH'nin bağımsız belirleyicilerini saptamak için uygulandı. Ayrıca ROC eğrisi analizi, tanısız doğruluğu değerlendirmek amacıyla gerçekleştirildi.

Bulgular: Çalışmaya dâhil edilen 1.216 hastanın 302'sinde (%24,8) ÇDH saptandı. Kritik ÇDH'si bulunan hastaların AIP değerleri, ÇDH bulunmayanlara kıyasla anlamlı olarak daha yüksekti (0.74 ± 0.28 'e karşı 0.59 ± 0.26 , $P < 0.001$). Çok değişkenli analizde AIP, ÇDH'nin bağımsız bir belirleyicisi olarak kaldı (olasılık oranı: 3.132; %95 güven aralığı: 1.626–6.030; $P = 0.001$). Diyabetes mellitus, yüksek HbA1c ve artmış LDL kolesterol düzeyleri de ÇDH ile bağımsız olarak ilişkili bulundu. AIP, ÇDH'yi öngörmeye orta düzeyde ayırt edici bir yetenek göstermiş olup, AUC değeri 0.689 ve duyarlılık ile özgüllük oranları %65.6 olarak bulundu.

Sonuç: AIP, NSTEMI hastalarında kritik ÇDH varlığıyla bağımsız olarak ilişkili bulunmuştur. Basit, ekonomik ve kolay erişilebilir bir parametre olması nedeniyle AIP, aterojenik yükü yansıtan ve ÇDH olasılığı yüksek hastaların belirlenmesine yardımcı olabilecek pratik bir gösterge niteliği taşıyabilir.

Anahtar Kelimeler: Akut koroner sendrom, plazma aterojenik indeksi, çok damar koroner arter hastalığı, ST elevasyonsuz miyokard enfarktüsü, öngördürücüler

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Vedat Hekimsoy¹

Veysel Ozan Tanık¹

Kürşat Akbuğa¹

Alperen Taş²

Ali Sezgin¹

Çağatay Tunca¹

Erhan Saraçoğlu¹

Bülent Özlek³

¹Department of Cardiology, Ankara Etilik City Hospital, Ankara, Türkiye

²Department of Cardiology, Kırşehir Training and Research Hospital, Kırşehir, Türkiye

³Department of Cardiology, Muğla Sıtkı Koçman University, Faculty of Medicine, Muğla, Türkiye

Corresponding author:

Bülent Özlek

✉ bulent_ozlek@hotmail.com

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Acute coronary syndromes (ACS) remain a major global cause of mortality.¹ Recent epidemiological observations indicate a shift in ACS presentation patterns, with an increasing proportion of patients now being diagnosed with non–ST–segment elevation myocardial infarction (NSTEMI) rather than ST–segment elevation myocardial infarction (STEMI).^{2–4} Individuals with NSTEMI are typically older, have multiple comorbidities, and more frequently present with severe multivessel coronary artery disease (MVD)—a condition linked to poorer prognoses and a greater likelihood of recurrent ischemic events.⁵ Therefore, early identification of NSTEMI patients who are more likely to have MVD is clinically relevant, as the presence of MVD reflects a higher anatomical disease burden.⁶ Despite advances in diagnostic modalities, accurately estimating coronary artery disease (CAD) severity in NSTEMI remains challenging in routine practice. Consequently, identifying simple, economical, and easily measurable biomarkers that can assist in estimating atherosclerotic burden and the likelihood of MVD has become an area of increasing clinical interest.

The atherogenic index of plasma (AIP), calculated as the logarithm of the ratio of triglycerides (TG) to high–density lipoprotein (HDL) cholesterol, is a key indicator of lipid metabolism.⁷ Beyond conventional lipid parameters, AIP is increasingly regarded as a biomarker reflecting plasma atherogenicity, owing to its association with cholesterol esterification, lipoprotein particle size, and the presence of remnant lipoproteins.⁸ Recent evidence suggests that AIP may outperform traditional single–lipid measures in predicting CAD risk.⁹ Prior studies have also demonstrated a relationship between AIP and several cardiovascular risk factors, including obesity, metabolic syndrome, and diabetes mellitus (DM).^{10–12} Moreover, elevated AIP levels have been correlated with greater CAD burden among patients with stable disease.¹³ However, although the association between AIP, cardiovascular risk factors, and CAD extent has been widely explored in stable CAD populations, limited evidence exists regarding its relationship with critical MVD specifically in NSTEMI patients. Therefore, this study aimed to determine whether AIP could predict MVD in individuals with NSTEMI.

Materials and Methods

Study Population

This single–center retrospective study included patients hospitalized with a diagnosis of NSTEMI who underwent coronary angiography (CAG) between January 2024 and December 2024. The diagnosis of NSTEMI was established in accordance with the latest European Society of Cardiology recommendations and the Fourth Universal Definition of Myocardial Infarction.^{14,15}

Patients were excluded if they met any of the following criteria: medically managed ACS, previous percutaneous coronary intervention (PCI), ongoing lipid–lowering therapy at admission, left ventricular ejection fraction (LVEF) < 50%, prior coronary artery bypass grafting, thyroid dysfunction (hypo– or hyperthyroidism) confirmed clinically or biochemically, estimated glomerular filtration rate (eGFR) < 30 mL/min/1.73 m², antibiotic administration during the hospitalization in which CAG was performed, a history of malignancy, evidence of severe hepatic dysfunction, or absence of complete lipid profile data.

ABBREVIATIONS

AIP	Atherogenic index of plasma
NSTEMI	Non–ST–segment elevation myocardial infarction
MVD	Multivessel
HDL	High–density lipoprotein
LDL	Low–density lipoprotein
HbA1c	Hemoglobin A1c
ACS	Acute coronary syndromes
CAD	Coronary artery disease
TG	Triglycerides
DM	Diabetes mellitus
CAG	Coronary angiography
PCI	Percutaneous coronary intervention
LVEF	Left ventricular ejection fraction
eGFR	Estimated glomerular filtration rate
LMCA	Left main coronary artery
LAD	Left anterior descending
RCS	Restricted cubic spline
ROC	Receiver operating characteristic
GRACE	Global Registry of Acute Coronary Events
TIMI	Thrombolysis in Myocardial Infarction
CCS	Chronic coronary syndrome
SYNTAX scores	Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery

The study protocol received institutional Ankara Etlik City Hospital Scientific Research Evaluation and Ethics Committee (Approval Number: AEŞH–BADEK–2025–0319, Date: 09.04.2025) and was conducted in accordance with the Declaration of Helsinki. Owing to its retrospective design, the committee waived the requirement for informed consent.

Demographic, clinical, and laboratory information were extracted from the hospital's electronic medical record system. Hypertension was defined as a systolic blood pressure ≥ 140 mmHg, a diastolic blood pressure ≥ 90 mmHg, or current use of antihypertensive agents. DM was defined as fasting plasma glucose ≥ 126 mg/dL, hemoglobin A1c $\geq 6.5\%$, or treatment with glucose–lowering medications. Current smoking status was defined as regular daily cigarette use.

Laboratory Measurements

Blood samples were collected from the antecubital vein in the early morning after a minimum fasting period of 12 hours, prior to the initiation of any lipid–lowering therapy. Total cholesterol and TG concentrations were determined using enzymatic assays, while HDL and low–density lipoprotein (LDL) cholesterol levels were measured using direct homogeneous methods. Complete blood counts, standard biochemical markers, and cardiac enzyme levels were analyzed using validated automated systems in the hospital's central laboratory.

The atherogenic index of plasma was calculated as the logarithm of the ratio of TG to HDL cholesterol: $AIP = \log(TG / HDL - \text{cholesterol})$.

Coronary Angiography

Conventional CAG was performed using the standard Judkins technique via either the radial or femoral approach, with at least four projections of the left coronary artery and two of the right

coronary artery. Nitroglycerin was administered when coronary spasm was suspected. Quantitative angiographic assessment was conducted according to a standardized protocol, evaluating maximal luminal narrowing from two orthogonal views.

All angiograms were independently reviewed by two experienced interventional cardiologists who were blinded to the patients' laboratory data. Critical CAD was defined as $\geq 70\%$ luminal diameter stenosis in at least one major epicardial vessel, or $\geq 50\%$ stenosis in the left main coronary artery (LMCA) or the proximal segment of the left anterior descending artery (LAD). The number of diseased vessels was determined by counting significant ($\geq 70\%$) stenoses in major arteries (LAD, left circumflex [LCx], and right coronary artery [RCA]) and their large branches (e.g., diagonal branch) with a reference diameter ≥ 2.0 mm. In the present study, we intentionally focused on a stricter angiographic definition of MVD, requiring critical stenosis in all three major epicardial coronary arteries. This approach is conceptually consistent with previous reports that have specifically examined LMCA and/or three-vessel disease, or triple-vessel CAD, as representing the most advanced spectrum of MVD in ACS/NSTEMI populations.^{16,17} When LMCA stenosis was present, it was classified as two-vessel disease regardless of concurrent LAD or LCx lesions.

Any discrepancies between the two cardiologists were resolved by consensus with a senior investigator. Based on angiographic findings, patients were categorized into single-vessel, two-vessel, or three-vessel disease groups.

Statistical Analysis

All statistical analyses were performed using SPSS version 23.0 software (SPSS Inc., Chicago, IL, USA). The normality of continuous variables was assessed using the Kolmogorov-Smirnov test. Variables with a normal distribution were expressed as mean \pm standard deviation and compared using the Student t-test, whereas those not following a normal distribution were reported as median (interquartile range) and evaluated with the Mann-Whitney U test. Categorical variables were described as frequencies and percentages, and intergroup differences were analyzed using the chi-square or Fisher's exact test, as appropriate. To determine the independent association of MVD, univariable analyses were first conducted, followed by multivariable logistic regression. Parameters with p-values below 0.05 in the multivariable model were considered independent predictors. The diagnostic and discriminative performance of AIP and other relevant variables for identifying MVD was further examined using receiver operating characteristic (ROC) curve analysis. To explore potential non-linear associations between AIP and the probability of MVD, AIP was modeled as a restricted cubic spline (RCS) with four knots placed at the 5th, 35th, 65th, and 95th percentiles of its distribution. Spline terms were incorporated into a multivariable logistic regression model, and non-linearity was assessed using a likelihood ratio test comparing the spline model to a model including a single linear AIP term. Statistical significance was defined as a two-tailed p-value of less than 0.05 for all tests. A post hoc power analysis was performed for the primary comparison of AIP values between patients with and without MVD. Using the observed group means, sample sizes, and a two-sided alpha level of

0.05, the standardized effect size (Cohen's d) was calculated as 0.57, corresponding to an estimated statistical power > 0.99 for detecting this difference.

Results

A total of 1,216 patients diagnosed with NSTEMI were included in the study, of whom 302 (24.8%) were found to have critical MVD. Among the remaining 914 patients without MVD, 610 (66.7%) had single-vessel disease, while 304 (33.3%) had two-vessel disease. The baseline demographic and clinical characteristics of patients with and without MVD are summarized in Table 1.

Patients in the MVD group had a significantly higher prevalence of hypertension and DM compared to those without MVD ($P < 0.05$ for both). No significant differences were observed between groups for age, sex, or smoking status ($P > 0.05$ for all). Regarding laboratory parameters, patients with MVD exhibited higher fasting plasma glucose, HbA1c, LDL cholesterol, triglycerides, and AIP values, along with lower HDL cholesterol levels ($P < 0.05$ for all). Serum creatinine levels were higher, and eGFR values were lower in the MVD group ($P < 0.05$ for both). LVEF did not differ significantly between the groups ($P = 0.191$).

The results of the univariable and multivariable logistic regression analyses for MVD predictors are presented in Table 2. In the univariable analysis, AIP, HbA1c, LDL cholesterol, reduced eGFR, hypertension, and DM were all significantly associated with MVD ($P < 0.05$ for all). In the multivariable analysis, AIP remained an independent predictor of MVD (odds ratio [OR]: 3.132, 95% confidence interval [CI]: 1.626–6.030, $P = 0.001$), together with DM (OR: 3.201, 95% CI: 2.432–3.822, $P = 0.001$), HbA1c (OR: 1.153, 95% CI: 1.038–1.280, $P = 0.008$), and LDL cholesterol (OR: 1.007, 95% CI: 1.003–1.012, $P = 0.002$). Reduced eGFR and the presence of hypertension did not retain statistical significance after adjustment ($P > 0.05$ for both).

The diagnostic performance of AIP, LDL cholesterol, and HbA1c in predicting MVD is summarized in Table 3 and illustrated in Figure 1. Among the three markers, AIP demonstrated the highest discriminatory ability, with an area under the curve (AUC) of 0.689 (95% CI: 0.658–0.720, $P < 0.001$) for identifying patients with MVD. The optimal cut-off value for AIP was 0.648, yielding 65.6% sensitivity and 65.6% specificity. In comparison, LDL cholesterol and HbA1c showed lower predictive capacities, with AUCs of 0.550 and 0.575, respectively.

In RCS analysis, the probability of MVD increased progressively across the AIP spectrum, with a steeper rise at higher values (Figure 2). A likelihood ratio test comparing the spline model with a simple linear term demonstrated a statistically significant deviation from linearity ($P = 0.018$), indicating that the association between AIP and MVD was not strictly linear.

Discussion

To the best of our knowledge, this study is the first to identify AIP as an independent predictor of critical MVD specifically among patients with NSTEMI. In our analysis, NSTEMI patients with MVD demonstrated significantly higher AIP values than those with single- or two-vessel disease. ROC curve analysis revealed that AIP showed better discriminatory performance than LDL cholesterol and HbA1c for detecting MVD. However, the AUC

Table 1. Baseline demographic, clinical, angiographic, and laboratory characteristics of NSTEMI patients with and without multivessel coronary artery disease

Variables	Patients without multivessel disease (n = 914)	Patients with multivessel disease (n = 302)	P
Demographic data			
Age, (years)	63.6 ± 13.5	63.9 ± 11.8	0.745
Male, n (%)	644 (70.5)	198 (65.6)	0.110
Active smoking, n (%)	569 (62.3)	181 (59.9)	0.433
Past medical history, n (%)			
Hypertension	551 (60.3)	205 (67.9)	0.018
Diabetes mellitus	217 (23.7)	124 (41.1)	< 0.001
COPD	77 (8.4)	28 (9.3)	0.671
Vital signs			
SBP, mmHg	150.9 ± 28.5	147.8 ± 28.7	0.180
DBP, mmHg	82.9 ± 16.2	82.7 ± 16.6	0.841
Heart rate, beats/min	86.0 ± 23.3	86.2 ± 23.3	0.928
CAG characteristics, n (%)			
One-vessel disease	610 (66.7)	0 (0)	< 0.001
Two-vessel disease	304 (33.3)	0 (0)	
Three-vessel disease	0 (0)	302 (100)	
Preadmission medications, n (%)			
Aspirin	307 (33.6)	108 (35.8)	0.516
ACEi/ARB	356 (38.9)	120 (39.7)	0.739
Beta-blocker	274 (30)	99 (32.8)	0.360
Laboratory parameters			
Hemoglobin, (g/dL)	13.4 ± 2.1	13.4 ± 2.0	0.856
White blood cells, (×10 ⁹ /L)	9.8 ± 3.4	9.9 ± 3.4	0.794
Platelets, (×10 ⁹ /L)	230.0 ± 67.2	233.9 ± 76.0	0.436
Serum creatinine, (mg/dL)	1.1 ± 0.6	1.2 ± 0.7	< 0.001
Estimated GFR, (mL/min/1.73 m ²)	80.0 ± 25.3	72.7 ± 27.0	< 0.001
ALT, (U/L)	20 (6-71)	21 (6-79)	0.283
AST, (U/L)	23 (5-76)	23 (6-65)	0.249
TSH, (mIU/L)	1.20 (0.63-4.40)	1.23 (0.72-4.70)	0.573
Blood glucose, (mg/dL)	145.1 ± 69.2	158.7 ± 78.9	0.002
HbA1c, (%)	6.7 ± 1.6	7.0 ± 1.8	0.004
Peak troponin T, (ng/mL)	1.145 (0.10-189.6)	1.285 (0.10-179)	0.154
Lipid profiles			
Total cholesterol, (mg/dl)	186.2 ± 48.4	194.1 ± 53.0	0.008
LDL cholesterol, (mg/dl)	119.8 ± 36.1	130.8 ± 41.9	< 0.001
HDL cholesterol, (mg/dl)	36.7 ± 9.3	34.1 ± 9.4	< 0.001
Triglycerides, (mg/dl)	131 (42-860)	179 (60-960)	< 0.001
Atherogenic index of plasma	0.59 ± 0.26	0.74 ± 0.28	< 0.001
Echocardiography			
LVEF, (%)	54.8 ± 4.4	53.8 ± 4.3	0.191

ACEi, Angiotensin-Converting Enzyme Inhibitor; ALT, Alanine Aminotransferase; ARB, Angiotensin II Receptor Blocker; AST, Aspartate Aminotransferase; CAG, Coronary Angiography; COPD, Chronic Obstructive Pulmonary Disease; DBP, Diastolic Blood Pressure; GFR, Glomerular Filtration Rate; HbA1c, Hemoglobin A1c; HDL, High-Density Lipoprotein; LDL, Low-Density Lipoprotein Cholesterol; LVEF, Left Ventricular Ejection Fraction; SBP, Systolic Blood Pressure; TSH, Thyroid-Stimulating Hormone.

Table 2. Univariable and multivariable logistic regression analyses for predictors of multivessel coronary artery disease in patients with NSTEMI

Variables	Univariable analysis		Multivariable analysis	
	OR (95% CI)	P	OR (95% CI)	P
Hypertension	1.747 (1.595-1.939)	0.013	1.727 (0.994-2.071)	0.107
Diabetes mellitus	3.872 (2.876-4.653)	< 0.001	3.201 (2.432-3.822)	0.001
GFR	0.995 (0.990-0.999)	0.030	1.002 (0.994-1.009)	0.663
HbA1c	1.149 (1.073-1.230)	< 0.001	1.153 (1.038-1.280)	0.008
LDL cholesterol	1.004 (1.001-1.006)	0.010	1.007 (1.003-1.012)	0.002
AIP	5.430 (3.972-8.381)	< 0.001	3.132 (1.626-6.030)	0.001

AIP, Atherogenic Index of Plasma; CI, Confidence Interval; DM, Diabetes Mellitus; GFR, Glomerular Filtration Rate; HbA1c, Hemoglobin A1c; LDL, Low-Density Lipoprotein; LVEF, Left Ventricular Ejection Fraction; OR, Odds Ratio.

Table 3. Receiver operating characteristic curve analysis of atherogenic index of plasma, LDL-C, and HbA1c for predicting multivessel coronary artery disease in patients with NSTEMI

Variables	AUC	P	95% Confidence Interval		Sensitivity (%)	Specificity (%)	Cut-off point
			Lower Bound	Upper Bound			
AIP	0.689	< 0.001	0.658	0.720	65.6	65.6	0.648
LDL-C	0.550	0.004	0.516	0.583	54	53	114.50
HbA1c	0.575	< 0.001	0.542	0.609	58	54	6.05

AIP, Atherogenic Index of Plasma; AUC, Area Under the Curve; HbA1c, Hemoglobin A1c; LDL-C, Low-Density Lipoprotein Cholesterol.

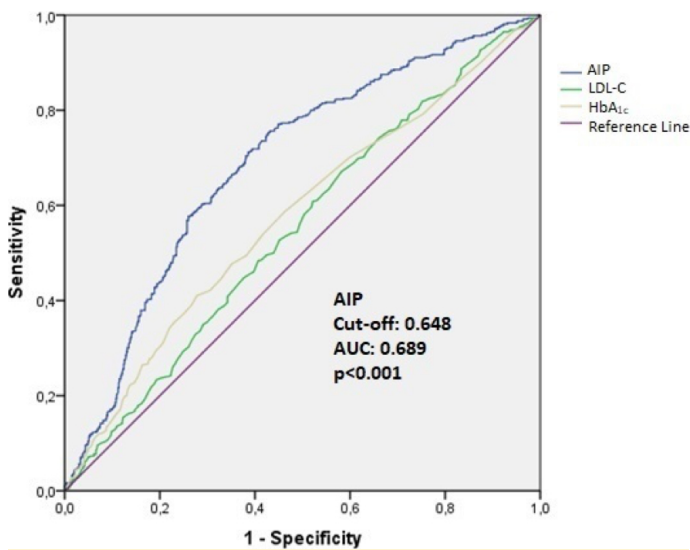


Figure 1. Comparison of receiver operating characteristic (ROC) curves for AIP, LDL-C, and HbA_{1c} in predicting multivessel coronary artery disease in patients with non-ST-segment elevation myocardial infarction.

AIP, Atherogenic Index of Plasma; AUC, Area under the curve; HbA_{1c}, Hemoglobin A1c; LDL-C, Low-density lipoprotein cholesterol.

value of 0.689 indicates only moderate discriminative ability. Therefore, the clinical relevance of AIP should be interpreted in the context of stronger prognostic indicators, such as troponin, Global Registry of Acute Coronary Events (GRACE) score, or the Thrombolysis in Myocardial Infarction (TIMI) score,¹⁴ which were not directly compared in our study because their primary roles are risk stratification and prognosis rather than assessment of

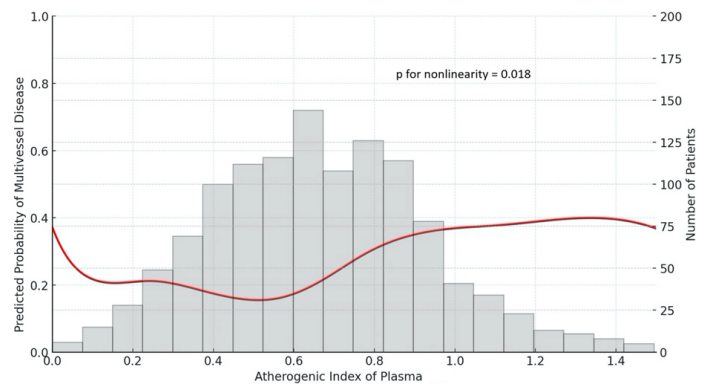


Figure 2. Restricted cubic spline curve illustrating the association between atherogenic index of plasma (AIP) and the predicted probability of multivessel disease. The red line represents the spline-derived predicted probability, and the gray bars depict the distribution of patients across AIP values.

anatomical disease burden. In this regard, AIP may still provide complementary value as a simple and accessible metabolic marker reflecting atherogenic burden.

The proportion of NSTEMI cases relative to STEMI has been steadily increasing, even though the overall incidence of ACS has declined in many developed countries over recent decades.^{18,19} Within the NSTEMI population, the presence of MVD is a marker of adverse prognosis,^{20,21} which is particularly relevant given that NSTEMI patients often experience higher long-term mortality after hospital discharge compared with those presenting with STEMI.^{22,23} In our cohort, MVD was detected in 24.8% of patients with NSTEMI. Although this rate is somewhat lower than in previous reports, it falls within the wide range observed across the

literature, likely reflecting differences in patient selection criteria, definitions of MVD, and population characteristics. For instance, Baumann et al.⁵ reported a prevalence of 42% among NSTEMI patients undergoing CAG in a contemporary registry. Conversely, a Portuguese study observed a lower prevalence of 18%, while other investigations have reported rates ranging from 40% to 60% among NSTEMI patients treated with PCI.^{17,24,25} Despite this variability, most studies consistently indicate that the presence of MVD is associated with poorer outcomes.²⁶ These findings highlight the clinical relevance of identifying MVD in NSTEMI.

AIP is a logarithmic index that reflects the relationship between fasting triglycerides and HDL cholesterol. It was first introduced as a marker of plasma atherogenicity, based on its inverse relationship with LDL particle size.⁷ Small dense LDL (sdLDL), an LDL subclass, is more atherogenic due to its smaller particle size, which facilitates penetration and retention within the arterial intima.²⁷ Furthermore, sdLDL particles are more susceptible to oxidative modification; oxidized LDL is then engulfed by macrophages, forming foam cells that contribute to atheroma development. The mechanisms underlying the enhanced atherogenicity of sdLDL include lipid peroxidation, increased expression of endothelial adhesion molecules, and activation of reactive oxygen species—all of which play integral roles in the progression of CAD.²⁸ Previous studies have identified sdLDL as a valuable biomarker for predicting atherosclerosis, and its clinical application has been encouraged.²⁹ However, sdLDL measurement remains limited in routine practice due to methodological complexity and high cost. AIP serves as a convenient and cost-effective surrogate for sdLDL, as elevated AIP values indicate smaller LDL particle size and a higher proportion of sdLDL.⁷ These associations reinforce the value of AIP as an accessible marker of atherogenic risk. The current study adds to this body of evidence by demonstrating that AIP correlates with the extent of CAD, thereby supporting its utility as a reliable indicator of atherosclerotic burden.

Several studies have explored the relationship between AIP and CAD severity in patients with chronic coronary syndrome (CCS). Wang et al.¹³ reported that AIP was not only an independent risk factor for CAD but also correlated with higher SYNTAX scores (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery), indicating a strong association with both disease occurrence and anatomical complexity. Similarly, Wu et al.³⁰ demonstrated that AIP independently predicted the severity of newly diagnosed CAD, particularly in individuals with normal glucose metabolism. Zhou et al.⁹ also confirmed that AIP is a powerful and independent predictor of CAD in patients with DM, with progressively increasing odds ratios across AIP quartiles. Furthermore, Cai et al.³¹ identified AIP as the lipid parameter most strongly associated with CAD among a broad panel of lipid indices in a large Chinese cohort. In addition, Mangalesh et al.³² found that AIP not only correlated with CAD severity but also predicted major adverse cardiovascular events during a three-year follow-up period, underscoring its prognostic value beyond the initial diagnosis.

The role of AIP has also been examined in patients with ACS. Two recent studies found that elevated AIP levels were significantly associated with both the presence and severity of ACS. Cai et al.³³ reported that AIP was independently associated with ACS

occurrence and lesion severity in very young adults (≤ 35 years), demonstrating stronger predictive power than traditional lipid parameters, particularly among men. Jin et al.³⁴ similarly found that AIP was independently associated with MVD in patients with acute myocardial infarction, especially among those with prediabetes. However, Jin et al.'s³⁴ cohort included both STEMI and NSTEMI patients, and the analysis did not differentiate between these subtypes. Their investigation mainly focused on the interaction between AIP and glucose metabolism rather than assessing AIP as an independent stratification tool within a specific ACS population. In contrast, our study concentrated exclusively on NSTEMI patients—a group characterized by distinct pathophysiological mechanisms and prognostic outcomes³⁵—and evaluated AIP specifically as a predictor of MVD. Moreover, the definition of MVD used in our study required critical stenosis in all three major epicardial coronary arteries. In contrast, Jin et al.³⁴ defined MVD as the involvement of two or more vessels. This distinction in MVD definitions across studies should be taken into account when comparing our results with previous literature. This stricter criterion may enhance the specificity of our findings and better represent advanced coronary atherosclerosis.

Although several previous studies have demonstrated the predictive value of AIP for assessing CAD severity in CCS or suspected CAD, its relevance in ACS—particularly in NSTEMI—remains insufficiently characterized. Several studies have linked higher AIP values with elevated SYNTAX scores, increased anatomical complexity, and higher odds of CAD in various metabolic contexts.^{9,13,30} Furthermore, investigations across diabetic, normoglycemic, and young adult populations have confirmed the consistency of AIP as a risk marker across diverse cardiovascular risk categories.^{9,28,33} However, most of these studies were conducted in patients undergoing elective CAG or in broader ACS cohorts without differentiating NSTEMI from other ACS types. This distinction is crucial because NSTEMI represents a unique subset of ACS, characterized by heterogeneous mechanisms, a higher prevalence of comorbidities, and often more extensive coronary involvement.³⁶ In addition, MVD in NSTEMI has been linked to poorer short- and long-term outcomes, yet reliable tools for early identification are still lacking in clinical practice.³⁷ Our study directly addresses this knowledge gap by focusing solely on NSTEMI patients and examining AIP's predictive ability for detecting MVD. We found that elevated AIP values were significantly associated with MVD, even after adjustment for HbA1c, LDL cholesterol, renal function, and LVEF. Among the analyzed parameters, AIP showed modest but better discriminative performance in ROC analysis than conventional metabolic indicators. These findings suggest that AIP may reflect atherogenic burden in NSTEMI and could offer additional clinical value when interpreted alongside established risk markers.

Study Limitations

This study is not without limitations, which should be carefully considered. First, because of its single-center, retrospective, and observational nature, a definitive causal relationship between elevated AIP levels and MVD in patients with NSTEMI cannot be established. In addition, the retrospective, single-center design of our study may further limit the external validity and generalizability of the results. Because patient characteristics and clinical practices may differ across centers and regions, caution

is required when extrapolating these findings to broader NSTEMI populations. Second, although the sample size was relatively large, all participants were drawn from a single tertiary hospital, which may have introduced selection bias and reduced generalizability of the findings. Third, the potential effects of unmeasured confounding factors, including lifestyle-related variables such as diet and physical activity, could not be fully excluded. Fourth, AIP values were calculated based on laboratory measurements obtained during a single hospitalization; therefore, longitudinal exposure or temporal changes in AIP levels were not evaluated, and the cumulative impact of sustained AIP elevation on the development of MVD in NSTEMI patients remains uncertain. Fifth, CAD severity in this study was determined by the number of major epicardial vessels with significant stenosis rather than by the SYNTAX score. Although the SYNTAX score provides valuable information regarding anatomical complexity, it does not necessarily reflect the overall extent of vessel involvement, which was the focus of our investigation. Finally, as the study cohort consisted primarily of patients of Turkish descent, the generalizability of our findings to other ethnic and geographic populations may be limited.

Conclusion

In conclusion, our study demonstrates that AIP is significantly associated with the presence of critical MVD in patients with NSTEMI. After adjustment for conventional cardiometabolic risk factors, AIP remained an independent predictor of MVD and showed better discriminative performance than the other evaluated parameters. Owing to its simplicity, affordability, and wide availability, AIP may serve as a practical and accessible indicator of atherogenic burden, helping identify NSTEMI patients who are more likely to have multivessel coronary involvement. Nevertheless, further large-scale, prospective, multicenter randomized studies involving diverse ethnic and demographic populations are warranted to validate and expand upon these findings.

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