THE ANATOLIAN JOURNAL OF CARDIOLOGY

Official journal of the TURKISH SOCIETY OF CARDIOLOGY

# The Association Between Atherogenic Index of Plasma and No-Reflow Phenomenon in Acute Coronary Syndrome

## ABSTRACT

**Background:** The atherogenic index of plasma (AIP) is a biomarker of plasma atherogenicity. Elevated AIP is linked with adverse cardiac events. We sought to examine the association of admission AIP and no-reflow phenomenon (NRP) in acute coronary syndrome (ACS) patient population treated with percutaneous coronary intervention (PCI).

**Methods:** Eight hundred eight-four ACS patients were included to statistical tests retrospectively and classified according to the occurrence of NRP: NRP (–) (n = 662) and NRP (+) (n = 186). AIP levels were calculated through the formula $\log_{10}$ (triglyceride-to-high-density lipoprotein cholesterol ratio).

**Results:** AIP levels were higher in NRP (+) patients compared to NRP (–) group patients. The receiver operating characteristic (ROC) curve analysis for AIP to predict NRP yielded an area under the ROC curve value 0.643 [95% confidence interval (CI): 0.596-0.690, $P < .001$]. AIP was associated with NRP in univariate logistic regression analysis [Odds Ratio (OR): 2.46; $P = .001$; CI: 1.44 (lower limit)-4.21 (upper limit)]. However, AIP did not emerge as a significant prognostic factor of NRP in multiple logistic regression analysis [OR: 2.11; $P = .422$; CI: 0.34 (lower limit)-13.11 (upper limit)]. On the other hand, peak troponin T (log10) was an independent prognostic factor for NRP [OR: 0.13; $P < .001$; CI: 0.10 (lower limit)-0.37 (upper limit)] occurrence.

**Conclusion:** The AIP level on admission is not a statistically significant prognostic factor of NRP. However, peak troponin T (log10) is an independent prognostic parameter of NRP.

**Keywords:** Acute coronary syndrome, atherogenic index of plasma, atherosclerosis, no-reflow phenomenon, troponin

## INTRODUCTION

Atherosclerosis-related cardiovascular disease (CVD), especially acute coronary syndrome (ACS), globally affects the world population. Percutaneous coronary intervention (PCI) is the main revascularization strategy in ACS.[1,2] However, despite significant advances in PCI in recent decades, a huge number of patients still develop insufficient myocardial perfusion because of poor microvascular perfusion which is defined as no-reflow phenomenon (NRP). It is known that NRP is linked with delayed functional recovery, left ventricular systolic impairment, heart failure, life-threatening arrhythmias, and death.[3,4] The underlying pathophysiology of NRP includes microvascular spasm, oxidative stress, reperfusion injury, distal embolization, alterations in endothelial functioning, and inflammation.[5,6]

Dyslipidemia is the leading risk factor in CVD and ACS pathophysiology.[7] Previous studies confirmed that increased triglycerides (TG) and low-density lipoprotein cholesterol (LDL-C) and lessened high-density lipoprotein cholesterol (HDL-C) have robust predictive capacity for subsequent adverse cardiac events.[8,9] Besides traditional lipid profiles, the atherogenic index of plasma (AIP), defined by logarithmic transformation of TG-to-HDL-C ratio, is considered as a plasma atherogenicity biomarker due to its association with cholesterol esterification, lipoprotein particle dimensions, and residue lipoproteins.[10,11] Numerous studies demonstrated a relationship among AIP and CVD risk factors such as obesity, hypertension



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**Received:** April 23, 2023
**Accepted:** August 24, 2023
**Available Online Date:** October 6, 2023

**Cite this article as:** Çelik İE, Öztürk S, Yarlıoğlu M, et al. The association between atherogenic index of plasma and no-reflow phenomenon in acute coronary syndrome. *Anatol J Cardiol.* 2023;27(12):712-719.

DOI:10.14744/AnatolJCardiol.2023.3381

(HT) and diabetes mellitus (DM).[12-14] The atherogenic index of plasma was also shown to be linked with adverse cardiac events and coronary artery disease (CAD) severity.[15,16] Moreover, increased AIP levels are linked with poor prognosis in ACS.[7,17] There are very limited data about the association of AIP and NRP in ACS patient population. Thus, we sought to explore the relationship among admission AIP levels and NRP in ACS patients who underwent revascularization of infarct-related artery (IRA) through PCI.

## METHODS

### Study Population

Clinical and angiographical data, and hospital records of 902 consecutive ACS patients treated with PCI between September 2019 and May 2021 were retrospectively evaluated. The exclusion criteria of the study were determined as follows: Infectious or inflammatory disease, statin usage, treatment with fibrinolytic agents, death during the periinterventional period, severe renal and/or liver impairment, malignancy, and hematologic disorder. In addition, patients with missing data were excluded. Because the study was designed in a retrospective manner, informed consent from the patients was waived with the approval of the study by the Local Ethics Committee (October 27, 2021/E-21-786). All study procedures were compatible with the Declaration of Helsinki.

Acute coronary syndrome diagnosis was performed by evaluating anamnesis, electrocardiography (ECG), imaging methods and cardiac enzymes of the patients. Patients with incipient symptoms that suggest myocardial ischemia and accompanying ST-segment elevation on ECG were diagnosed as ST-segment elevated myocardial infarction (STEMI).[1] Patients with incipient symptoms that suggest myocardial ischemia without ST-segment elevation on ECG that accompany troponin increase greater than the upper limit of normal value were diagnosed as non-ST-segment elevated myocardial infarction (NSTEMI). Patients with incipient symptoms that suggest myocardial ischemia, no ST-segment elevation on ECG with no troponin increase were diagnosed as unstable angina (UA).[2] Hyperlipidemia was defined if total cholesterol (TC) above 200 mg/dL and/or a LDL-C above 130 mg/dL were detected in blood tests or previous diagnosis of hyperlipidemia. HT was diagnosed as blood pressure measurement ≥140/90 mm Hg on 2 different office visits or treatment for a previous diagnosis of HT. DM was diagnosed by fasting glucose levels ≥ 126 mg/dL, nonfasting glucose levels ≥ 200 mg/dL or a previous DM diagnosis. Active smokers were defined as patients who smoke regularly in the recent 6 months.

### Coronary Angiography and Interventions

Quantitative coronary angiography (CAG) and PCI (Siemens Axiom Artis Zee 2011; Siemens Healthcare, Erlangen, Germany) were applied through standard Judkins method. The CAG videos were assessed by 2 interventional cardiologists blinded to data of the patients. The diagnosis of significant lesions was visually made if there is 50% stenosis or greater in at least 1 of the major coronary arteries, including left anterior descending artery (LAD), circumflex artery, and right coronary artery, or their major branches. In case of disagreement between these 2 cardiologists, a consensus decision was made. All patients received antiaggregant and anticoagulant medications based on the current guidelines. During CAG and PCI procedures and follow-up of the patients, the operators and/or physicians were free for the decision of revascularization type and technique and administration of further medical therapies such as glycoprotein IIb/IIIa inhibitor, sodium nitroprusside and/or adenosine. Successful PCI was described as minimum stenosis diameter below 20% with a final Thrombolysis in Myocardial Infarction (TIMI) grade 3 flow pattern with no major complications.

Epicardial blood flow in the IRA before and after PCI was analyzed through TIMI flow grade scoring system.[18] The NRP was diagnosed if there is a final TIMI flow grade less than 3 with no dissection, residual stenosis, thrombus, or vasospasm after PCI.[19] Angiographic thrombus burden (TB) was used and the patients were categorized into low TB (grades 1, 2, or 3) or high TB groups (grades 4 or 5) according to their thrombus score.[20] Two-dimensional transthoracic echocardiography was applied to all patients (Vivid S60N; Vingmed-General Electric, Horten, Norway) during their hospital stay and left ventricular ejection fraction (LVEF) was measured through 2-dimensional biplane Simpson's method.

### Laboratory Procedures

Peripheral blood samples were acquired on admission through an antecubital vein. Total complete blood count test was performed by using an automated blood cell counter (Sysmex SF-3000 Hematology Analyzer, USA). Serum levels of cardiac enzymes, biochemical parameters, C-reactive protein (CRP), and fasting lipid panel were measured through standard methods at the biochemistry laboratory of the hospital. The AIP was calculated through the formula $\log_{10}$ (TG-to-HDL-C ratio).

### Statistical Analysis

Statistical tests were exerted by using the Statistical Package for the Social Sciences Statistics, version 22.0 (SPSS, Inc, Chicago, Ill, USA). Categorical variables were given as counts and percentages and compared by the chi-square test or Fisher's exact test. In order to evaluate the distribution of continuous variables, the Kolmogorov–Smirnov test was applied. Afterward, comparison of normally distributed continuous variables was exerted through independent samples *t*-test. On the other hand, comparison of abnormally distributed continuous variables was carried out by applying

## HIGHLIGHTS

- The atherogenic index of plasma levels were higher in patients with no-reflow phenomenon (NRP) than in the patient group without NRP.
- The atherogenic index of plasma did not emerge as a significant prognostic factor of NRP in multiple logistic regression analysis.
- Peak troponin T (log10) was an independent prognostic parameter for NRP occurrence.

Mann–Whitney *U*-test and the results were given as median and interquartile ranges (percentiles 25$^{th}$ and 75$^{th}$). The receiver operating characteristic (ROC) curve analysis was applied in order to assess the cutoff values for the sensitivity and specificity of AIP to predict NRP.

Binary logistic regression analysis was applied to test the prognostic parameters of NRP. Variables that could be associated with NRP such as age, gender, DM, STEMI, peak troponin T, CRP, LVEF, baseline TIMI flow grade, thrombus burden, number of implanted stents and AIP were included in univariate analysis. Due to abnormal distribution of peak troponin T and CRP, logarithmic transformations were applied to these variables before being included in regression model in order to yield an approximately normal distribution. Afterward, the variables which were identified as $P < .1$ in univariate analysis were incorporated into multiple logistic regression model. The goodness-of-fit assumption was examined by the Hosmer–Lemeshow method and satisfied when p value was more than .05. A 2-sided $P < .05$ was defined as statistically significant for all tests.

## RESULTS

Nine hundred two ACS patients treated with PCI were enrolled consecutively and 54 patients were excluded. There remained 848 patients for statistical analyses. Afterward, the patients were classified in accordance with the NRP occurrence in the IRA: NRP (–) (n = 662) and NRP (+) (n = 186). NRP occurred in 21.9% of the patients. Table 1 indicates the comparison of baseline demographics and features of the patients. Age, gender, HT, current smokers, previous MI, family history of CAD, blood pressure, and heart rate were similar between groups. Preadmission medications including aspirin, $P_2Y_{12}$ inhibitor, angiotensin–aldosterone system antagonists and beta-blocker therapy were also comparable among groups. The NRP (+) group patients had significantly lower body mass index and LVEF compared to NRP (–) patients ($P = .001$ and $P < .001$, respectively). Besides, the percentage of patients with DM and hypercholesterolemia were significantly increased in NRP (+) patients ($P = .025$ and $P = .020$, respectively). Patients who developed NRP more frequently suffered from STEMI but were less likely to suffer from NSTEMI and UA ($P < .001$).

Laboratory parameters of the patients are demonstrated in Table 2. Hemoglobin, platelet count, and glucose levels were comparable among groups, whereas white blood cell count was significantly higher NRP (+) patient group. Creatinine level was higher in NRP (+) patients than patients with NRP (–), however estimated glomerular filtration rate was similar between the groups. The median of peak cardiac enzymes and CRP were significantly increased in NRP (+) patients ($P < .001$ for all). Lipid panel results including TC, HDL-C, LDL-C and non-HDL-C were comparable between groups. However, TG levels were increased in NRP (+) patient group at a significant level. AIP levels were also higher in NRP (+) patient group than the NRP (–) patients (0.55 ± 0.39, 0.48 ± 0.28, $P = .002$, respectively) as indicated in Figure 1. ROC curve analysis for AIP to predict NRP demonstrated an area under the ROC curve value 0.643 [95% confidence interval (CI): 0.596-0.690, $P < .001$] as demonstrated in Figure 2. The cutoff value of AIP (0.55) was associated with 65.0% sensitivity and 63.0% specificity.

**Table 1. Baseline Characteristics and Preadmission Medications of the Study Population**

| | No-Reflow Phenomenon [n (%)] | | |
|---|---|---|---|
| **Variables** | **No (n = 662)** | **Yes (n = 186)** | ***P*** |
| Age (years) | 59.4 ± 12.1 | 61.8 ± 11.9 | .790 |
| Men, n (%) | 525 (79.3) | 141 (75.8) | .165 |
| Body mass index (kg/m$^2$) | 26.9 ± 4.1 | 26.6 ± 3.4 | .001 |
| Hypertension, n (%) | 315 (47.5) | 97 (52.1) | .514 |
| Diabetes mellitus, n (%) | 197 (29.7) | 74 (39.7) | .025 |
| Current smoker, n (%) | 354 (53.4) | 114 (61.2) | .125 |
| Hypercholesterolemia, n (%) | 124 (18.7) | 51 (27.4) | .020 |
| Previous myocardial infarction, n (%) | 126 (19.0) | 54 (29.0) | .073 |
| Family history of coronary artery disease, n (%) | 146 (22) | 38 (20.5) | .486 |
| Systolic blood pressure (mm Hg) | 129 ± 22 | 127 ± 21 | .597 |
| Diastolic blood pressure (mm Hg) | 76±13 | 76±15 | .412 |
| Heart rate (beats/min) | 79 ± 15 | 85 ± 17 | .309 |
| **Clinical presentation, n (%)** | | | |
| ST-segment elevated myocardial infarction | 445 (67.2) | 172 (92.4) | <.001 |
| Non-ST-segment elevated myocardial infarction | 154 (23.2) | 6 (3.3) | |
| Unstable angina pectoris | 63 (9.6) | 8 (4.3) | |
| Left ventricular ejection fraction (%) | 50 ± 10 | 48 ± 11 | <.001 |
| **Preadmission medications, n (%)** | | | |
| Aspirin | 195 (29.4) | 67 (36.0) | .287 |
| $P_2Y_{12}$ inhibitor | 75 (11.3) | 19 (5.6) | .473 |
| Angiotensin–aldosterone system antagonists | 234 (35.3) | 74 (39.7) | .166 |
| Beta-blocker | 179 (27.0) | 62 (33.3) | .233 |

Data are presented as mean ± SD or number (%).

Angiographic features of the groups are given in Table 3. Multivessel disease ($P = .001$), number of diseased coronary artery ($P = .001$), percentage of patients with high-grade thrombus burden ($P < .001$) and baseline TIMI flow grade below 3 ($P < .001$) were higher in NRP (+) group patients. Chronic total occlusion rates were similar among groups and the LAD was the most frequent culprit vessel in both groups. The NRP group patients underwent longer stent length with lower stent diameter implantation that accompany higher number of implanted stents compared to those who did not develop NRP. As for the treatment strategy, the percentage

**Table 2. Laboratory Parameters of the Study Population**

| Variables | No-Reflow Phenomenon [n (%)] No (n = 662) | Yes (n = 186) | *P* |
|---|---|---|---|
| Hemoglobin, g/dL | 14.2 ± 1.9 | 14.1 ± 1.9 | .750 |
| White blood cells, ×10⁹/L | 10.7 ± 3.2 | 14.6 ± 4.7 | <.001 |
| Platelets, ×10⁹/L | 251 ± 92 | 243 ± 60 | .240 |
| Glucose, mg/dL | 141 ± 66 | 151 ± 65 | .253 |
| Creatinine, mg/dL | 1.06 ± 0.56 | 1.16 ± 0.49 | .040 |
| Estimated GFR (mL/min/1.73 m²) | 80.71 ± 22.54 | 75.10 ± 26.72 | .202 |
| Peak creatine kinase-MB, U/L | 15 (4.95-43.50) | 27 (14.0-68.50) | <.001 |
| Peak troponin T, ng/mL | 279 (232–1389) | 1376 (695-1923) | <.001 |
| C-reactive protein, mg/dL | 5.10 (3.0-16.40) | 18.25 (7.70-39.10) | <.001 |
| Total cholesterol, mg/dL | 182 ± 46 | 175 ± 45 | .931 |
| Triglycerides, mg/dL | 127 (95-178) | 151 (119-203) | <.001 |
| High-density lipoprotein, mg/dL | 38 ± 9 | 36 ± 10 | .070 |
| Low-density lipoprotein, mg/dL | 111 ± 38 | 117 ± 35 | .100 |
| Non-HDL, mg/dL | 136 ± 41 | 143 ± 47 | .098 |
| Atherogenic index of plasma | 0.48 ± 0.28 | 0.55 ± 0.39 | .002 |

Data are presented as mean ± SD or median (IQR).
GFR, glomerular filtration rate; HDL, high-density lipoprotein; IQR, interquartile range; MB, myocardial band.

of patients who underwent direct stenting was higher in NRP (–) patients, whereas NRP occurrence was more prevalent in patients who underwent balloon pre-dilatation and post-dilatation. The rates of mechanical thrombus aspiration and glycoprotein IIb/IIIa inhibitor usage were similar among groups.

Predictors of NRP assessed by logistic regression analysis are demonstrated in Table 4. Age, DM, STEMI, peak troponin T (log10), CRP (log10), baseline TIMI flow grade, number of implanted stents, and AIP were found as significant prognostic factors linked with NRP in univariate analysis. Multiple logistic regression analysis yielded peak troponin T (log10) [OR: 0.13; *P* <.001; CI: 0.10 (lower limit)-0.37 (upper limit)] as a statistically prognostic factor of NRP. AIP did not emerge as a significant prognostic parameter of NRP [OR:2.11; *P* = .422; CI: 0.34 (lower limit)-13.11 (upper limit)].

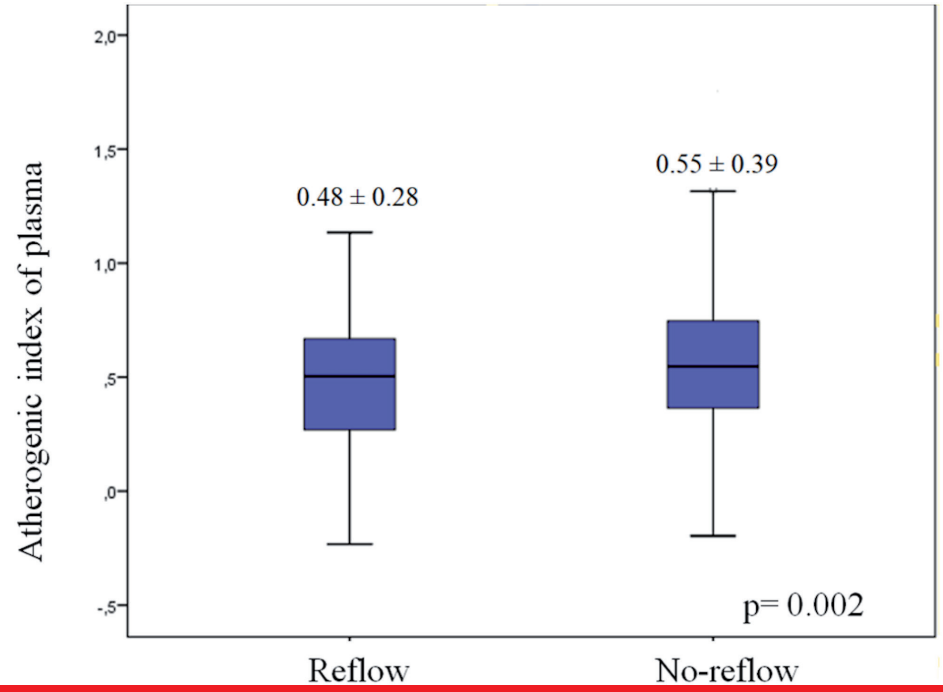


**Figure 1. Comparison of atherogenic index of plasma levels in patients with reflow and no-reflow phenomenon.**

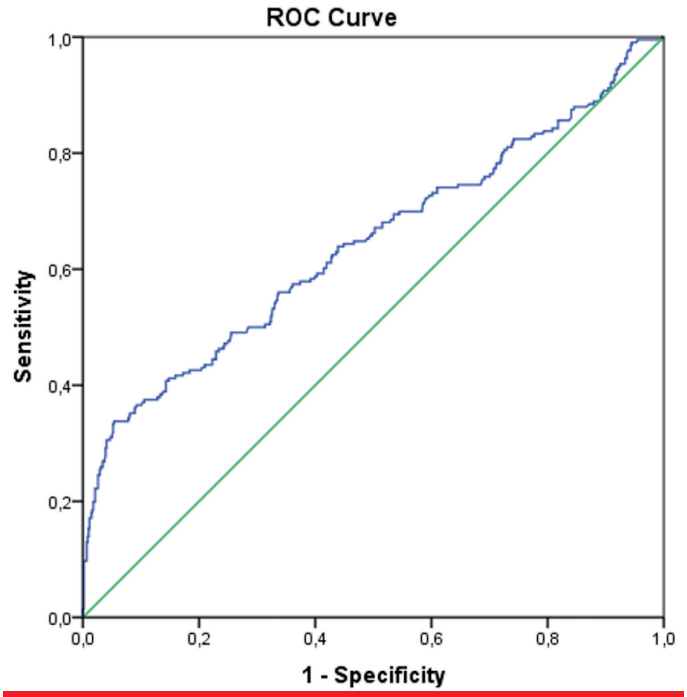


**Figure 2. Receiver operating characteristic curve analysis of atherogenic index of plasma to predict no-reflow phenomenon.**

## DISCUSSION

We investigated the association among AIP and NRP in ACS patients who underwent PCI and found that AIP levels are higher in patients who developed NRP. However, AIP level on admission did not emerge as a significant prognostic factor for NRP in multiple logistic regression analysis. On the other hand, logarithmically transformed peak troponin T level was a statistically significant prognostic factor of NRP.

The NRP is frequently observed after PCI in ACS patients and related with adverse outcomes such as left ventricular remodeling, life-threatening arrhythmias, increased hospitalization and mortality.[4] Therefore, prediction of NRP is a crucial issue in order to improve outcomes of ACS. The pathogenesis of NRP is multifactorial and involves various parameters linked with endothelial functioning and also increased oxidative stress and inflammation.[5,6]

Dyslipidemia is amongst the substantial risk factors in CVD and ACS pathophysiology. The vast majority of atherogenic dyslipidemia is characterized by diminished serum HDL-C concentration, elevated TG-rich lipoproteins and small dense LDL-C levels.[7-9] However, despite the prognostic significance of traditional lipid profiles in atherosclerotic process, it has been emphasized that AIP, a novel plasma atherogenicity marker, is associated with the development of atherogenesis.[15] Recent data also demonstrated

**Table 3. Angiographic and Procedural Characteristics of the Study Population**

| | No-Reflow Phenomenon [n (%)] | | |
|---|---|---|---|
| **Variables** | **No (n = 662)** | **Yes (n = 186)** | ***P*** |
| Multivessel disease, n (%) | 259 (39.1) | 96 (51.6) | .001 |
| Chronic total occlusion, n (%) | 24 (3.7) | 6 (3.2) | .520 |
| **Infarct-related artery, n (%)** | | | |
| Left anterior descending | 293 (44.2) | 96 (51.6) | .270 |
| Left circumflex | 164 (24.8) | 33 (17.8) | |
| Right | 207 (31.2) | 57 (30.6) | |
| Left main | 1 (0.1) | 0 (0) | |
| Number of diseased coronary artery | 1.53 ± 0.74 | 1.78 ± 0.84 | .001 |
| Thrombus aspiration, n (%) | 5 (0.8) | 5 (2.6) | .300 |
| High-grade thrombus burden, n (%) | 64 (9.7) | 54 (29.1) | <.001 |
| Baseline TIMI flow grade <3, n (%) | 528 (79.7) | 166 (89.2) | <.001 |
| Number of implanted stents | 1.30 ± 0.61 | 1.56 ± 0.50 | .021 |
| **Type of intervention, n (%)** | | | |
| Direct stenting | 243 (34.8) | 30 (16.1) | <.001 |
| Stenting after predilatation | 392 (59.2) | 141 (75.8) | |
| Postdilatation | 156 (23.5) | 63 (33.8) | |
| Stent diameter (mm) | 3.20 ± 0.39 | 3.05 ± 0.47 | .001 |
| Total length of stent (mm) | 19.48 ± 4.96 | 20.56 ± 6.24 | .018 |
| Glycoprotein IIb/IIIa inhibitor use, n (%) | 163 (24.6) | 49 (26.3) | .613 |

Data are presented as mean ± SD or number (%).
TIMI, thrombolysis in myocardial infarction.

**Table 4. Predictors of No-Reflow Phenomenon by Logistic Regression Analysis**

| | Univariate | | Multiple | |
|---|---|---|---|---|
| | Odds Ratio (Lower Limit–Upper Limit) | *P* | Odds Ratio (Lower Limit–Upper Limit) | *P* |
| Age (years) | 0.98 (0.97-0.99) | .021 | 0.97 (0.92-1.02) | .293 |
| Gender | 0.77 (0.52-1.11) | .166 | .. | .. |
| Diabetes mellitus | 1.46 (1.04-2.03) | .025 | 0.80 (0.27-2.34) | .689 |
| STEMI | 10.19 (4.42-23.44) | <.001 | 1.70 (0.43-6.72) | .447 |
| Peak troponin T (log10) | 0.30 (0.22-0.41) | <.001 | 0.13 (0.10-0.37) | <.001 |
| C-reactive protein (log10) | 0.29 (0.21-0.40) | <.001 | 0.88 (0.36-2.14) | .792 |
| LVEF | 1.00 (0.97-1.04) | 0.540 | .. | .. |
| Baseline TIMI flow grade | 3.13 (2.15-11.59) | <.001 | 1.24 (0.30-5.02) | .758 |
| Thrombus burden | 1.26 (0.53-2.99) | .591 | .. | .. |
| Number of implanted stents | 0.67 (0.42-1.07) | .099 | 0.65 (0.34-1.26) | .211 |
| Atherogenic index of plasma | 2.46 (1.44-4.21) | .001 | 2.11 (0.34-13.11) | .422 |

LVEF, left ventricular ejection fraction; STEMI, ST-segment elevated myocardial infarction; TIMI, thrombolysis in myocardial infarction.

the predictive capacity of AIP to detect severity of ACS. For example, Ma et al[21] demonstrated that higher AIP level on admission is related with adverse cardiac events in type 2 DM patients who suffer from ACS and treated with PCI. Cai et al[7] also showed AIP is independently related with ACS in very young patients. In another study, increased AIP levels tended to associate with adverse cardiovascular events.[22] Suleymanoglu et al[17] reported that AIP is an independent predictor of NRP in STEMI patients after primary PCI. In our study consisting of whole ACS population, AIP was linked with NRP in univariate analysis, but this association seemed to be mediated by other confounding factors and we could not prove that AIP is a statistically prognostic factor of NRP. On the other hand, we demonstrated that logarithmically transformed peak troponin T level is a significant prognostic factor for NRP occurrence.

Although the potential mechanisms underlying high AIP levels and NRP are not exactly known yet, numerous possible explanations have been proposed. One of the most possible underlying mechanisms between AIP and NRP may be the increased inflammatory activity that prone revascularized vessel to NRP. Many studies demonstrated the relationship between systemic inflammation and NRP.[23,24] Karabag et al[25] showed that elevated CRP and higher TG values in STEMI patients have a significant association with NRP. It was also reported that lipolytic products of TG carry a risk for activation of proinflammatory, procoagulant, and proapoptotic signaling mechanisms.[26] Meanwhile, recent evidence confirmed that HDL-C has various favorable effects in the vasculature such as cholesterol efflux from macrophages, antioxidant effect, suppression of inflammation in the vasculature, and enhancement of endothelium functioning, suggesting a contributory role for HDL-C as an anti-inflammatory particle.[27] Thus, increased TG levels and low HDL-C may be responsible for inflammatory processes that might cause NRP. We evaluated CRP as an inflammatory marker in our study. C-reactive protein was linked with NRP development in univariate analysis but similar to AIP, CRP did not yield as a significant prognostic parameter for NRP in multiple logistic regression analysis.

Another possible mechanism that links AIP and NRP is elevated oxidative stress. It is known that increased vascular levels of reactive oxygen species, such as lipid hydroperoxide, total antioxidant capacity, oxidative stress index, and paraoxonase 1 activity, might contribute to NRP development.[5,6] The importance of TGs in atherosclerotic process has been emphasized recently, which is known to be related with increased oxidative and inflammatory status.[26] However, HDL-C acts as an antioxidant in plasma, which is the body compartment exposed to oxidative stress.[27] Therefore, the association of higher TG and lower HDL-C with NRP might be the consequence of increased oxidative stress.

Apart from the abovementioned pathophysiological mechanisms that also play role in atherosclerosis progression, NRP is a mechanoimmunological process which is independent from atherosclerosis. For example, procedural and mechanic factors such as high thrombotic burden, delayed presentation, high pressure balloon inflations, and use of debulking tools, and also distal embolization, play role in the pathophysiology of NRP.[28] Such factors may have confounded a probable independent relationship between AIP and NRP in our study.

The independent association between troponin levels and NRP may not be surprising which is a finding consistent with a recent study.[29] It can be suggested that impaired myocardial perfusion subsequent to NRP occurrence might be the link between NRP and troponin increase. On the other hand, this association might be at a pathophysiological level. A recent study suggested association between inflammatory markers and peak troponin levels in ACS patient population.[30] Given the association of inflammation in both NRP occurrence and troponin release from cardiomyocytes, it is logical to suggest that this association might be a consequence of increased inflammatory activity. Our data also demonstrated a correlation between logarithmically transformed peak troponin

levels and CRP, which is a well-known inflammation marker ($r = 0.11$, $P = .001$) (data not presented).

The study has many limitations. First, we did not carry out the other diagnostic approaches of myocardial perfusion, such as coronary magnetic resonance imaging. Second, consecutive AIP measurements could provide us to understand the effect of consecutive changes of AIP in this process more precisely. Finally, this was a single center and retrospectively designed study. For instance, lack of many variables including duration of patients' admission to the hospital might have affected the results. Prospectively designed multicenter studies are required in order to investigate the association between AIP and NRP more comprehensively. Therefore, our observational and retrospectively designed study should be considered hypothesis-generating only.

In conclusion, AIP level on admission is not a statistically significant prognostic factor of NRP in ACS patients. However, peak troponin T (log10) is an independent prognostic parameter of NRP occurrence.

**Data Availability Statement:** The data used to support the findings of this study are available from the corresponding author upon reasonable request.

**Ethics Committee Approval:** All procedures performed in studies involving human participants were in accordance with the ethical standards of the Institutional and/or National Research Committee and with the Helsinki Declaration and its later amendments or comparable ethical standards. The study protocol was approved by the Local Ethics Committee of the hospital (October 27, 2021/E-21-786).

**Informed Consent:** Informed consent from the patients was waived with the approval of the study protocol by the Local Ethics Committee of the hospital (October 27, 2021/E-21-786).

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept – İ.E.Ç., M.Y., O.B., O.A., M.D., Ş.Y., S.Ö., S.N.M.; Design – İ.E.Ç., M.Y., O.B., O.A., M.D., Ş.Y., S.Ö., S.N.M.; Supervision – M.Y., M.D., S.Ö., S.N.M.; Resources – İ.E.Ç., M.Y., O.B., O.A., Ş.Y.; Materials – İ.E.Ç., M.Y., O.B., O.A., M.D., Ş.Y., S.Ö., S.N.M.; Data Collection and/or Processing – İ.E.Ç., M.Y., O.B., O.A., M.D., Ş.Y.; Analysis and/or Interpretation – İ.E.Ç., M.Y., S.Ö., S.N.M.; Literature Search – İ.E.Ç., M.Y., O.B., Ş.Y., S.Ö.; Writing – İ.E.Ç., M.Y., O.B., S.Ö.; Critical Review – İ.E.Ç., M.Y., O.B., O.A., M.D., Ş.Y., S.Ö., S.N.M.

**Declaration of Interests:** The authors have no conflict of interest to declare.

**Funding:** The authors declared that this study has received no financial support.

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