European Review for Medical and Pharmacological Sciences 2023; 27: 3993-4005

Atherogenic index of plasma and triglyceride-glucose index to predict more advanced coronary artery diseases in patients with the first diagnosis of acute coronary syndrome

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Abstract. – OBJECTIVE: Coronary heart disease (CHD) is the most common cause of mortality and morbidity. Acute coronary syndrome (ACS) is the most advanced form of the CHD spectrum. The triglyceride-glucose index (TGI) and atherogenic plasma index (AIP) are associated with future cardiovascular events. This study investigated the association of these parameters with the severity of CAD and prognosis in the first-diagnosed ACS patients.

PATIENTS AND METHODS: Our study was designed retrospectively, including 558 patients. Patients were divided into four subgroups: high and low TGI and high and low AIP. SYNTAX scores, in-hospital mortality, major adverse cardiac events (MACE), and survival were compared at 12-month follow-up.

RESULTS: More three-vessel disease and higher SYNTAX scores have been detected in the high AIP and TGI groups. More MACEs have been observed in high AIP and TGI groups than low groups. AIP and TGI were found to be independent predictors for SYNTAX ≥23. While AIP has been found to be an independent risk factor for MACE, TGI has not been detected as an independent risk factor. In addition to AIP, age, three-vessel disease, and lower EF were the independent risk factors for MACE. Survival was lower in high TGP and AIP groups.

CONCLUSIONS: AIP and TGI are costless bedside parameters that can be easily calculated. These parameters can predict the severity of CAD in first-diagnosed ACS patients. Besides, AIP is an independent risk factor for MACE. AIP and TGI parameters can guide our treatment in this patient population.

Key Words:
Acute coronary syndrome, Atherogenic index of plasma, Triglyceride-glucose index, SYNTAX score.

Introduction

Coronary heart disease (CHD) is the most common cause of morbidity and mortality[1,2]. Acute coronary syndrome (ACS) is the most severe type of CHD[3,4]. Thus, it is important to detect patients with a high risk for future adverse cardiovascular events (CVE) to take precautions in advance. ACS consists of ST-elevation ACS (STE-ACS) and non-ST-elevation ACS (NSTE- myocardial infarction and unstable angina)[5,6].

Hypertriglyceridemia (HTG) was found to be an independent risk factor for glucose metabolism disorders and was associated with elevated levels of glucose[7-9]. Metabolic syndrome (MetS) is one of the most significant risk factors for cardiovascular diseases (CVD). High levels of triglyceride (TG) and fasting blood glucose (FBG) are the constituents of MetS[10,11]. The triglyceride-glucose (TyG) index consisting of those components of MetS has a significant association with insulin resistance (IR) and has been demonstrated to be an indicator of IR[12-14]. Several recent studies[15,16] have found a relation between the TyG index and vascular diseases. Though most studies[17-19] regarding the TyG index centered on metabolic diseases, no studies have excessively investigated the role of this index in patients with a first-time ACS. So, one of the objectives of this study was to evaluate the effects of the TyG index on cardiovascular outcomes in this patient population.

The combination of high levels of fasting blood TG and low levels of high-density lipoprotein cholesterol (HDL-c) has been named atherogenic

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dyslipidemia[20]. Low-density lipoprotein- cholesterol (LDL-c) particle has a pivotal role in the development of CHD. A superior relationship between small dense LDL-C (sdLDL) particles and premature atherosclerosis compared to large LDL-C particles has been found by Gentile et al[21]. Nevertheless, the measurement of sdLDL has been found to be more complicated, due to the complexity and cost of the measurement method. The atherogenic index of plasma (AIP) reflects a correlation with smaller LDL-c particles and increased fractional esterification rate for cholesterol in plasma[22-25]. AIP formulated as $\log^{10}$ [TG/ HDL-c] by Dobiasova et al[22] has also been associated with obesity, hypertension, diabetes mellitus (DM), CHD, and CVE. AIP was also a better predictor of CHD compared to other traditional pro-atherogenic lipid profiles[26-29].

We therefore aimed at investigating the association between TyG index and AIP and the severity of CHD based on SYNTAX [the anatomical synergy between percutaneous coronary intervention (PCI) with taxus and cardiac surgery] score and the impact of these parameters on cardiovascular outcomes in patients with a first diagnosis of ACS.

Patients and Methods

Patient Selection and Study Design

We retrospectively analyzed the data of 1,154 consecutive patients with a diagnosis of ACS who underwent urgent coronary angiography (CA) in Ankara City Cardiovascular Hospital and Ankara Yüksek Ihtisas University Training and Research Hospital between January 2017 and December 2018. Patients with a history of previous myocardial infarction, prior stent placement, or bypass grafting were excluded from the study to obtain a more homogeneous study group in the ACS group. Patients on a statin and triglyceride-lowering medication were also excluded. Other exclusion criteria were as follows: incomplete lipid profile, heart failure, malignancy, severe renal insufficiency, nephrotic syndrome, myocarditis, infectious endocarditis, active infection, and systemic diseases. Our study was conducted after the approval of Ankara City Cardiovascular Hospital and Ankara Yüksek Ihtisas University Training and Research Hospital Ethical Committee, and informed consent was obtained from all patients.

Of this study population, 420 patients had previously CAD, a history of stent implantation, CABG, and 176 patients had other exclusion criteria. The remaining 558 patients met the inclusion criteria for the study. Patients were divided into the following groups, according to the median value of TGI and AIP: low TGI index group and high TGI index group, and low AIP index and high AIP index group (Figure 1).

Trained physicians recorded clinical data, including demographic features, medical history, laboratory parameters. Risk factors for CHD comprised of cigarette smoking, hyperlipidemia [total cholesterol (TC) levels of 200 mg/dl or higher], family history of CHD (first-degree relatives before the age of 55 in men and 65 years in women), hypertension (systolic blood pressure ≥140 and/or diastolic ≥90 mmHg or on anti-hypertensive treatment), DM (FBG of 126 mg/dl or higher or 2-h serum glucose of the oral glucose tolerance test ≥200 mg/dl or the use of anti-diabetic medication) were recorded. BMI was calculated according to the formula as weight/height^2, kg/m^2.

ACS population consisted of NSTE-ACS and STE-ACS. CA was performed by standard Judkins techniques *via* radial or femoral approach. During cardiac catheterization, nitroglycerin was given to all patients with suspicion of having a coronary spasm. Each coronary artery was viewed on at least two different planes. All the coronary angiograms were recorded on compact disks (DICOM format). In need, PCI was carried out by using standard techniques. CHD was determined on the quantitative CA as coronary stenosis ≥50% luminal diameter narrowing. ACS group was classified according to 1-, 2- or 3-vessel disease. The number of vessels with coronary artery lesion was calculated by counting the major coronary artery stenosis ≥50%, including the left main (LM), left anterior descending (LAD), left circumflex (LCX), right coronary artery (RCA), and main branches (diagonal, etc.) bigger than 1.5 mm. The SYNTAX score was calculated by two interventional cardiologists blinded to patients' clinical and laboratory data. For all coronary lesions with >50% diameter stenosis in a vessel >1.5 mm, SYNTAX score calculator 2.28 (available at: www.syntaxscore.com) was used to determine the SYNTAX score.

Follow-up data of all patients for 12 months for major adverse cardiovascular events (MACEs) was acquired from hospital records or by interviewing patients and their families in person or by phone. MACEs were defined as the composite of cardiac death, nonfatal myocardial infarction,

target vessel revascularization (TVR), congestive heart failure (CHF), and nonfatal stroke. Cardiac death was accepted as death primarily due to acute myocardial infarction (MI), CHF, and malignant arrhythmia.

Laboratory Analysis

Blood samples were drawn from each patient's antecubital vein on admission and the first morning after at least 12-h fasting. Biochemical parameters such as TC, TG, LDL-c, HDL-c, fasting blood glucose, creatinine, troponin-I and C-reactive protein (CRP), white blood cell count (WBC), platelet count, and hemoglobin concentration were measured by utilizing the standard methods.

Statistical Analysis

All statistical analyses were performed using SPSS for Windows version 21.0 (IBM Corp., Armonk, NY, USA). Since continuous variables did not show normal distribution, they were given a median and interquartile range (IQR). The Kolmogorov-Smirnov test was used to evaluate the distribution of continuous variables. The Mann-Whitney U test was used to compare two groups that did not show normal distribution. The χ^2 and Fisher's Exact tests were used in the comparison of categorical variables between groups.

Patients were divided into groups, as mentioned earlier, with the median value of TGI and AIP, respectively. For correlation analysis, Spearmen's correlation analysis was used to evaluate the correlation of SYNTAX score with TGI and AIP parameters. Patients with correlation coefficient <0.25 were assessed as 'weak correlation', ≥0.25 and <0.50 as 'moderate correlation', ≥0.50 and <0.75 as 'strong correlation', and ≥0.75 as very strong correlation.

Independent risk factors affecting SYNTAX score ≥23 were evaluated by binary logistic regression analysis. Univariate analysis and multivariate logistic regression analysis with the Enter method were used to determine the independent predictors of SYNTAX score ≥23. ROC analysis was also performed to determine the best discriminative values of TGI and AIP for the SYNTAX score ≥23.

Cox regression analysis was performed to determine the risk factors for MACE and in-hospital mortality. All variables were first included in

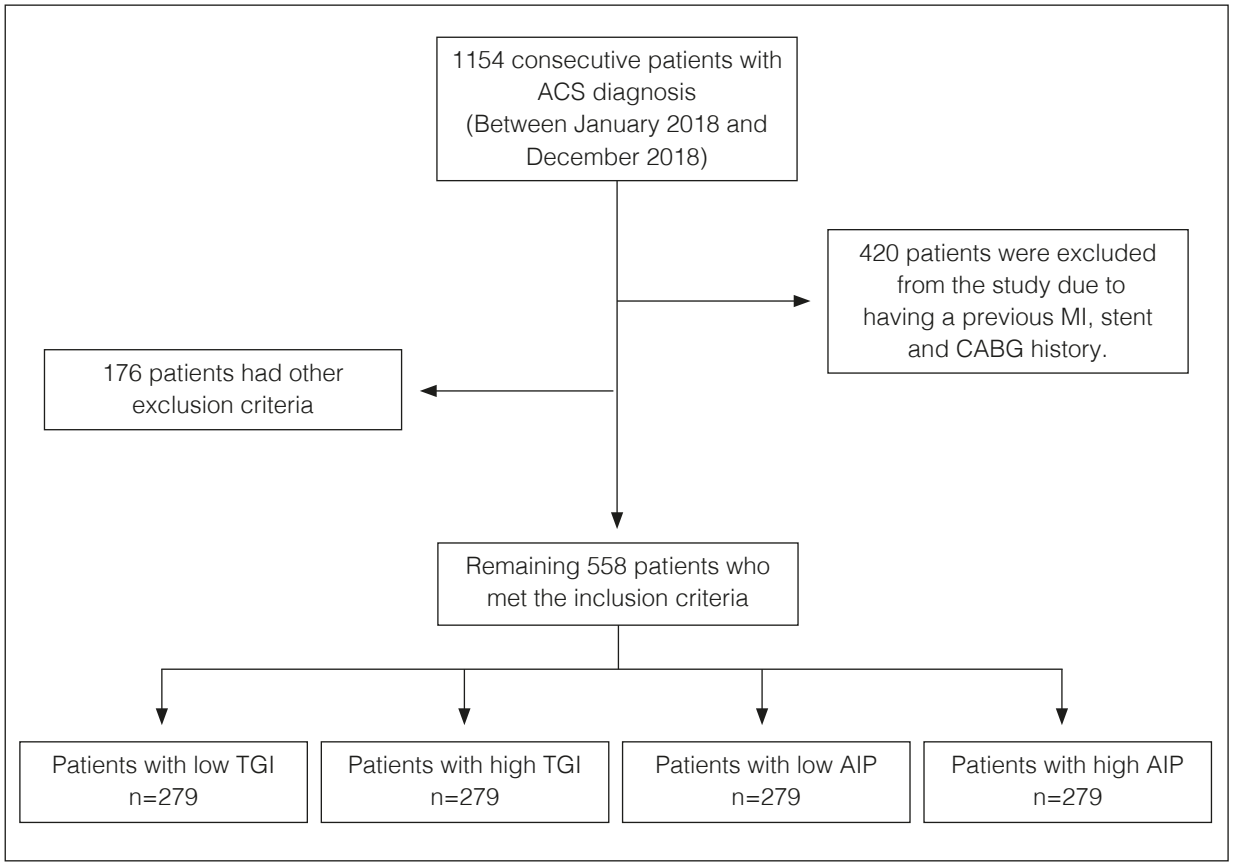

Figure 1. Flow chart of the study population.

univariate Cox Regression analysis. Variables with *p*-value below 0.10 were assumed as potential risk factors and included in multivariate Cox Regression analysis. MACE rates and survival times in the groups were evaluated by Kaplan-Meier analysis. The *p*-value below 0.05 was considered to be statistically significant.

Results

Since AIP and TGI groups were non-homogeneously distributed, the patients were divided into two subgroups, according to the median value. The median values for TGI and AIP were 0.50 and 4.65, respectively. AIP and TGI groups were divided into high and low groups, according to those median values.

The demographic and angiographic characteristics of ACS groups based on AIP subgroups are shown in Table I. The BMI of the high AIP group was significantly higher than the low AIP group (p=0.015). Hyperlipidemia (p<0.001) and family history (p=0.005) were significantly higher in the high AIP group. Although DM was more common in the high AIP group, it could not reach statistical significance (p=0.067). The three-vessel disease was more common in the high AIP group, while single vessel disease was more common in the low AIP group. The SYNTAX score of the high AIP group was significantly higher than the the score of the low AIP group (p<0.001). There was no significant difference between the two groups in terms of the ACS type. Both PCI and CABG treatment were performed more in the high AIP group. In-hospital mortality of the study population was found to be 2.9% (Table I). In-hospital mortality was higher in the high AIP group (1.1% *vs.* 4.7%, p=0.022). MACEs occurred as 34.1% in the high AIP group and 15.1% in the low AIP group (p<0.001). While there was no difference for both groups in terms of non-fatal CVE (p=0.339), cardiac death (p=0.001), non-fatal MI (p=0.006), TVR (p=0.001) and CHF (p=0.001) were found to be more common in the high AIP group. Laboratory parameters of ACS groups with low and high AIP are shown in Table I. While glucose and TG are higher in the high AIP group, HDL-c and LVEF were lower. There was no statistical difference between the two groups in terms of other parameters.

The demographic and angiographic properties of ACS groups with low and high TGI are shown in Table II. The BMI of the high TGI group was significantly higher than in the low TGI group (p=0.012). Hyperlipidemia (p<0.001), DM (p<0.001), and family history (p=0.005) were found to be significantly higher in the high TGI group. The three-vessel disease was more common in the high TGI group, while single vessel disease was more common in the low TGI group. The SYNTAX score of the high TGI group was found to be significantly higher than the score of the low TGI group [24 (10.5) *vs.* 14 (10), p<0.001]. There was no significant difference between the two groups in terms of the ACS type. In-hospital mortality and MACE, according to TGI subgroups, are shown in Table II. In-hospital mortality was higher in the high AIP group (1.1% *vs.* 4.7%, p=0.022). MACE's were detected to be 35.8% in the high TGI group and 13.3% in the low TGI group (p<0.001). Non-fatal CVE (p=0.026), cardiac death (p<0.001), non-fatal MI (p<0.001), TVR (p<0.001) and CHF (p=0.001) were more common in the high TGI group. Laboratory parameters of ACS groups with low and high TGI are shown in Table II. While glucose and TG were higher in the high TGI group, HDL-c and LVEF parameters were lower. Also, WBC was higher in the high TGI group (p=0.036). There was no statistical difference between the two groups in terms of other parameters.

Correlation analyses are shown in Figure 2. According to Spearman's rho correlation test, a strong positive and statistically significant correlation was found between the patients' SYNTAX scores and TGI (r=0.538, p<0.001). A moderately positive and statistically significant correlation was found between the patients' SYNTAX scores and AIP (r=0.418, p<0.001). Best discriminative values of TGI and AIP for the SYNTAX score ≥23 were found to be 4.8897 and 0.5101 in ROC analysis, respectively (Figure 3).

We performed univariate and multiple logistic regression analyses for the SYNTAX ≥23 score predictors, as depicted in Table III. In univariate regression analysis, age, BMI, family history, LDL, DM, hyperlipidemia, LVEF, AIP, and TGI were associated with a SYNTAX score ≥ of 23 (p<0.05; see Table III for p). High AIP and TGI values have been found to be independent predictors of SYNTAX score ≥23 after multiple logistic regression analysis (OR=1.378; 95% CI: 1.106-1.716; p=0.004 and OR=1.610; 95% CI: 1.317-1.968; p<0.001, respectively).

Cox regression analysis was performed to determine the risk factors for MACE and in-hospital

Table I. Demographic and angiographic features, In-hospital mortality and MACE, and laboratory parameters of the study population, according to AIP subgroups (n=558).

Variables	Total (n=558)	Low AIP (≤0.50, n=279)	High AIP (>0.50, n=279)	*p*-value
Age	59 (18)	60 (18)	59 (17)	0.415
BMI, kg/m²	26 (3.2)	25.7 (3.5)	26.1 (3.3)	**0.015**
Male, n (%)	422 (75.8)	201 (72.0)	221 (79.5)	**0.040**
Hyperlipidemia, n (%)	193 (34.6)	54 (19.4)	139 (49.8)	**<0.001**
Diabetes Mellitus, n (%)	213 (38.2)	96 (34.4)	117 (41.9)	0.067
Hypertension, n (%)	219 (39.2)	114 (40.9)	105 (37.6)	0.435
Current smoker, n (%)	189 (33.9)	85 (30.5)	104 (37.3)	0.089
Family History, n (%)	86 (15.4)	31 (11.1)	55 (19.7)	**0.005**
Glucose, mg/dL	108 (30)	103 (29)	113 (36)	**<0.001**
Creatinine, mg/dL	0.91 (0.26)	0.88 (0.26)	0.92 (0.28)	0.093
Triglyceride, mg/dL	132 (46)	110 (30)	154 (31)	**<0.001**
Total cholesterol, mg/dL	181 (55)	180 (58)	184.5 (54)	0.266
LDL-C, mg/dL	116 (41)	115 (44)	120 (40)	0.098
HDL-C, mg/dL	41 (8)	44.5 (7)	39 (9)	<0.001
Hemoglobine, g/dL	14.2 (2.3)	14.2 (2.1)	14.1 (2.5)	0.853
WBC,10^3/mm³	10.9 (4.4)	10.8 (4.3)	11.0 (4.5)	0.205
Platelet, 10^3/mm³	236 (84)	234 (78)	245 (88)	0.286
Neutrophil, 10^3/mm³	7.5 (4.7)	7.5 (4.4)	7.4 (4.8)	0.934
CRP,mg/L	4.5 (6.9)	4.3 (5.8)	4.8 (8.9)	0.062
LVEF, %	49 (15)	50 (15)	47 (13)	**<0.006**
Peak troponin-T, ng/mL	2.9 (9.9)	2.94 (13.4)	2.83 (8.4)	0.577
Angiographic findings				
One vessel disease, n (%)	152 (27.2)	97 (34.8)	55(19.7)	**<0.001**
Three vessel disease, n (%)	189 (33.9)	76 (27.2)	113 (40.5)	**0.001**
SYNTAX score	19 (12.6)	15.0 (10)	23.5 (12)	**<0.001**
ACS subtype and treatment				
STE-ACS, n (%)	318 (57)	158 (56.6)	160 (57.3)	0.864
NSTE-ACS, n (%)	240 (43)	121 (43.4)	119 (42.7)	0.932
CABG, n (%)	55 (9.9)	27 (9.7)	28 (10.0)	0.887
PCI and CABG, n (%)	40 (7.2)	13 (4.7)	27 (9.7)	**0.032**
Medical, n (%)	8 (1.4)	8 (2.9)	0 (0)	**0.007**
Only PCI, n (%)	462 (82.8)	234 (83.9)	228 (81.7)	0.501
In hospital mortality, n (%)	16 (2.9)	3 (1.1)	13 (4.7)	0.022
MACE, n (%)	137 (24.6)	42 (15.1)	95 (34.1)	<0.001
Cardiac death, n (%)	28 (5)	5 (1.8)	23 (8.2)	0.001
Non-fatal MI, n (%)	42 (7.5)	12 (4.3)	30 (10.8)	0.006
TVR, n (%)	76 (13.6)	25 (9.0)	51 (18.3)	0.001
Non-fatal CVE, n (%)	10 (1.8)	3 (1.1)	7 (2.5)	0.339
CHF,n (%)	58 (10.4)	17 (6.1)	41 (14.7)	0.001

Data are given as n (%) and median (IQR; interquartile range). ACS, Acute coronary syndrome; BMI, body mass index; CABG, coronary artery bypass grafting; NSTE-ACS, Non-ST elevation ACS; PCI, percutaneous coronary intervention; STE-ACS, ST elevation ACS; SYNTAX, The anatomical synergy between PCI with taxus and cardiac surgery. CHF, congestive heart failure; MI, myocardial infarction; MACE, major adverse cardiac events; CVE, cerebrovascular events; TVR, target vessel revascularization CRP, C-reactive protein; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LVEF, left ventricular ejection fraction; WBC, white blood cell.

mortality. In univariate analysis, age, three-vessel disease, family history, smoking, DM, EF, CRP, AIP, and TGI were found statistically significant for MACE ($p<0.05$; see Table IV for p). As a result of multivariate analysis, age, three-vessel disease, EF, and AIP, which were significant in univariate analysis, were determined to be independent risk factors. After a multivariate analysis, TGI lost its statistical significance (HR for AIP=1.324; 95% CI: 1.157-1.515; $p<0.001$ and HR for TGI=0.977; 95% CI: 0.919-1.040; $p=0.466$). After removing AIP from the model, multivariate Cox regression analysis was again performed by the Enter method. Although TGI approached the statistically significant value as a risk factor, it did not reach significance (HR=1.049; 95% CI: 0.999-1.101; $p=0.053$) (Table V).

Kaplan-Meier analysis for MACE occurrence time is shown for AIP and TGI subgroups in Table VI. High TGI and AIP groups had MACEs

Table II. Demograpic and angiographic features , In-hospital mortality and MACE, and laboratory parameters of the study population, according to TGI subgroups (n=558).

Variables	Total (n=558)	Low TGI (≤0.50, n=279)	High TGI (>0.50, n=279)	*p*-value
Age	59 (18)	60.58±11.79	60.27±12.62	0.758
BMI, kg	26 (3.2)	25.9 (3.2)	26.04 (3.3)	**0.012**
Male, n (%)	422 (75.8)	221 (79.5)	201 (72.0)	**0.040**
Hyperlipidemia, n (%)	193 (34.6)	55 (19.7)	138 (49.5)	**<0.001**
Diabetes Mellitus, n (%)	213 (38.2)	58 (20.8)	155 (55.6)	**<0.001**
Hypertension, n (%)	219 (39.2)	100 (35.8)	119 (42.7)	0.100
Current smoker, n (%)	189 (33.9)	103 (36.9)	86 (30.8)	0.128
Family History, n (%)	86 (15.4)	31 (11.1)	55 (19.7)	**0.005**
Glucose, mg/dL	108 (30)	98 (17)	124 (39)	**<0.001**
Creatinine, mg/dL	0.91 (0.26)	0.9 (0.26)	0.91 (0.28)	0.483
Triglyceride, mg/dL	132 (46)	111 (32)	153.5 (35)	**<0.001**
Total cholesterol, mg/dL	181 (55)	177 (53)	186 (55)	0.076
LDL-C, mg/dL	116 (41)	116 (44)	117 (41)	0.349
HDL-C, mg/dL	41 (8)	42 (8)	41 (9)	**<0.001**
Hemoglobine, g/dL	14.2 (2.3)	14.3 (2.1)	14.1 (2.4)	0.864
WBC, $10^3/mm^3$	10.9 (4.4)	10.5 (4.3)	11.1 (4.7)	**0.036**
Platelet, $10^3/mm^3$	236 (84)	234 (80)	246 (86)	0.149
Neutrophil, $10^3/mm^3$	7.5 (4.7)	7.15 (4.3)	7.8 (5.0)	0.111
CRP,mg/L	4.5 (6.9)	4.3 (6.0)	5.0 (8.5)	0.086
LVEF, %	49 (15)	50 (14)	45 (13)	**0.001**
Peak troponin-T, ng/mL	2.9 (9.9)	2.57 (12.7)	3.18 (8.91)	0.612
Angiographic findings				
One vessel disease, n (%)	152 (27.2)	95 (34.1)	57 (20.4)	**<0.001**
Three vessel disease, n (%)	189 (33.9)	73 (26.2)	116 (41.6)	**0.001**
SYNTAX score	19 (12.6)	14 (10)	24 (10.5)	**<0.001**
ACS subtype and treatment				
STE-ACS, n (%)	318 (57)	154 (55.2)	164 (58.8)	0.393
NSTE-ACS, n (%)	240 (43)	125 (44.8)	115 (41.2)	0.392
CABG, n (%)	55 (9.9)	17 (6.1)	39 (13.6)	**<0.003**
PCI and CABG, n (%)	40 (7.2)	10 (3.6)	30 (10.8)	**0.002**
Medical, n (%)	8 (1.4)	7 (2.5)	1 (0.4)	0.068
Only PCI, n (%)	462 (82.8)	242 (86.7)	220 (78.9)	**0.014**
In hospital mortality, n (%)	16 (2.9)	3 (1.1)	13 (4.7)	**0.022**
MACE, n (%)	137 (24.6)	37 (13.3)	100 (35.8)	**<0.001**
Cardiac death, n (%)	28 (5)	4 (1.4)	24 (8.6)	**<0.001**
Non-fatal MI, n (%)	42 (7.5)	9 (3.2)	33 (11.8)	**<0.001**
TVR, n (%)	76 (13.6)	23 (8.2)	53 (19.0)	**<0.001**
Non-fatal CVE, n (%)	10 (1.8)	1 (0.4)	9 (3.2)	**0.026**
CHF, n (%)	58 (10.4)	12 (4.3)	46 (16.5)	**<0.001**

Data are given as n (%) and median (IQR; interquartile range). ACS, Acute coronary syndrome; BMI, body mass index; CABG, coronary artery bypass grafting; NSTE-ACS, Non-ST elevation ACS; PCI, percutaneous coronary intervention; STE-ACS, ST elevation ACS; SYNTAX, The anatomical synergy between PCI with taxus and cardiac surgery. CHF, congestive heart failure; MI, myocardial infarction; MACE, major adverse cardiac events; CVE, cerebrovascular events; TVR, target vessel revascularization CRP, C-reactive protein; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LVEF, left ventricular ejection fraction; WBC, white blood cell.

(Figure 4). The patients were divided into high AIP, low AIP, high TGI, low TGI, and both AIP and TGI high groups (Table VI). There was no difference between high TGI, AIP, and both AIP and TGI high groups in terms of MACE occurrence time. Kaplan-Meier LongRank curve for MACE in 5 groups are presented in Figure 4. Survival times, according to AIP and TGI groups, are presented in Table VII. The average survival time in high TGI and AIP groups was lower than in low TGI and AIP groups. Survival Kaplan-Meier graphs for AIP and TGI are given in Figure 5.

Discussion

In this study, high TGI and AIP levels were found to be independent predictors for an advanced form of CAD. High TGI and AIP groups

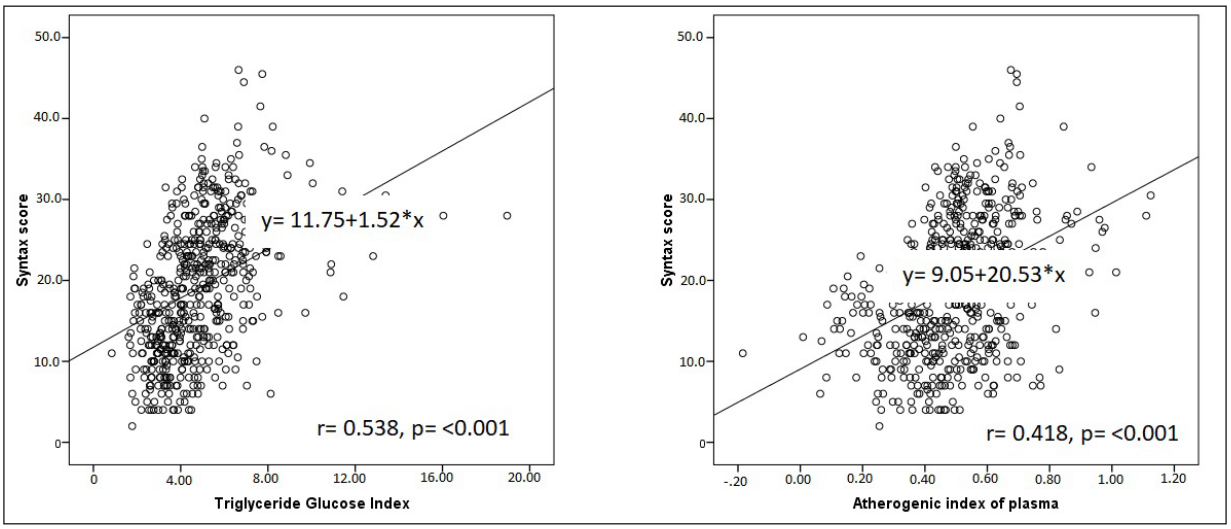

Figure 2. Correlation of AIP and TGI with SYNTAX score by Spearman analysis.

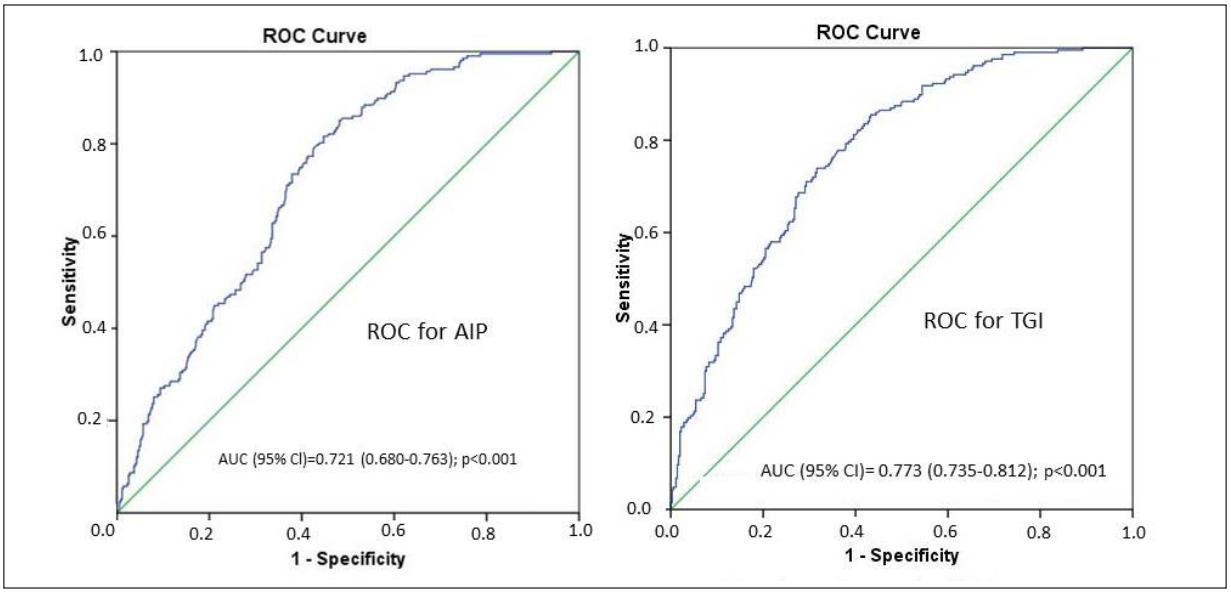

Figure 3. ROC analyses of AIP and TGI to predict SYNTAX score ≥23. AUC; Area under curve.

had higher SYNTAX scores compared to lower groups. In addition, MACEs were more detected in high AIP and TGI groups in the 12-month follow-up. Cardiac death, non-fatal MI, TVR, and CHF that constitute MACEs occurred more often in high TGI and AIP groups at 12-month follow-up compared to the low groups.

While non-fatal CVE occurred more in the high TGI group than in the low group, no statistically significant difference was observed between the high and low AIP groups in non-fatal CVE. Freiberg et al[30] found a close association between high fasting TG levels and ischemic stroke. However, hyperglycemia was associated with stroke and poor prognosis after stroke[31]. Since TGI is the product of TG and glucose parameters, it can be expected to increase the risk of ischemic stroke if it is high. AIP was not associated with stroke in the study performed by Koca et al[32]. In this trial, there was also no difference between high and low AIP groups in terms of non-fatal stroke.

Insulin resistance is one of the primary mechanisms in the development of MetS[17,33,34]. High TGI is a good indicator of insulin resistance. In this study, the BMI of the patients in the high

Table III. Multivariate logistic regression analysis showing the predictors of the SYNTAX ≥23.

	Univariate OR (95% CI)	p	Multivariate OR (95% CI)	p
Age	1.017 (1.003-1.032)	**0.018**	1.023 (1.003-1.043)	**.026**
BMI	1.133 (1.064-1.206)	**<0.001**	1.149 (1.066-1.238)	**<0.001**
Family history	1.776 (1.118-2.822)	**0.015**	1.479 (0.821-2.666)	.193
Hypertension	1.147 (0.806-1.633)	0.447	0.702 (0.445-1.108)	.129
Current smoker	0.838 (0.581-1.208)	0.344	1.012 (0.625-1.64)	.960
LDL	1.009 (1.004-1.015)	**0.001**	1.017 (1.01-1.024)	**<0.001**
Diabetes Mellitus	1.675 (1.178-2.381)	**0.004**	0.664 (0.388-1.137)	.135
Hyperlipidemia	1.568 (1.096-2.242)	**0.014**	2.112 (1.261-3.535)	**.004**
LVEF	0.949 (0.930-0.968)	**<0.001**	0.953 (0.93-0.976)	**<0.001**
WBC	1.005 (0.959-1.053)	0.842	0.955 (0.88-1.037)	.278
Neutrophil	1.008 (0.970-1.047)	0.699	0.998 (0.937-1.063)	.956
CRP	1.010 (1.000-1.021)	0.06	1.003 (0.993-1.014)	.567
Peak troponin	0.998 (0.993-1.003)	0.395	0.997 (0.989-1.005)	.415
AIP	1.719 (1.519-1.945)	**<0.001**	1.378 (1.106-1.716)	**.004**
TGI	1.727 (1.503-1.985)	**<0.001**	1.610 (1.317-1.968)	**<0.001**
Constant			-9.159	**<0.001**

Accuracy=76.6%. AIP, atherogenix index of plasma; BMI, body mass index; CRP, C-reactive protein; LDL, low-density lipoprotein; LVEF, left ventricular ejection fraction; TGI, triglyceride-glucose index.

Table VI. Univariate and multivariate Cox proportional hazards regression analysis for MACE.

	Univariate HR (95% CI)	p	Multivariate HR (95% CI)	p
Age	1.043 (1.029-1.058)	**<0.001**	1.041 (1.024-1.058)	**<0.001**
Male	0.757 (0.522-1.097)	0.141		
Three vessel disease	3.013 (2.147- 4.228)	**<0.001**	2.362 (1.660-3.360)	**<0.001**
BMI	1.023 (0.968-1.082)	0.415		
Family history	1.682 (1.122-2.521)	**0.012**	1.379 (0.899-2.117)	0.141
Hypertension	1.346 (0.962-1.885)	0.083	1.202 (0.840-1.721)	0.315
Current smoker	1.209 (1.114-1.411)	**0.012**	1.030 (0.674-1.574)	0.392
Diabetes Mellitus	1.755 (1.255-2.453)	**0.001**	1.420 (0.972-2.075)	0.07
Hyperlipidemia	1.130 (0.799-1.598)	0.489		
Creatinine	1.307 (1.016-1.682)	**0.037**	0.823 (0.553-1.225)	.338
LVEF	0.915 (0.898-0.932)	**<0.001**	0.926 (0.909-0.942)	**<0.001**
CRP	1.008 (1.004-1.013)	**0.001**	1.003 (0.997-1.009)	0.331
AIP	1.314 (1.199-1.441)	**<0.001**	1.324 (1.157-1.515)	**<0.001**
TGI	1.127 (1.088-1.167)	**<0.001**	0.977 (0.919-1.040)	0.466

AIP, atherogenix index of plasma; BMI, body mass index; CRP, C-reactive protein; LDL, low-density lipoprotein; LVEF, left ventricular ejection fraction; TGI, triglyceride-glucose index.

TGI group was higher. This finding is compatible with abdominal obesity, which is one of the basic diagnostic criteria of MetS. In other studies[35,36], high TGI was found to be a risk factor for the development of DM, while DM was found to be statistically higher in the high TGI group in this study population. High AIP has also been found[37] to be a risk factor for the development of DM. However, this study showed no difference in DM between high and low AIP groups. Since these groups were not followed in terms of DM development, it does not mean that AIP is not a risk factor for DM.

HTG, low LDL, and high TG/HDL ratio have been associated[38,39] with thrombus formation caused by plaque rupture. In addition to that, AIP is an independent risk factor for CAD development in both men and women[37]. High triglyceride and low HDL cholesterol levels have been found[40] to be at least as strong predictors of vascular events as metabolic syndrome in a population of patients with angiographically determined coronary artery disease. AIP has been found[41] to be a risk factor for multi-vessel disease in patients with stable CAD. Nevertheless, high TGI was found[42]

to be an independent risk factor in terms of the severity of CAD in NSTE-ACS patients. In this study, more three-vessel disease was found in the high AIP and TGI group. Also, AIP and TGI were detected to be independent risk factors for high SYNTAX scores in patients with first-diagnosed ACS.

In our study, EF was significantly lower in high TGI and AIP groups compared to low groups. Also, more three-vessel diseases and higher SYNTAX scores in high AIP and TGI groups indicate that the ischemic burden is higher in these groups. The lower EF in the high TGI and AIP groups can be explained by myocardial stunning caused by ischemic load due to advanced CAD. The CABG procedure as a treatment in high TGI and AIP groups is also in line with the more advanced CAD in this patient group.

It has been reported[43] that the high TG/HDL ratio is a strong independent predictor of all-cause mortality in patients with ACS after coronary

Table V. Cox regression analysis of risk factors with Enter method after exclusion of AIP from the model.

	Multivariate OR (95% CI)	p
Age	1.039 (1.021-1.057)	**<0.001**
BMI	0.985 (0.92-1.053)	0.652
Family history	1.335 (0.852-2.09)	0.207
Hypetension	1.332 (0.903-1.964)	0.149
Current smoker	1.123 (0.725-1.741)	0.603
Diabetes Mellitus	1.286 (0.871-1.9)	0.206
Hyperlipidemia	1.220 (0.817-1.824)	0.331
LVEF	0.922 (0.905-0.94)	**<0.001**
CRP	1.005 (0.998-1.011)	0.149
Peak troponin	0.993 (0.986-1.001)	0.084
Male	1.152 (0.752-1.765)	0.514
Three vessel disease	2.595 (1.81-3.72)	**<0.001**
LDL	0.998 (0.992-1.004)	0.452
Creatinine	0.830 (0.552-1.246)	0.368
TGI	1.049 (0.999-1.101)	0.053

BMI, body mass index; CRP, C-reactive protein; LDL, low-density lipoprotein; LVEF, left ventricular ejection fraction; TGI, triglyceride-glucose index.

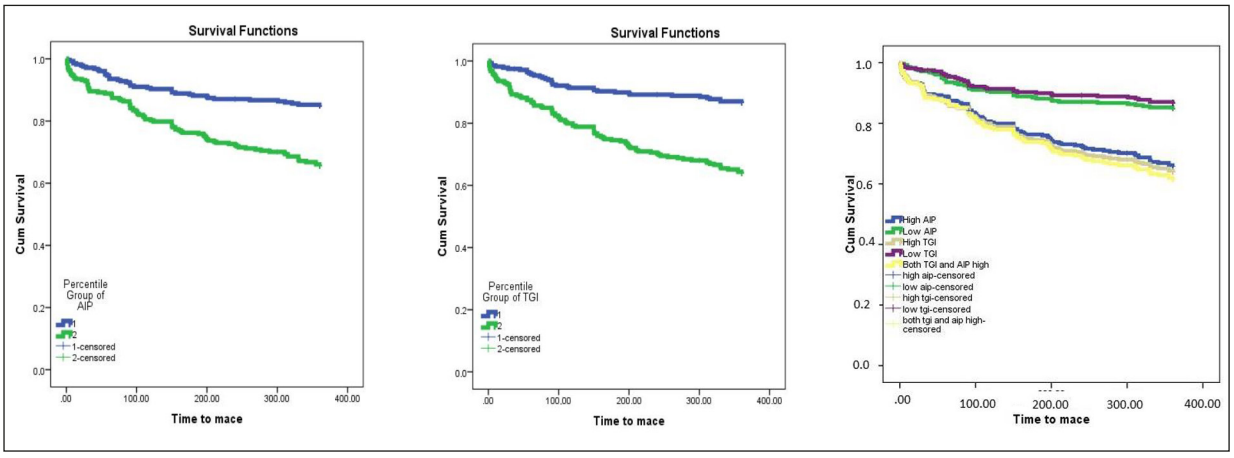

Figure 4. Kaplan-Meier curve for MACE in AIP, TGI and among 5 groups.

revascularization. High TGI has been found to be a strong risk factor associated with future cardiovascular events in stable CAD patients[44]. In this study, we found higher in-hospital mortality and MACE in the high AIP and TGI groups at a 12-month follow-up after ACS. While AIP was found to be an independent risk factor for MACE in 12-month follow-up with multivariate Cox regression analysis, TGI was detected not to be an independent risk factor. However, after AIP was removed from the model, TGI was found not

Table VI. Kaplan-Meier LogRank Test among 5 groups.

	Mean occurence time of MACE (95% CI)	p
High AIP group	284.5 (265.6-303.4)[a]	**<0.001**
Low AIP group	322.2 (309.3-335.0)[b]	
High TGI group	277.9 (259.3- 296.9)[a]	
Low TGI group	329.4 (317.5 – 341.4)[b]	
Both AIP and TGI high	271.8 (254.6-289.1)[a]	

[a,b]There is no difference between groups containing the same letter.

to be an independent risk factor for MACE. TGI not being an independent risk factor for MACE in a 12-month follow-up contradicts with the abovementioned studies. In other studies[42,44], if TGI was evaluated as a risk factor together with AIP, it could lose its significance as a risk factor. So, it can be concluded that AIP is a better risk factor than TGI for cardiovascular events after ACS. Age, low EF, and severe vascular disease are independent risk factors for high MACE and low survival in the short and long term[45]. In this study, age, three-vessel disease, low EF, and AIP have been found to be independent risk factors for MACEs.

The no-reflow phenomenon is one factor that increases the MACE rate by causing inadequate recovery of the infarct area and reverse left ventricular remodeling[46]. AIP has been found[47] to be an independent risk factor for no-reflow in STEMI patients undergoing PCI. In addition, this parameter has been found to be a better predictor than only TG and HDL-c levels[47]. Although there is evidence[48] that hyperglycemia is associated with no-reflow after PCI in ACS, the no-reflow study of TGI in patients with ACS is not yet available in the literature.

Although TGI was not a risk factor for MACE in our study; cardiac death, CHF, TVR, non-ischemic CVE, and non-fatal MI were more common in the high TGI group than in the low group. Also, the high TGI group's survival time was found to be statistically lower at the 12-month follow-up. There was no difference among high TGI, high AIP, and both high AIP and TGI groups in terms of survival. However, these three groups were found to have lower survival times than the low AIP and TGI groups.

Table VII. Kaplan-Meier LogRank Test for survival in AIP and TGI groups.

	Mean survival time (95% CI)	p
Low AIP	354.7 (349.6-359.7)	**<0.001**
High AIP	336.3 (326.2-346.4)	
Low TGI	355.9 (351.6-360.3)	**<0.001**
High TGI	335.0 (339.7-351.2)	

Limitations

The study can be counted as a single-center and retrospective study. A prospective study is required to support the findings due to the limitations arising from the internal design of the retrospective study.

Conclusions

TGI, consisting of metabolic syndrome components, and AIP, a good indicator of atherogenic dyslipidemia, do not require additional costs, and their

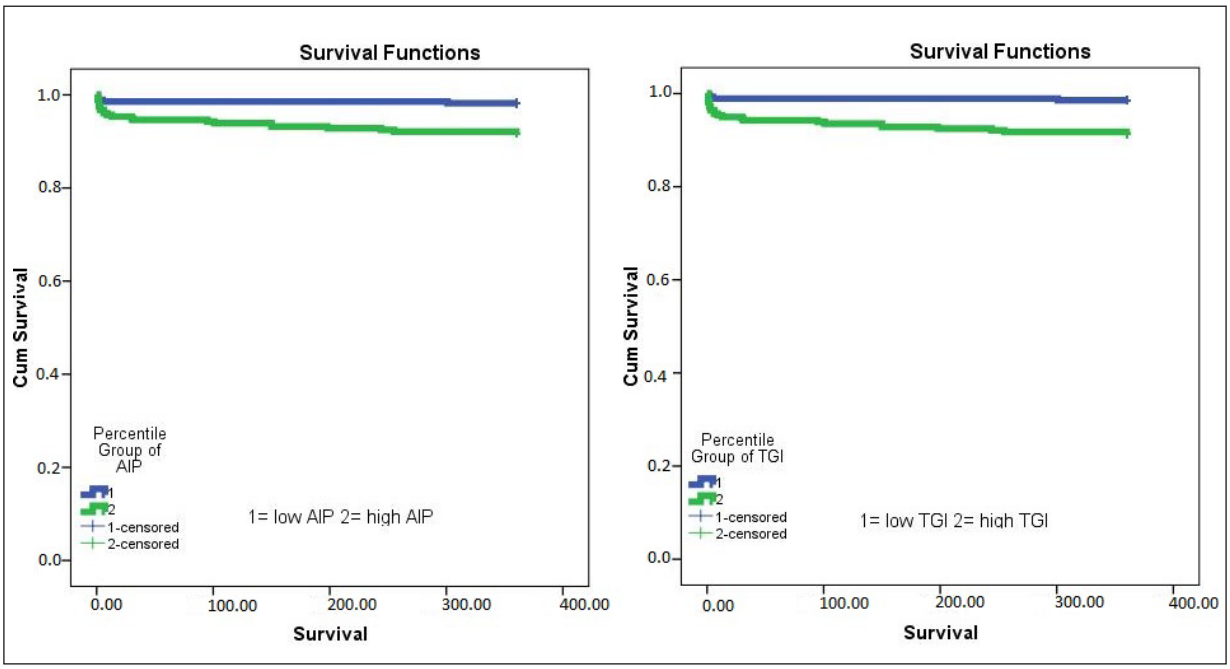

Figure 5. Survival curves for AIP and TGI groups.

calculations are not complicated. These parameters can be used to predict the severity of coronary artery disease in patients with first-diagnosed ACS. AIP is a better predictor than TGI for cardiovascular outcomes in patients with the first diagnosed ACS.

Authors' Contributions

All authors made substantial contributions to (1) conception and design of the study, and acquisition, analysis and interpretation of data, (2) drafting or revising the manuscript to include important intellectual content, and (3) approval of the final version of the manuscript readily to be published.

Conflict of Interest

The authors do not have any potential conflict of interest regarding the research, authorship and/or publication of this article.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Ethics Approval

This retrospective study was approved by the Republic of Turkey's Ministry of Health (No.: E2-22-2775) as well as by Ankara City Cardiovascular Hospital and Ankara Yüksek Ihtisas University Training and Research Hospital Ethics Committee.

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