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Original Article

The Role of Atherogenic and Triglyceride/Glucose Indices in Patients with Multivessel Disease

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Abstract

Objective: Coronary artery disease (CAD) is a major cause of global mortality. Multivessel disease (MVD) is linked to poorer clinical outcomes. Insulin resistance (IR) is a key factor in CAD progression. The triglyceride-glucose (TyG) index and atherogenic index of plasma (AIP) are emerging biomarkers related to IR and cardiovascular risk. Their role in predicting CAD severity is not fully established. This study aimed to evaluate the prognostic value of TyG and AIP indices in assessing CAD severity and distinguishing MVD from single-vessel disease (SVD).

Methods: This retrospective study involved 244 patients undergoing coronary angiography from January 2022 to January 2024. Patients were classified into MVD (n=116) and SVD (n=128) groups. Data on demographics, cardiovascular risk factors, and metabolic parameters were collected. TyG and AIP indices were calculated. Logistic regression and receiver operating characteristic (ROC) curve analyses assessed their predictive value for MVD.

Results: Patients in the MVD group were older than those in the SVD group (64.9±8.3 vs. 60.1±7.8 years; p<0.001) and had a higher prevalence of diabetes mellitus (56.9% vs. 31.3%; p<0.001). In multivariable analysis, the TyG index (odds ratio [OR]: 6.71; 95% confidence interval [CI]: 2.75–16.35; p<0.001) and AIP (OR: 1.66; 95% CI: 1.22–2.24; p=0.001) were identified as independent predictors of MVD. ROC analysis demonstrated that the TyG index had superior diagnostic accuracy compared with AIP (area under the curve: 0.718 vs. 0.643).

Conclusion: TyG and AIP indices are useful biomarkers for CAD severity assessment. The TyG index demonstrated greater predictive accuracy. These indices may enhance clinical risk stratification and treatment decisions. Prospective studies are needed to validate these findings across populations.

Keywords: Atherogenic index of plasma; coronary artery disease; multivessel disease; risk stratification; triglyceride-glucose index.

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Çok Damarlı Hastalığı Olan Hastalarda Aterojenik ve Trigliserit/Glukoz İndekslerinin Rolü

Özet

Amaç: Koroner arter hastalığı (KAH), dünya genelinde mortalitenin önde gelen nedenlerinden biridir. Çoklu damar hastalığı (ÇDH), daha kötü klinik sonuçlarla ilişkili olup hastalık yükünün artmasıyla karakterizedir. İnsülin direnci, KAH'nin gelişimi ve progresyonunda temel patofizyolojik mekanizmalardan biridir. Trigliserid-glukoz indeksi (TGİ) ve aterojenik plazma indeksi (APİ), insülin direnci ve kardiyovasküler risk ile ilişkili yeni biyobelirteçler olarak tanımlanmaktadır. Ancak bu indekslerin KAH şiddetini öngörmedeki ve çoklu damar hastalığını tek damar hastalığından (TDH) ayırt etmedeki klinik değerleri henüz net değildir. Bu çalışmada, TGİ ve APİ'nin KAH şiddetinin değerlendirilmesindeki prognostik değerinin araştırılması ve ÇDH ile TDH'nin ayırt edilmesindeki rollerinin incelenmesi amaçlanmıştır.

Yöntem: Bu retrospektif çalışmaya, Ocak 2022–Ocak 2024 tarihleri arasında koroner anjiyografi uygulanan 244 hasta dahil edilmiştir. Hastalar ÇDH (n=116) ve TDH (n=128) olmak üzere iki gruba ayrılmıştır. Demografik özellikler, kardiyovasküler risk faktörleri ve metabolik parametrelere ilişkin veriler kaydedilmiştir. TGİ ve APİ hesaplanmıştır. Bu indekslerin ÇDH'yi öngörmedeki performansını değerlendirmek amacıyla lojistik regresyon ve ROC eğrisi analizleri uygulanmıştır.

Bulgular: ÇDH grubundaki hastalar TDH grubuna göre daha ileri yaşta idi (64,9±8,3'e karşı 60,1±7,8 yıl; p<0,001) ve diyabet prevalansı daha yüksekti (%56,9'a karşı %31,3; p<0,001). Çok değişkenli analizde TGİ (OR: 6,71; %95 GA: 2,75–16,35; p<0,001) ve APİ (OR: 1,66; %95 GA: 1,22–2,24; p=0,001) ÇDH'nin bağımsız öngördürücüleri olarak saptandı. ROC analizinde TGİ'nin tanısal doğruluğu APİ'ye kıyasla daha yüksekti (AUC: 0,718'e karşı 0,643).

Sonuç: TGİ ve APİ indeksleri, koroner arter hastalığı şiddetinin değerlendirilmesinde yararlı biyobelirteçlerdir. TGİ indeksinin öngördürücü doğruluğu daha yüksek bulunmuştur. Bu indeksler, klinik risk sınıflamasını ve tedaviye yönelik karar süreçlerini geliştirebilir. Bulguların farklı popülasyonlarda doğrulanması için prospektif çalışmalara ihtiyaç vardır.

Anahtar sözcükler: Aterojenik plazma indeksi; koroner arter hastalığı; çoklu damar hastalığı; risk sınıflaması; trigliserid-glukoz indeksi.

Introduction

Cardiovascular diseases continue to account for the majority of deaths worldwide, with coronary artery disease (CAD) representing a substantial share of this burden, as reported by World Health Organization statistics.[1] The healthcare burden of CAD remains significant due to its widespread prevalence; however, proactive screening and optimized clinical management can substantially reduce this impact.[1] Coronary angiography (CAG) remains the standard diagnostic tool for CAD, providing detailed information on coronary anatomy. The extent and severity of multivessel disease (MVD) can be reliably determined.[2]

Insulin resistance (IR) serves as a primary metabolic driver for CAD, impairing glycemic control and accelerating the transition to type 2 diabetes mellitus (DM). Simultaneously, it fuels the atherosclerotic process, correlating with heightened disease severity and unfavorable clinical prognoses.[3]

In recent years, the triglyceride-glucose index (TyG) and plasma atherogenic index of plasma (AIP) have emerged as innovative biomarkers for assessing IR and cardiovascular risks.[4,5] By integrating fasting serum triglycerides and glucose metrics, the TyG provides a quantitative measure of insulin sensitivity. Similarly, the AIP reflects disturbances in the lipid profile and serves as an effective tool in predicting atherogenic potential. Literature indicates that both indices are significant predictors of diabetes, metabolic syndrome, and cardiovascular events. However, data on the impact of TyG and AIP on the severity of CAD remain limited.[5]

This research aims to evaluate the efficacy of the AIP and TyG as prognostic indicators for determining the extent and severity of CAD. By examining the prognostic value of TyG and AIP in differentiating between multivessel and single-vessel lesions, the clinical role of these indices in CAD management will be better understood. In this context, the study seeks to enhance the understanding of the effects of IR and lipid dysfunction on CAD and to optimize treatment strategies based on these insights.

Materials and Methods

Study Population and Design

The present retrospective and cross-sectional research analyzed data from 450 consecutive patients who received their first coronary angiographic assessment over a 2-year period, starting from January 2022. Patients admitted with a diagnosis of acute coronary syndrome (ACS) were included in the study. Individuals under the age of 18, patients with unavailable survival follow-up, those with missing laboratory data, pregnant or breastfeeding women, individuals with severe chronic diseases (such as liver, kidney, or hematological disorders), and patients who had undergone prior coronary revascularization were not included in the analysis. Ultimately, 244 patients were included for analysis. The patients were divided into two groups: Those with ≥50% stenosis in two or more coronary arteries (multivessel lesions, n=116) and those with ≥50% stenosis in a single epicardial coronary artery (single-vessel disease, n=128) (Fig. 1).

Data Collection

Clinical data for this investigation were retrieved directly from the hospital's electronic health record database. Demographic information, cardiovascular risk factors, and medical histories of the patients were recorded. Demographic characteristics included age, sex, height, and body weight. We recorded essential predictors of cardiovascular health, such as patient smoking status and diagnoses of diabetes, hypertension, or dyslipidemia. Clinical assessments also incorporated ejection fraction measurements, while body mass index (BMI) was computed through the conventional formula (kg/m^2).

Laboratory Analyses

Venous blood samples were obtained after at least 8 h of fasting. Measurements included creatinine, fasting plasma glucose, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and total cholesterol. Samples were collected from the antecubital vein in the morning hours. Serum was separated after centrifugation. Lipid profile analyses were performed using the enzymatic method on a Beckman Coulter AU5800 device.

The TyG and AIP were calculated using the following formulas, respectively:[4,5]

TyG=ln (Fasting glucose [mg/dL] × Triglycerides [mg/dL]/2) and AIP=log10 (Triglycerides [mmoL/L]/HDL [mmoL/L]).

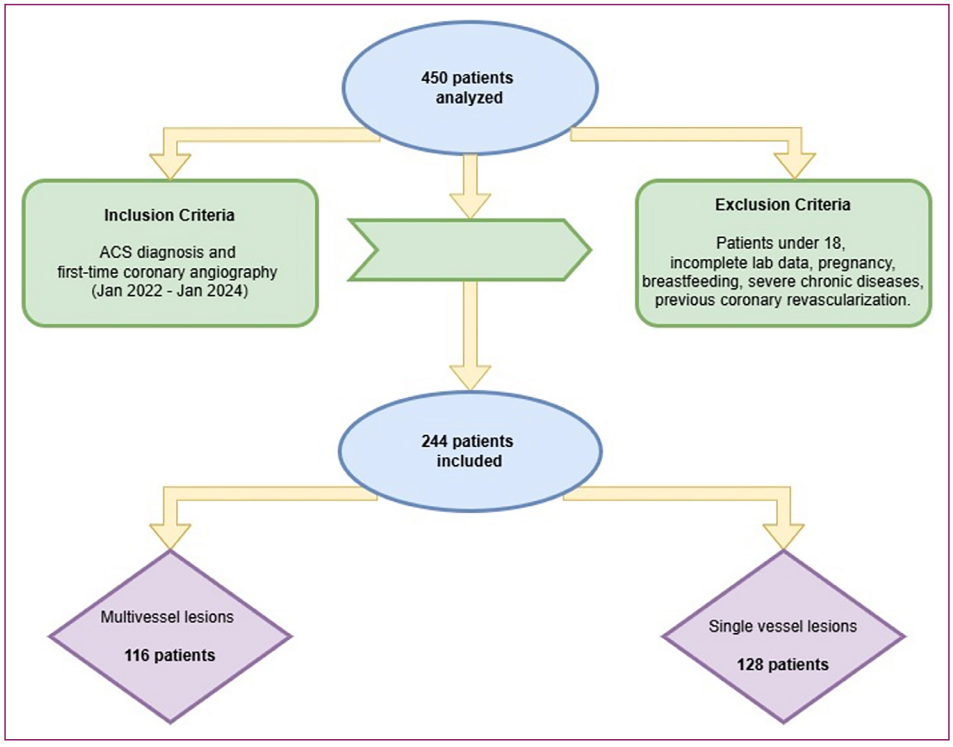


Figure 1. Study flowchart.

Diabetes and ACS Definitions

DM was identified by the administration of antidiabetic agents or insulin, alongside diagnostic thresholds of fasting glucose ≥7.0 mmoL/L or 2-h post-challenge glucose ≥11.1 mmoL/L. Concurrently, ACS was categorized as a range of conditions, including ST-elevation myocardial infarction, non-ST-segment elevation myocardial infarction, and unstable angina. The severity of CAD is measured using CAG, considering the degree of stenosis (%50 or greater) in the arteries. If stenosis of 50% or more is detected in two or more major vessels, it is classified as multivessel disease; if only one vessel is affected, it is classified as single-vessel disease.[6]

Ethics Approval and Informed Consent

Adhering to the ethical principles of the Declaration of Helsinki, this research was authorized by the Mardin Artuklu University (Date: 07.05.2024, Decision no: 2024/5-4). Due to the study's retrospective nature, the institutional board granted a waiver for informed consent from participants.

Statistical Analysis

Statistical processing was executed using the Statistical Package for the Social Sciences version 25.0 (IBM Corp., Armonk, New York, USA). Continuous variables were expressed according to their distribution (normality checked by the Shapiro–Wilk); normally distributed data used mean±standard deviation, whereas non-normal data used medians. To compare MVD and SVD cohorts, we utilized t-tests or Mann–Whitney U protocols, with Chi-square analysis applied to categorical percentages.

To identify independent predictors of multivessel CAD, both univariate and multivariable logistic regression models were constructed. Multivariate regression included variables demonstrating $p<0.10$ in univariate screening, alongside established clinical confounders such as AIP, TyG, age, and gender. The TyG and AIP indices were analyzed in separate multivariable models to avoid collinearity. For multivariable regression analyses, the AIP was standardized (per 1 standard deviation increase) to improve model stability, whereas the TyG was analyzed per 1-unit increase. Descriptive analyses and figures were based on original values. To evaluate the diagnostic accuracy of AIP and TyG in identifying CAD severity, receiver operating characteristic (ROC) curve analysis was employed. The Youden index served as the basis for determining optimal cutoff thresholds, with statistical significance defined by $p<0.05$.

Results

Out of 244 participants, 116 were classified into the MVD cohort and 128 into the SVD group. The MVD subjects exhibited a significantly higher mean age (64.9±8.3 vs. 60.1±7.8 years; $p<0.001$) and a greater prevalence of DM (56.9% vs. 31.3%; $p<0.001$). Conversely, variables such as sex distribution ($p=0.117$), BMI ($p=0.087$), and family history ($p=0.823$) showed no statistical disparity. Both hypertension ($p=0.064$) and smoking ($p=0.058$) were more frequent in the MVD group, though these trends did not reach the standard significance threshold (Table 1).

Laboratory evaluations revealed that the MVD group had significantly elevated levels of fasting blood glucose (158.4±53.7

Table 1. Demographic characteristics and clinical findings

Features	Total n=244	Multivessel disease n=116	Single-vessel disease n=128	p
Age (years)	62.4±8.4	64.9±8.3	60.1±7.8	**<0.001**
Gender, male, n (%)	143(58.6)	74 (63.8)	69 (53.9)	0.117
BMI (kg/m^2)	26.0±2.1	26.3±2.3	25.8±1.9	0.087
Diabetes mellitus, n (%)	106 (43.3)	66 (56.9)	40 (31.3)	**<0.001**
Hypertension, n (%)	130 (53.3)	69 (59.5)	61 (47.7)	0.064
Smoking, n (%)	117 (48.0)	63 (54.3)	54 (42.2)	0.058
Family history, n (%)	88 (36.1)	41 (35.3)	47 (36.7)	0.823
LV EF (%)	53.2±7.8	52.3±8.2	53.9±7.5	0.119
Hemoglobin (g/dL)	12.3±1.9	12.6±2.0	12.2±1.6	0.103
Leukocyte (10^3/uL)	9.8±1.9	9.9±1.7	9.7±2.0	0.319
Fasting blood glucose (mg/dl)	143.4±48.0	158.4±53.7	129.8±37.3	**<0.001**
Creatinine (mg/dl, IQR)	0.93±0.27	0.96±0.28	0.90±0.26	0.104
Uric acid (mg/dL)	5.6±1.4	5.8±1.4	5.5±1.3	0.063
Triglyceride (mg/dL)	165.0±46.4	175.6±45.5	155.3±45.3	**0.001**
LDL (mg/dL)	116.4±28.9	120.8±30.3	112.5±27.1	**0.025**
HDL (mg/dL)	38.3±7.8	37.0±6.5	39.5±8.7	**0.013**
TyG	9.3±0.4	9.5±0.4	9.1±0.4	**<0.001**
AIP	0.62±0.16	0.66±0.14	0.58±0.17	**<0.001**

BMI: Body mass index; DM: Diabetes mellitus; HTN: Hypertension; LVEF: Left ventricular ejection fraction; LDL: Low-density lipoprotein cholesterol; HDL: High-density lipoprotein cholesterol; TyG: Triglyceride–glucose index; AIP: Atherogenic index of plasma.

vs. 129.8±37.3 mg/dL; p<0.001) and triglycerides (175.6±45.5 vs. 155.3±45.3 mg/dL; p=0.001). Furthermore, LDL was higher (p=0.025), and HDL was lower (p=0.013) in the MVD cohort. Notably, both the TyG and AIP were markedly higher in patients with multivessel involvement (p<0.001), reinforcing the strong association between MVD and these metabolic markers (Table 1).

In the regression analysis evaluating factors associated with MVD, age, DM, smoking, fasting glucose, HDL, LDL, uric acid, BMI, TyG, AIP, and hypertension were identified as potential predictors in univariate analysis (p<0.1). In addition, the gender variable was included in the model based on its clinical relevance.

In the multivariable analysis adjusted for the TyG, age (odds ratio [OR]: 1.07, 95% confidence interval [CI]: 1.03–1.12, p<0.001), DM (OR: 2.02, 95% CI: 1.09–3.76, p=0.025), and smoking (OR: 2.04, 95% CI: 1.10–3.79, p=0.023) emerged as independent predictors of MVD. Notably, the TyG demonstrated a powerful association, with an OR of 6.71 (95% CI: 2.75–16.35, p<0.001) per unit increase. Conversely, LDL (OR: 1.00, 95% CI: 0.99–1.01, p=0.279) and HDL (OR: 0.99, 95% CI: 0.95–1.04, p=0.914) were not independently associated with the disease. To prevent multicollinearity, triglycerides and fasting glucose were omitted as they are constituent components of the TyG (Table 2).

In the multivariable analysis including the AIP, age (OR: 1.07, 95% CI: 1.03–1.11, p<0.001), AIP (OR: 1.66, 95% CI: 1.22–2.24, p=0.001), DM (OR: 2.28, 95% CI: 1.28–4.07, p=0.005), and LDL cholesterol (OR: 1.01, 95% CI: 1.00–1.02, p=0.043) were identified as independent predictors of multivessel CAD. Due to high collinearity with the AIP, triglycerides and HDL cholesterol were excluded from the multivariable model (Table 3).

ROC curve analysis demonstrated that the TyG had an AUC of 0.718 (95% CI: 0.653–0.782, p<0.001), with an optimal cutoff of 9.3 (69% sensitivity, 66.4% specificity). For the AIP, the AUC was 0.643 (95% CI: 0.574–0.712, p<0.001), using a cutoff of 0.63 (62.1% sensitivity, 59.4% specificity). These results show that TyG offers higher diagnostic accuracy for MVD, but AIP could also be a valuable biomarker in clinical evaluation (Fig. 2).

Discussion

This study aimed to assess the relevance of metabolic markers, including the AIP and the TyG, in patients with MVD. Early diagnosis of MVD is crucial for determining treatment strategies. In recent years, biochemical parameters such as AIP and the TyG have garnered increasing attention for their role in assessing cardiovascular risk in these patients.[7,8] Our findings reveal a strong relationship between AIP and TyG indexes as independent predictors of MVD. The study highlights the potential utility of these indices in predicting the severity of CAD and their value as potential biomarkers.

In this study, significant associations were found between the MVD group and age, DM, smoking, and metabolic parameters (especially fasting blood glucose, triglycerides, LDL, HDL, TyG, and AIP). These findings are consistent with previous reports showing that established cardiovascular risk factors

Table 2. Regression analysis of factors associated with multivessel coronary artery disease, including the TyG index

Variables	Univariable		Multivariable	
	OR (95% CI)	p	OR (95% CI)	p
Age	1.07 (1.04–1.11)	**<0.001**	1.07 (1.03–1.12)	**<0.001**
Gender	1.50 (0.90–2.51)	0.118	1.84 (0.98–3.46)	0.056
BMI	1.11 (0.98–1.25)	0.089	–	
Diabetes mellitus	2.90 (1.71–4.90)	**<0.001**	2.02 (1.09–3.76)	**0.025**
Hypertension	1.61 (0.97–2.67)	0.065	–	
Smoking	1.62 (0.98–2.70)	0.059		
Uric acid	1.19 (0.99–1.43)	0.064	–	
LDL	1.01 (1.00–1.01)	0.027	1.00 (0.99–1.01)	0.279
HDL	0.95 (0.92–0.99)	0.015	0.99 (0.95–1.04)	0.914
TyG	6.78 (3.31–13.90)	**<0.001**	6.71 (2.75–16.35)	**<0.001**

Univariable and multivariable logistic regression analyses of factors associated with multivessel coronary artery disease, including the TyG index. Variables with p<0.10 in univariable analysis and clinically relevant covariates were considered for inclusion in the multivariable model. Triglycerides and fasting blood glucose were not included because they are components of the TyG index. Odds ratios for the TyG index are reported per 1-unit increase. OR: Odds ratio; CI: Confidence interval; BMI: Body mass index; LDL: Low-density lipoprotein cholesterol; HDL: High-density lipoprotein cholesterol; TyG: Triglyceride–glucose index.

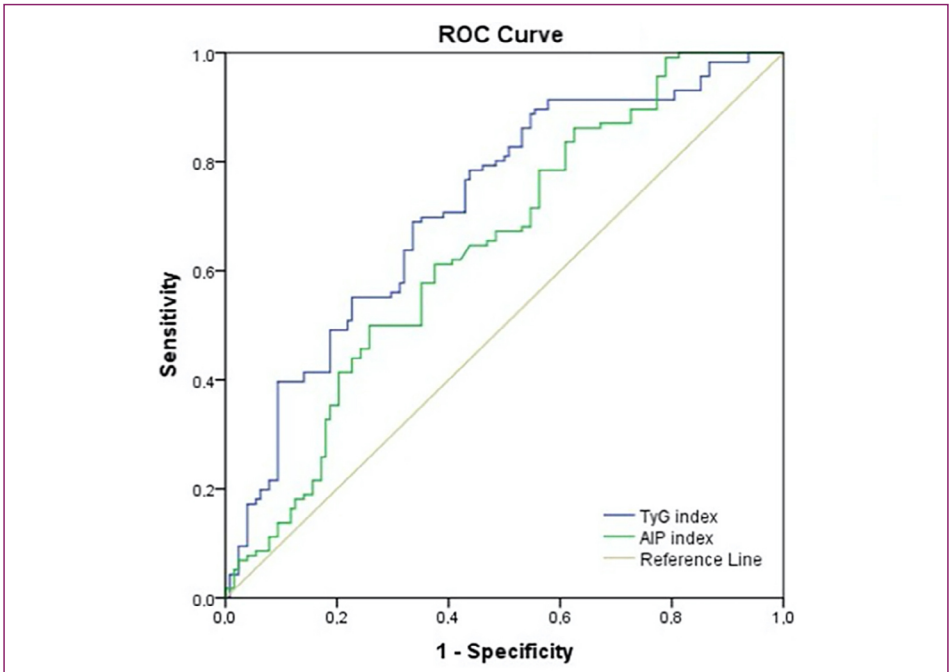
Table 3. Regression analysis of factors associated with multivessel coronary artery disease, including the AIP index

Variables	Univariable		Multivariable	
	OR (95% CI)	p	OR (95% CI)	p
Age	1.07 (1.04–1.11)	**<0.001**	1.07 (1.03–1.11)	**<0.001**
Gender	1.50 (0.90–2.51)	0.118	1.97 (1.10–3.52)	0.022
BMI	1.11 (0.98–1.25)	0.089	–	
Diabetes mellitus	2.90 (1.71–4.90)	**<0.001**	2.28 (1.28–4.07)	**0.005**
Hypertension	1.61 (0.97–2.67)	0.065	–	
Smoking	1.62 (0.98–2.70)	0.059		
Uric acid	1.19 (0.99–1.43)	0.064	–	
LDL	1.01 (1.00–1.01)	0.027	1.01 (1.00–1.02)	**0.043**
AIP	1.69 (1.28–2.23)	**<0.001**	1.66 (1.22–2.24)	**0.001**

Univariable and multivariable logistic regression analyses of factors associated with multivessel coronary artery disease, including the AIP index. Variables with a p<0.10 in univariable analysis and clinically relevant covariates were considered for inclusion in the multivariable model. Triglycerides and HDL cholesterol were not included because they are components of the AIP index. Odds ratios for the AIP index are reported per 1 standard deviation increase. OR: Odds ratio; CI: Confidence interval; BMI: Body mass index; LDL: Low-density lipoprotein cholesterol; AIP: Atherogenic index of plasma.

such as diabetes and smoking contribute to the development of MVD.[9] Furthermore, the higher mean age observed in the MVD group likely reflects the cumulative effect of arterial aging on CAD.[10] The significantly higher prevalence of DM in the MVD group supports the effect of IR and metabolic syndrome on coronary pathology.[11]

Metabolic parameters play a significant role in the development and prognosis of cardiovascular diseases. In our study, metabolic changes such as high triglycerides, low HDL, high LDL, and impaired fasting blood glucose levels were observed in the MVD group. These changes, reflecting the fundamental biological processes of atherosclerosis, increase the cardiovascular risk of the patients.[12] Specifically, abnormalities in triglyceride and HDL levels can accelerate atherogenic processes and trigger the development of MVD.[13] High AIP levels in patients with MVD indicate increased atherogenic risk associated with cardiovascular diseases, suggesting that this parameter may be useful in the early prediction of cardiovascular complications. TyG, reflecting the relationship between triglycerides and fasting glucose, indicates IR, whereas AIP, representing the triglyceride/HDL ratio, reveals atherogenic potential.[13,14] A study by Simental-Mendía et al.[15] demonstrated a strong relationship between the TyG, metabolic syndrome, and cardiovascular diseases. Similarly, Wang et al.[6] reported that the TyG is effective in predicting cardiovascular disease risk in a cohort in China. Furthermore, high TyG and AIP indices stand out as important indicators affecting the prognosis of atherosclerosis.[14] The combined assessment of AIP and TyG indices could provide higher accuracy in diagnosing the early stages of cardiovascular diseases. In the literature, there are studies with varying results using these indices together. In a study by Wu et al.,[14] the relationship between the TyG, the AIP, and the severity of newly onset CAD was examined. The study found that the TyG was not related to the severity of CAD, but AIP showed a significant relationship



Parameters	AUC	95% CI	p Değeri	Sensitivity (%)	Specificity (%)
TyG	0.718	0.653 - 0.782	**<0.001**	69	66.4
AIP	0.643	0.574 - 0.712	**<0.001**	62.1	59.4

Figure 2. Diagnostic performance of TyG and AIP indices in MVD: ROC analysis results.

ROC: Receiver operating characteristic; TyG: Triglyceride-glucose index; AIP: Atherogenic index of plasma; AUC: Area under the curve; CI: Confidence interval; MVD: Multivessel disease.

only in patients with normal glucose levels. However, in our study, both indices predicted the prognosis of MVD, with TyG standing out as a stronger biomarker. These findings suggest that both TyG and AIP could be valuable tools in the evaluation of cardiovascular diseases.

Understanding the metabolic parameters associated with the development of MVD is crucial for the early diagnosis of cardiovascular diseases. The analyses found that the TyG and AIP were independently associated with MVD. The TyG, which includes fasting blood glucose and triglyceride levels, emerges as a strong biomarker associated with metabolic syndrome and may play a significant role in the development of MVD.[15] These findings support the idea that the TyG could be a practical and effective biomarker in the early stages of cardiovascular diseases. Furthermore, the AIP, which measures the balance between triglycerides and HDL, reflects how the disruption of this balance increases atherosclerosis risk.[16] These data suggest that both parameters could play an important role in clinical applications, especially in assessing the risk of MVD in patients.

In our study, the TyG provided stronger results with high accuracy rates in the diagnosis of MVD. This finding indicates that the TyG could be a valuable biomarker for predicting CAD, and particularly MVD prognosis.[17] Although the AIP had a lower accuracy rate, it could still serve as an important adjunct tool in clinical evaluations.[6]

Limitations

There are several constraints to this research, notably its single-center and retrospective nature, which may affect the broader applicability of the findings. Furthermore, metabolic markers were determined using only a baseline measurement. In addition, the results were obtained based on a single measurement of the metabolic parameters evaluated in this study. Future prospective studies could provide a more detailed assessment of the dynamic changes of these parameters and their impact on long-term prognosis. In addition, information on pre-admission lipid-lowering therapy was not consistently available and therefore could not be included in the analysis. However, all laboratory measurements were obtained at hospital admission, before any in-hospital modification of lipid-lowering therapy, which may partially mitigate the impact of prior treatment on the observed associations.

Conclusion

The TyG and AIP indices emerged as independent predictors of MVD. Their use in routine clinical assessment may improve risk stratification in patients with MVD. Furthermore, these parameters may serve as potential biomarkers for early detection of cardiovascular diseases and for determining treatment strategies.

Disclosures

Ethics Committee Approval: The study was approved by the Mardin Artuklu University Ethics Committee (no: 2024/5-4, date: 07/05/2024).

Informed Consent: The requirement for individual informed consent was waived due to the retrospective design of the study.

Conflict of Interest Statement: The authors declare that they have no conflict of interest.

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