International Journal of General Medicine

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Correlation Between Triglyceride-Glucose Index (TyG Index), Monocyte to High-Density Lipoprotein Cholesterol Ratio (MHR), and the Severity of Coronary Artery Disease

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Objective: To explore the relationship between the triglyceride-glucose index (TyG), the monocyte to high-density lipoprotein cholesterol ratio (MHR) and the severity of coronary artery disease (CAD) under different glucose metabolism states.

Methods: A retrospective analysis was conducted on 526 patients who underwent coronary angiography (CAG) for the first time in the Affiliated Hospital of Xuzhou Medical University from January 2024 to January 2025. Among them, there were 122 patients in the non-CAD group and 404 patients in the CAD group. According to the Gensini score, the CAD group was further divided into a mild group (n = 147) and a moderate-to-severe group (n = 257). Meanwhile, they were divided into normal glucose regulation (NGR), prediabetes (Pre-DM), and diabetes mellitus (DM) groups according to the glucose metabolism state. Multivariate Logistic regression, restricted cubic spline (RCS), and receiver operating characteristic (ROC) curve analyses were used.

Results: Both the TyG index and MHR were independent risk factors for the occurrence and severity of CAD ($P<0.05$). In the DM group, the TyG index was significantly associated with the severity of CAD (*OR*=4.30, 95% *CI*: 1.48–12.49, $P<0.01$); in the NGR group, MHR was significantly associated with the severity of CAD (*OR*=436.1, 95% *CI*: 15.4–12342, $P<0.001$). RCS analysis suggested a significant linear positive correlation between the TyG index and the severity of CAD (*P*-overall=0.006, *P*-non-linear =0.917), while there was a non-linear relationship between MHR and the severity of CAD (*P*-overall=0.007, *P*-non-linear=0.033). ROC analysis showed that the area under the curve (AUC) of the combined prediction was 0.655, higher than that of the TyG index (0.618) and MHR (0.631).

Conclusion: TyG index and MHR can serve as independent biomarkers of new-onset CAD severity. In DM patients, TyG offers greater predictive value, while MHR is more predictive in NGR individuals.

Keywords: coronary artery disease severity, triglyceride-glucose index, monocyte to high-density lipoprotein cholesterol ratio, glucose metabolic states, gensini scores

Introduction

Coronary artery disease (CAD) is a leading cause of mortality worldwide, characterized by myocardial ischemia and hypoxia due to coronary artery constriction or obstruction.[1] Early and accurate diagnosis of CAD is essential, with coronary angiography (CAG) being the gold standard for identifying the disease, where stenosis of ≥50% in the main coronary artery confirms its presence.[2] The Gensini score, a widely used angiographic scoring system, evaluates the severity of CAD by quantifying both the degree of stenosis and the anatomical location of lesions, thus providing a comprehensive assessment of coronary atherosclerotic burden.[3] However, the invasive and costly nature of CAG deters

Received: 15 October 2025
Accepted: 23 December 2025
Published: 25 December 2025

some early-stage patients from undergoing this critical diagnostic procedure. Consequently, there is a pressing need to identify reliable and accessible serum biomarkers. Insulin resistance, inflammatory processes, and dysregulated lipid metabolism represent key mechanisms driving the progression of CAD.[4] Insulin resistance (IR) exacerbates atherosclerosis through various pathways such as inducing abnormal glucose homeostasis, increasing inflammation and oxidative stress, and causing dyslipidemia, thereby promoting the occurrence and development of CAD.[5] The triglyceride-glucose index (TyG), as an alternative indicator of IR, is closely related to the progression and poor prognosis of CAD.[6,7] Monocytes are key cells in vascular inflammation and atherosclerosis,[8] while high-density lipoprotein-cholesterol (HDL-C) has anti-inflammatory, anti-oxidative, and anti-atherosclerotic effects.[9] The monocyte to high-density lipoprotein cholesterol ratio (MHR) can reflect the interaction between inflammation and abnormal lipid metabolism and is closely related to all-cause mortality, cardiovascular mortality, in-hospital mortality, adverse events, and the severity of coronary artery lesions.[10–12] However, the association between the TyG index and MHR with the severity of CAD across varying glucose metabolism states remains elusive. This study sought to elucidate the roles of TyG and MHR in the context of different glucose metabolism conditions, thereby providing a foundation for the early identification and management of CAD.

Materials and Methods

Ethical Statement

The study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was obtained from the Institutional Review Board of Xuzhou Medical University Affiliated Hospital (Approval Number: XYFY2025-KL179-01). Given the retrospective design of the study, which relied exclusively on anonymized data extracted from electronic medical records without any direct patient contact or intervention, the requirement for individual informed consent was formally waived by the Institutional Review Board.

Research Subjects

We studied patients undergoing initial coronary angiography (CAG) treatment at the Affiliated Hospital of Xuzhou Medical University from January 1, 2024, to January 1, 2025. For the purpose of this study, a separate random sampling technique was applied to select both CAD patients and non-CAD individuals. Specifically, 450 CAD patients and 150 non-CAD individuals were randomly selected from a pool of eligible individuals. Exclusion criteria were as follows: ①patients aged<18 years; ②patients with a previous diagnosis of CAD, or a history of myocardial infarction, percutaneous coronary intervention (PCI), or coronary artery bypass grafting (CABG); ③patients with concurrent malignant tumors, infectious diseases, severe hepatic or renal insufficiency, or thyroid dysfunction; ④patients with incomplete clinical data. Ultimately, a total of 526 subjects were included, consisting of 404 CAD patients and 122 non-CAD individuals. According to the Gensini score, the CAD group was further divided into a mild lesion group (N = 147) and a moderate-to-severe lesion group (N = 257) according to the Gensini score (Figure 1).

Methods

Baseline data included age, gender, height, weight, blood pressure, smoking and drinking status, clinical history (hypertension, diabetes, cerebral infarction), and medication use (antihypertensive drugs, antidiabetic drugs, antiplatelet drugs). The results of CAG and echocardiographic parameters (left ventricular ejection fraction [LVEF]) were recorded. Venous blood was collected within 24 hours after admission to measure complete blood count, blood lipids, liver and kidney function, fasting plasma glucose (FPG), and glycated hemoglobin (HbA1c), and to calculate the TyG index and MHR. TyG index=Ln [triglyceride (TG, mg/dL) × fasting plasma glucose (FPG, mg/dL)/2], MHR=monocytes (10^9/L)/HDL-C(mmol/L). Two senior cardiologists independently assessed coronary artery stenosis based on CAG results, with both assessors being blinded to all clinical and laboratory data (eg, patient demographics, comorbidities, lab results) to minimize potential bias. A total of 526 patients, consisting of 404 patients in the CAD group and 122 non-CAD individuals, were included. In the CAD group, patients were divided into mild, moderate, and severe lesion groups based on the tertiles of Gensini score, and the moderate and severe lesion groups were combined. Finally, they were divided

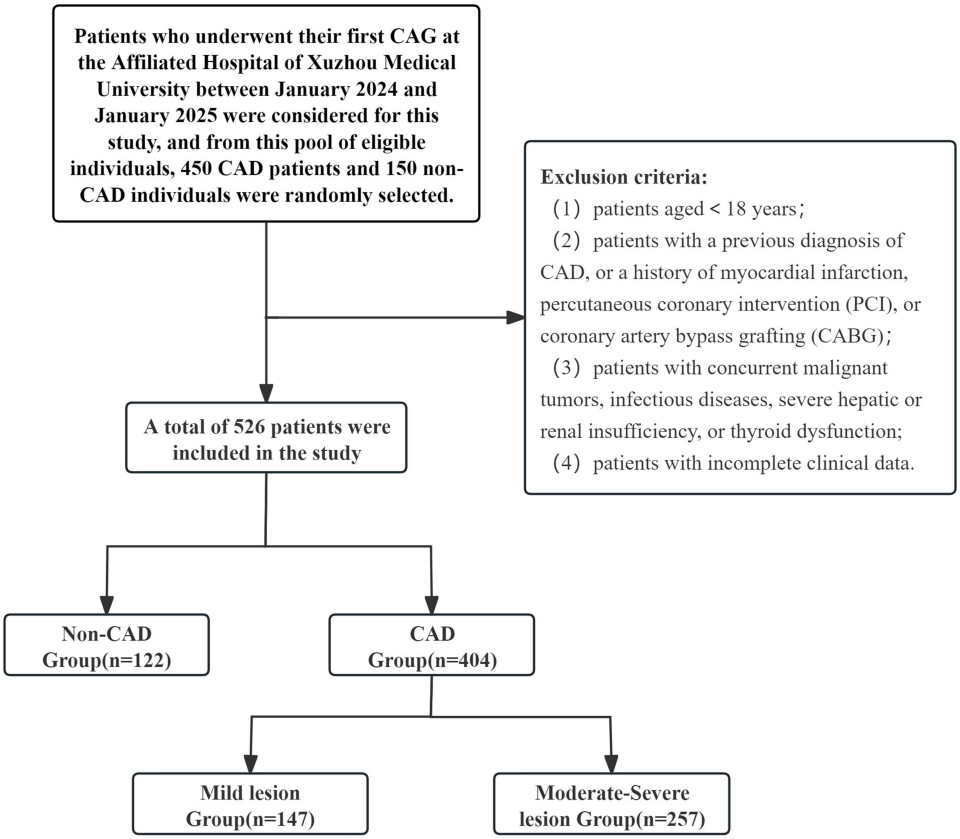

Figure 1 Flow chart of patient recruitment.
Abbreviations: CAD, coronary artery disease; CAG, coronary angiography.

into the mild lesion group (n=147, Gensini≤20) and the moderate-severe lesion group (n=257, Gensini>20) (Table 1). Additionally, according to the patients' glucose metabolism status, CAD patients were divided into the normal glucose regulation (NGR) group, the prediabetes (Pre-DM) group, and the diabetes mellitus (DM) group. NGR was defined as HbA1c<5.7% and no history of diabetes; patients with 5.7%≤HbA1c<6.5% and no history of diabetes were classified as the prediabetes group; patients with a history of diabetes or HbA1c≥6.5% were in the DM group.[13]

Table 1 Comparison of Clinical Data Between Non-CAD Group and CAD Group

Variables	Group 1 (n = 122)	Group 2 (n = 147)	Group 3 (n = 257)	*P*
Male, n (%)	62 (50.82%)	82 (55.78%)	169 (65.76%)	0.012
Age (years)	61.50 (54.25,70.00)	64.00 (57.50,71.00)	64.00 (56.00,70.00)	0.246
BMI (kg/m^2)	25.39 (23.24,27.28)	24.90 (22.87,27.29)	24.77 (22.89,27.36)	0.749
Smoking, n (%)	26 (21.31%)	40 (27.21%)	85 (33.07%)	0.055
Drinking, n (%)	21 (17.21%)	26 (17.69%)	50 (19.46%)	0.838
TC (mmol/L)	4.29 (3.58,4.89)	4.12 (3.39,4.83)	4.25 (3.30,4.96)	0.582
TG (mmol/L)	1.38 (1.11,1.77)	1.29 (0.96,1.90)	1.52 (1.12,2.21)	0.003
HDL-C (mmol/L)	1.02 (0.88,1.26)	1.04 (0.90,1.19)	0.95 (0.81,1.11)	<0.001
LDL-C (mmol/L)	2.29 (1.72,2.79)	2.15 (1.58,2.72)	2.17 (1.59,2.80)	0.517
sdLDL-C (mmol/L)	0.80 (0.59,1.25)	0.80 (0.52,1.13)	0.84 (0.60,1.34)	0.114
ApoA (g/L)	1.27 (1.15,1.47)	1.31 (1.13,1.46)	1.23 (1.07,1.36)	0.001
ApoB (g/L)	0.81 (0.65,0.97)	0.79 (0.64,1.00)	0.84 (0.67,1.05)	0.151

(*Continued*)

https://doi.org/10.2147/IJGM.S570395

Table 1 (Continued).

Variables	Group 1 (n = 122)	Group 2 (n = 147)	Group 3 (n = 257)	*P*
Lipoprotein(a) (mg/L)	162.50 (88.00,327.25)	156.00 (105.00,285.50)	215.00 (116.00,452.00)	0.002
HbA1c (%)	5.70 (5.30,6.00)	5.80 (5.45,6.20)	5.90 (5.60,6.60)	<0.001
FPG (mmol/L)	4.92 (4.52,5.34)	5.03 (4.62,5.86)	5.30 (4.76,6.73)	<0.001
White blood cell ($\times10^9$/L)	5.80 (4.90,7.10)	5.90 (4.90,7.05)	6.40 (5.40,7.70)	0.006
Neutrophil ($\times10^9$/L)	3.49 (2.75,4.23)	3.39 (2.71,4.47)	3.77 (3.12,4.82)	0.001
Lymphocytes ($\times10^9$/L)	1.75 (1.40,2.08)	1.90 (1.50,2.20)	1.80 (1.40,2.20)	0.518
Monocyte ($\times10^9$/L)	0.36 (0.30,0.45)	0.37 (0.30,0.45)	0.41 (0.34,0.51)	<0.001
Hemoglobin (g/L)	136.79 ± 13.41	139.03 ± 15.48	137.72 ± 15.16	0.456
Platelets ($\times10^9$/L)	224.81 ± 50.21	218.87 ± 53.55	218.07 ± 52.97	0.488
TbIL (μmol/L)	9.45 (7.62,12.65)	10.10 (7.30,14.00)	9.40 (7.00,12.10)	0.167
Scr (μmol/L)	57.50 (50.00,68.00)	61.00 (51.00,71.50)	62.00 (54.00,71.00)	0.061
LVEF (%)	62.00 (60.00,65.00)	62.97 (60.00,65.00)	62.00 (59.00,65.00)	0.557
Hypertension, n (%)	59 (48.36%)	89 (60.54%)	153 (59.53%)	0.077
Diabetes, n (%)	15 (12.30%)	26 (17.69%)	73 (28.40%)	<0.001
Cerebral infarction, n (%)	13 (10.66%)	17 (11.56%)	42 (16.34%)	0.218
Antihypertensive drugs, n (%)	47 (38.52%)	75 (51.02%)	130 (50.58%)	0.060
Antidiabetic drugs, n (%)	12 (9.84%)	23 (15.65%)	67 (26.07%)	<0.001
Antiplatelet drugs, n (%)	8 (6.56%)	14 (9.52%)	29 (11.28%)	0.347
TyG index	8.60 (8.33,8.87)	8.61 (8.26,8.96)	8.84 (8.49,9.23)	<0.001
MHR	0.35 (0.26,0.49)	0.37 (0.27,0.45)	0.43 (0.33,0.56)	<0.001

Note: Group 1: non-CAD, Group 2: Gensini Scores≤20, Group 3: Gensini Scores>20.

Abbreviations: CAD, coronary artery disease; BMI, body mass index; TG, Triglyceride; TC, Total cholesterol; LDL-C, Low-density lipoprotein cholesterol; HDL-C, High-density lipoprotein cholesterol; sdLDL-C, small dense low-density lipoprotein cholesterol; ApoA, Apolipoprotein A; ApoB, Apolipoproteins B; HbAlc, Glycated hemoglobin A1c; FPG, fasting plasma glucose; Scr, Serum creatinine; TbIL, Total bilirubin; LVEF, Left ventricular ejection fraction; MHR, monocyte to HDL-C ratio; TyG index, triglyceride-glucose index.

Statistical Analysis

Statistical analysis was performed using SPSS 27.0 and R 4.2.0. Continuous variables with a normal distribution were presented as mean±standard deviation (SD), while those with a non-normal distribution were presented as median (interquartile range). Categorical variables were presented as frequencies and percentages. For comparisons between groups, the *t*-test, Mann–Whitney *U*-test, or χ^2-test was selected according to the data type. The relationships between the TyG index, MHR, and CAD were evaluated by multivariate Logistic regression, and the results were presented as odds ratios (*OR*) and 95% confidence intervals (*CI*). Restricted cubic splines (RCS) were further used to analyze the linear or non-linear trends, and the receiver operating characteristic (ROC) curve was used to evaluate the predictive efficacy and calculate the optimal cut-off value. A two-sided test was used, and a *P*-value<0.05 was considered statistically significant.

Results

Baseline Characteristics of the Non-CAD Group and the CAD Group

A total of 526 patients were included in this study, including 122 cases of non-CAD and 404 cases of newly diagnosed CAD. Among them, CAD patients were divided into mild lesion group (≤20) and moderate-severe lesion group (>20) according to Gensini score. There were statistically significant differences among the three groups in terms of gender, triglyceride (TG), HDL-C, apolipoprotein A (ApoA), lipoprotein(a), HbA1c, FPG, TyG index, MHR, white blood cell, monocyte, diabetes and use of antidiabetic drugs (*P*<0.05) (Table 1).

Relationship Between TyG Index and MHR and CAD

The TyG index was divided into Q1-Q4 groups according to quartiles. Logistic regression showed that after adjusting for traditional risk factors and drug treatment, the TyG index was significantly associated with CAD (*P*<0.05) (Table 2). As a continuous variable, the TyG index was significantly associated with an increased risk of CAD (*OR*=1.85, 95% *CI*:

Table 2 Association Between the TyG Index and CAD

Variables	Coronary artery Disease					
	Model1		Model2		Model3	
	OR (95% CI)	*P*	*OR* (95% CI)	*P*	*OR* (95% CI)	*P*
TyG index	2.00 (1.37 ~ 2.93)	<0.001	2.18 (1.47 ~ 3.21)	<0.001	1.85 (1.07 ~ 3.20)	0.029
Q1	Reference		Reference		Reference	
Q2	0.92 (0.54 ~ 1.57)	0.756	0.99 (0.58 ~ 1.71)	0.976	0.91 (0.51 ~ 1.62)	0.738
Q3	1.26 (0.72 ~ 2.19)	0.419	1.32 (0.75 ~ 2.32)	0.332	1.30 (0.68 ~ 2.46)	0.426
Q4	3.04 (1.57 ~ 5.87)	<0.001	3.54 (1.81 ~ 6.92)	<0.001	2.73 (1.14 ~ 6.55)	0.024
P-trend	<0.001		<0.001		0.019	

Note: Model 1 is unadjusted. Model 2 is adjusted for age and sex. Model 3 is adjusted for age, sex, BMI, TC, LDL-C, HDL-C, ApoA, ApoB, Lipoprotein(a), hypertension, antihypertensive drugs, antidiabetic drugs and smoking.
Abbreviations: *OR*, Odds ratio; *CI*, Confidence interval; TyG index, triglyceride-glucose index.

1.07–3.20, $P<0.05$); as a categorical variable, the risk of CAD in the Q4 group was 2.73 times higher than that in the Q1 group (*OR*=2.73, 95% CI: 1.14–6.55, $P<0.05$). Similarly, the MHR was divided into Q1-Q4 groups. After multivariable adjustment, the MHR was significantly associated with CAD ($P<0.05$) (Table 3). The MHR as a continuous variable was significantly associated with the risk of CAD (*OR*=4.92, 95% CI: 1.09–22.12, $P<0.05$); as a categorical variable, the risk in the Q4 group was 2.56 times higher than that in the Q1 group (*OR*=2.56, 95% CI: 1.23–5.32, $P<0.05$).

Relationship Between TyG Index, MHR and the Severity of CAD

Logistic regression indicated a positive correlation between the TyG index and the severity of CAD ($P<0.01$) (Table 4). After adjusting for confounding factors in the quartile groups, the risk of moderate-to-severe lesions in the Q4 group was 5.22 times higher than that in the Q1 group (*OR*=5.22, 95% *CI*: 2.18–12.53, $P<0.001$). Similarly, the MHR was significantly associated with the severity of CAD ($P<0.05$) (Table 5). In the quartile groups, the risk of moderate-to-severe lesions in the Q4 group was 2.62 times higher than that in the Q1 group (*OR*=2.62, 95% *CI*: 1.25–5.47, $P<0.05$).

Relationship Between TyG Index, MHR and the Severity of CAD Under Different Glucose Metabolism States

In the NGR and Pre-DM groups, there was no significant difference in the association between the TyG index and the severity of CAD; however, in the DM group, a significant correlation was observed (*OR*=4.30, 95% CI: 1.48–12.49, $P<0.01$) (Table 6). The MHR was significantly associated with the severity of CAD in the NGR group (*OR*=436.1, 95% CI: 15.4–12342, $P<0.001$) (Table 7), but no correlation was found in the Pre-DM and DM groups.

Table 3 Association Between the MHR and CAD

Variables	Coronary Artery Disease					
	Model1		Model2		Model3	
	OR (95% CI)	*P*	*OR* (95% CI)	*P*	*OR* (95% CI)	*P*
MHR	7.06 (2.05 ~ 24.31)	0.002	6.06 (1.69 ~ 21.70)	0.006	4.92 (1.09 ~ 22.12)	0.038
Q1	Reference		Reference		Reference	
Q2	1.97 (1.14 ~ 3.41)	0.016	1.92 (1.10 ~ 3.36)	0.022	1.84 (1.01 ~ 3.40)	0.050
Q3	2.06 (1.18 ~ 3.59)	0.011	1.97 (1.12 ~ 3.50)	0.020	1.90 (1.00 ~ 3.61)	0.050
Q4	2.83 (1.57 ~ 5.09)	<0.001	2.68 (1.45 ~ 4.95)	0.002	2.56 (1.23 ~ 5.32)	0.012
P-trend	<0.001		0.003		0.023	

Note: Model 1 is unadjusted. Model 2 is adjusted for age and sex. Model 3 is adjusted for age, sex, BMI, TC, TG, LDL-C, ApoA, ApoB, Lipoprotein(a), hypertension, antihypertensive drugs, antidiabetic drugs and smoking.
Abbreviations: *OR*, Odds ratio; *CI*, Confidence interval; MHR, monocyte to HDL-C ratio.

Table 4 Association Between the TyG Index and the Severity of CAD

Variables	Severity of CAD					
	Model1		Model2		Model3	
	OR (95% CI)	*P*	*OR* (95% CI)	*P*	*OR* (95% CI)	*P*
TyG index	1.97 (1.38 ~ 2.81)	<0.001	2.06 (1.44 ~ 2.96)	<0.001	2.39 (1.41 ~ 4.07)	0.001
Q1	Reference		Reference		Reference	
Q2	1.56 (0.89 ~ 2.73)	0.120	1.67 (0.95 ~ 2.95)	0.076	1.81 (0.97 ~ 3.37)	0.061
Q3	1.77 (1.01 ~ 3.11)	0.047	1.77 (1.01 ~ 3.14)	0.049	2.04 (1.04 ~ 3.98)	0.037
Q4	3.52 (1.91 ~ 6.50)	<0.001	4.09 (2.17 ~ 7.71)	<0.001	5.22 (2.18 ~ 12.53)	<0.001
P-trend	<0.001		<0.001		<0.001	

Note: Model 1 is unadjusted. Model 2 is adjusted for age and sex. Model 3 is adjusted for age, sex, BMI, TC, LDL-C, HDL-C, ApoA, ApoB, lipoprotein(a), hypertension, antihypertensive drugs, antidiabetic drugs, and smoking.
Abbreviations: *OR*, Odds ratio; *CI*, Confidence interval; TyG index, triglyceride-glucose index; CAD, coronary artery disease.

Table 5 Association Between the MHR and the Severity of CAD

Variables	Severity of CAD					
	Model1		Model2		Model3	
	OR (95% CI)	*P*	*OR* (95% CI)	*P*	*OR* (95% CI)	*P*
MHR	8.02 (2.47 ~ 26.08)	<0.001	6.89 (2.10 ~ 22.65)	0.001	5.08 (1.25 ~ 20.64)	0.023
Q1	Reference		Reference		Reference	
Q2	1.62 (0.93 ~ 2.84)	0.090	1.59 (0.90 ~ 2.80)	0.107	1.37 (0.74 ~ 2.55)	0.314
Q3	2.17 (1.22 ~ 3.85)	0.008	2.08 (1.17 ~ 3.72)	0.013	1.85 (0.98 ~ 3.52)	0.059
Q4	3.14 (1.73 ~ 5.70)	<0.001	2.92 (1.58 ~ 5.40)	<0.001	2.62 (1.25 ~ 5.47)	0.011
P-trend	<0.001		<0.001		0.008	

Note: Model 1 is unadjusted; Model 2 is adjusted for age and sex; Model 3 is adjusted for age, sex, BMI, TG, TC, LDL-C, ApoA, ApoB, lipoprotein(a), hypertension, diabetes, and smoking.
Abbreviations: *OR*, Odds ratio; *CI*, Confidence interval; MHR, monocyte to HDL-C ratio.; CAD, coronary artery disease.

Table 6 Association Between the TyG Index and Severity of CAD Under Different Glucose Metabolism Statuses

Variables	Severity of CAD					
	Model1		Model2		Model3	
	OR (95% CI)	*P*	*OR* (95% CI)	*P*	*OR* (95% CI)	*P*
NGR						
TyG index	1.89 (0.94 ~ 3.83)	0.075	1.90 (0.93 ~ 3.88)	0.076	1.85 (0.65 ~ 5.25)	0.246
Q1	Reference		Reference		Reference	
Q2	1.79 (0.69 ~ 4.65)	0.231	1.88 (0.72 ~ 4.95)	0.198	1.64 (0.54 ~ 4.93)	0.381
Q3	1.12 (0.44 ~ 2.86)	0.811	1.16 (0.45 ~ 2.99)	0.759	1.13 (0.35 ~ 3.61)	0.842
Q4	3.06 (1.12 ~ 8.37)	0.030	3.06 (1.11 ~ 8.41)	0.030	3.35 (0.79 ~ 14.18)	0.100
P-trend	0.070		0.071		0.183	
Pre-DM						
TyG index	2.09 (1.06 ~ 4.12)	0.033	1.93 (0.95 ~ 3.93)	0.070	2.24 (0.75 ~ 6.68)	0.149
Q1	Reference		Reference		Reference	
Q2	1.12 (0.44 ~ 2.87)	0.811	1.16 (0.44 ~ 3.03)	0.763	1.07 (0.36 ~ 3.18)	0.906
Q3	2.06 (0.78 ~ 5.46)	0.146	2.01 (0.75 ~ 5.40)	0.167	2.39 (0.76 ~ 7.51)	0.135
Q4	2.36 (0.88 ~ 6.34)	0.088	2.17 (0.76 ~ 6.23)	0.150	1.63 (0.33 ~ 8.02)	0.546
P-trend	0.049		0.087		0.237	

(*Continued*)

Table 6 (Continued).

Variables	Severity of CAD					
	Model1		Model2		Model3	
	OR (95% CI)	*P*	*OR* (95% CI)	*P*	*OR* (95% CI)	*P*
DM						
TyG index	1.75 (0.93 ~ 3.28)	0.081	2.00 (1.04 ~ 3.87)	0.038	4.30 (1.48 ~ 12.49)	0.007
Q1	Reference		Reference		Reference	
Q2	2.08 (0.71 ~ 6.09)	0.183	2.20 (0.72 ~ 6.77)	0.168	1.93 (0.56 ~ 6.62)	0.294
Q3	2.48 (0.82 ~ 7.47)	0.107	3.22 (0.99 ~ 10.40)	0.051	4.28 (1.15 ~ 15.95)	0.030
Q4	2.08 (0.71 ~ 6.09)	0.183	2.89 (0.92 ~ 9.09)	0.069	5.73 (1.00 ~ 32.89)	0.050
P-trend	0.205		0.077		0.027	

Note: Model 1 is unadjusted; Model 2 is adjusted for age and sex; Model 3 is adjusted for age, sex, BMI, TC, LDL-C, HDL-C, ApoA, ApoB, Lipoprotein(a), hypertension, antihypertensive drugs, and smoking.
Abbreviations: *OR*, Odds ratio; *CI*, Confidence interval; TyG index, triglyceride-glucose index; CAD, coronary artery disease; NGR, normoglycemia; Pre-DM, pre-diabetes mellitus; DM, diabetes mellitus.

Table 7 Association Between the MHR and Severity of CAD Under Different Glucose Metabolism Statuses

Variables	Severity of CAD					
	Model1		Model2		Model3	
	OR (95% CI)	*P*	*OR* (95% CI)	*P*	*OR* (95% CI)	*P*
NGR						
MHR	90.23 (8.49 ~ 959.14)	<0.001	126.45 (9.85 ~ 1622)	<0.001	436.10 (15.41 ~ 12,342)	<0.001
Q1	Reference		Reference		Reference	
Q2	2.26 (0.87 ~ 5.88)	0.096	2.31 (0.87 ~ 6.12)	0.092	2.15 (0.69 ~ 6.71)	0.188
Q3	3.24 (1.22 ~ 8.63)	0.018	3.40 (1.23 ~ 9.40)	0.018	3.94 (1.16 ~ 13.36)	0.028
Q4	5.71 (2.01 ~ 16.24)	0.001	6.09 (2.01 ~ 18.43)	0.001	7.41 (1.82 ~ 30.10)	0.005
P-trend	0.001		0.002		0.005	
Pre-DM						
MHR	6.62 (0.89 ~ 48.97)	0.064	5.64 (0.77 ~ 41.08)	0.088	3.49 (0.34 ~ 35.78)	0.293
Q1	Reference		Reference		Reference	
Q2	1.26 (0.49 ~ 3.22)	0.633	1.13 (0.43 ~ 2.95)	0.803	1.00 (0.34 ~ 2.98)	0.997
Q3	3.43 (1.25 ~ 9.40)	0.017	3.38 (1.21 ~ 9.50)	0.021	3.17 (0.96 ~ 10.45)	0.058
Q4	3.43 (1.25 ~ 9.40)	0.017	3.08 (1.09 ~ 8.75)	0.034	2.94 (0.83 ~ 10.42)	0.095
P-trend	0.005		0.010		0.031	
DM						
MHR	1.42 (0.33 ~ 6.05)	0.634	1.24 (0.31 ~ 4.92)	0.762	1.92 (0.32 ~ 11.63)	0.478
Q1	Reference		Reference		Reference	
Q2	0.73 (0.24 ~ 2.20)	0.576	0.90 (0.29 ~ 2.79)	0.851	1.00 (0.28 ~ 3.57)	0.996
Q3	0.73 (0.24 ~ 2.20)	0.576	0.68 (0.22 ~ 2.10)	0.504	0.55 (0.15 ~ 2.10)	0.384
Q4	1.00 (0.32 ~ 3.12)	1.000	0.86 (0.27 ~ 2.76)	0.801	1.03 (0.21 ~ 4.99)	0.973
P-trend	0.880		0.791		0.992	

Note: Model 1 is unadjusted. Model 2 is adjusted for age and sex. Model 3 is adjusted for age, sex, BMI, TC, TG, LDL-C, ApoA, ApoB, Lipoprotein(a), hypertension, antihypertensive drugs, and smoking.
Abbreviations: *OR*, Odds ratio; *CI*, Confidence interval; MHR, monocyte to HDL-C ratio; CAD, coronary artery disease; NGR, normoglycemia; Pre-DM, pre-diabetes mellitus; DM, diabetes mellitus.

RCS Analysis to Investigate the Relationship Between TyG Index, MHR and the Severity of CAD Lesions

RCS-logistic regression analysis showed that the TyG index was significantly linearly and positively correlated with the severity of CAD lesions. Without adjustment, an elevated TyG index was associated with the severity of CAD lesions

(*P*-overall<0.001, *P*-non-linear=0.917) (Figure 2A). After adjusting for confounding factors, the linear association still existed (*P*-overall=0.006, *P*-non-linear=0.941) (Figure 2B). The MHR showed a non-linear relationship with the severity of CAD. Without adjustment, an elevated MHR significantly increased the risk of CAD (*P*-overall<0.001, *P*-non-linear = 0.014) (Figure 3A). After adjustment, the non-linear relationship remained significant (*P*-overall=0.007, *P*-non-linear =0.033) (Figure 3B). The RCS curve suggested that the risk was relatively low when the MHR was <0.537, and the risk of moderate to severe lesions increased significantly after exceeding this threshold.

Predictive Values of TyG Index and MHR for the Severity of CAD

ROC curve analysis revealed that the AUCs of the TyG index, MHR, and their combination for predicting the severity of CAD were 0.618, 0.631, and 0.655, respectively (all *P*<0.001) (Table 8 and Figure 4). The optimal cut-off values were 8.978 (Youden index 0.209), 0.456 (0.222), and 0.660 (0.242), respectively.

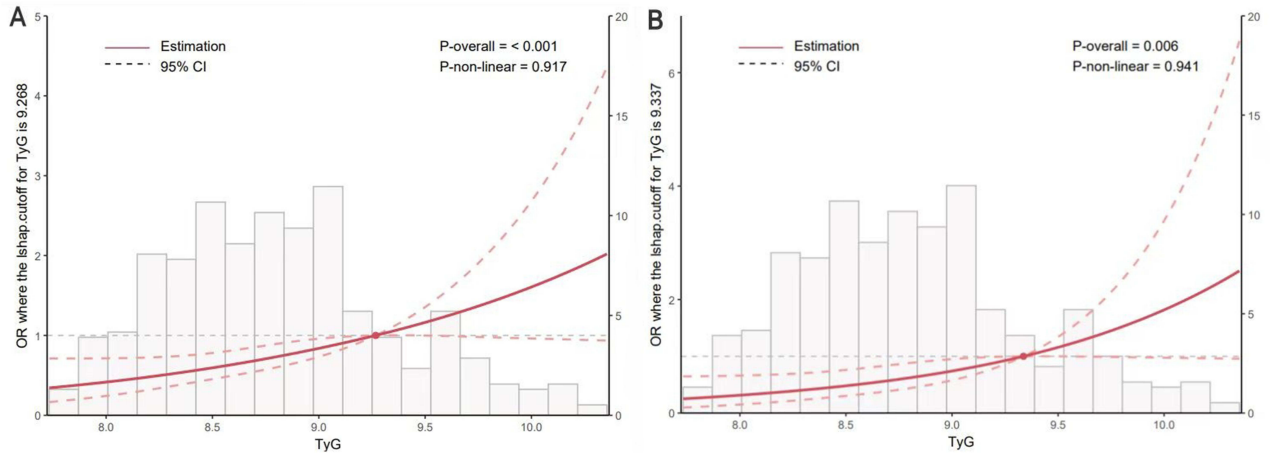

Figure 2 Association between the TyG index and severity of CAD with the RCS function; Panel (**A**) unadjusted; Panel (**B**) adjusted for age, sex, BMI, TC, HDL-C, LDL-C, ApoA, ApoB, Lipoprotein(a), hypertension, antihypertensive drugs, smoking.
Abbreviations: TyG index, triglyceride-glucose index; CI, Confidence interval.

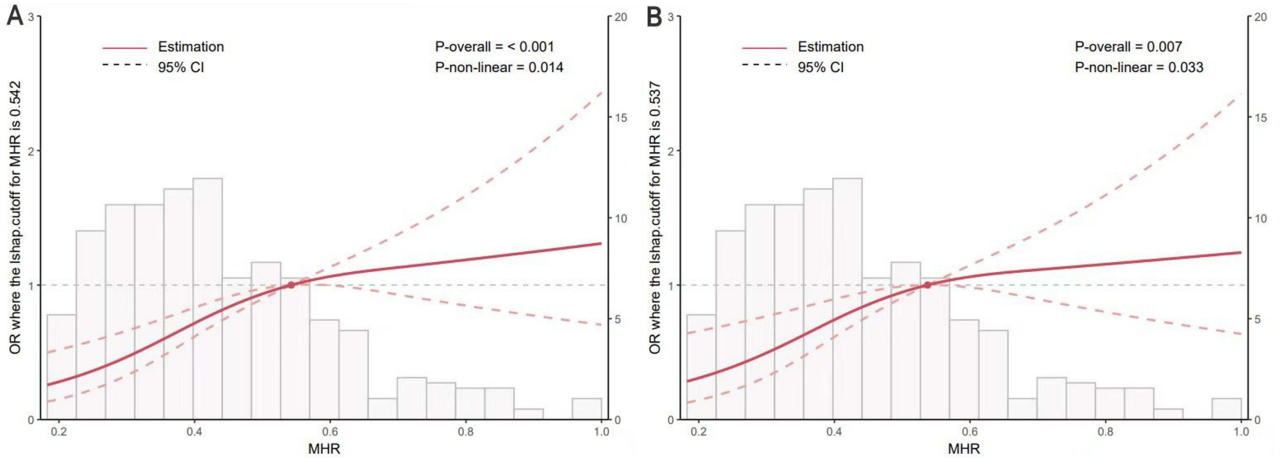

Figure 3 Association between the MHR and severity of CAD with the RCS function; Panel (**A**) unadjusted; Panel (**B**) adjusted for age, sex, BMI, TC, TG, LDL-C, ApoA, ApoB, Lipoprotein(a), hypertension, antihypertensive drugs, smoking.
Abbreviations: MHR, Monocyte to HDL-C ratio; CI, Confidence interval.

Table 8 ROC Curve Analysis

Indicators	Sensitivity (%)	Specificity (%)	Best Cut-Off Point	AUC	95% CI	*P*
TyG index	0.440	0.769	8.978	0.618	(0.562–0.675)	<0.001
MHR	0.467	0.755	0.456	0.631	(0.575–0.688)	<0.001
Combined	0.514	0.728	0.660	0.655	(0.599–0.711)	<0.001

Abbreviations: AUC, Area Under the Curve; *CI*, Confidence interval.

Discussion

The present study examined the associations between the TyG index, MHR, and the presence and severity of CAD. Notably, the predictive utility of these markers varied across distinct glucose metabolism states. Specifically, the TyG index exhibited greater predictive value in patients with DM, while the MHR demonstrated a more pronounced effect in the NGR population. Although the combined use of these markers improved the predictive efficacy, the AUC remained moderate. These findings suggest that both metabolic disturbances and inflammation-lipid imbalance contribute to the progression of CAD, corroborating the conclusions of prior investigations.

The incidence and mortality of cardiovascular diseases are significantly higher in patients with type 2 diabetes mellitus (T2DM) compared to the non-diabetic population. IR is considered the core feature of T2DM and metabolic syndrome, and it is also an independent risk factor for cardiovascular diseases.[14] The mechanisms by which IR leads to cardiovascular diseases primarily involve chronic hyperglycemia, dyslipidemia, inflammation, and endothelial

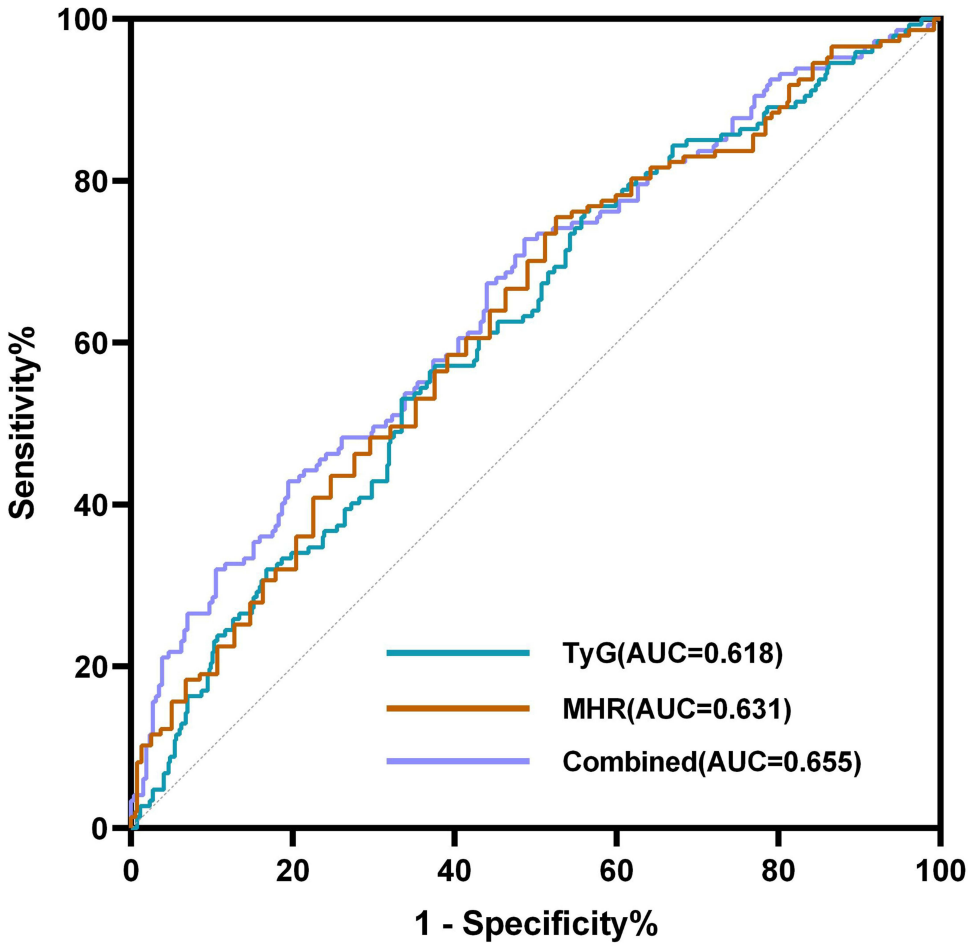

Figure 4 ROC curve analysis of the TyG index and MHR for CAD prediction.
Abbreviations: ROC curve, receiver operator characteristic curve; AUC, area under the curve; TyG index, triglyceride-glucose index; MHR, Monocyte to HDL-C ratio.

https://doi.org/10.2147/IJGM.S570395

dysfunction. IR promotes endothelial dysfunction by reducing the production of nitric oxide (NO) through the PI3K/Akt pathway in endothelial cells and increasing the production of reactive oxygen species (ROS) mediated by MAPK/ERK activation, as well as enhancing the generation of pro-thrombotic factors and pro-inflammatory markers, thereby accelerating the formation of atherosclerosis and increasing the risk of cardiovascular diseases.[15] The gold standard for evaluating IR is the hyperinsulinemic euglycemic clamp (HIEC), but its complex technology, long duration, and high cost limit its clinical application.[16] In contrast, the TyG index has been proven to be a simple and reliable alternative indicator of IR, and it has been shown to be superior to the classic homeostasis model assessment of insulin resistance (HOMA-IR) in clinical applications.[17]

The TyG index has been shown to predict the risk of adverse cardiovascular events in patients with diabetes and acute coronary syndrome,[18] and is associated with the incidence of arteriosclerosis and the severity of coronary stenosis.[19,20] However, the relationship between the TyG index and the severity of CAD across different glycemic states remains unclear. Some studies have found the TyG index to be associated with CAD severity only in patients with DM, but not in those with NGR or Pre-DM.[21,22] Conversely, a large-scale prospective study reported a positive correlation between the TyG index and CAD severity across various glucose metabolic states.[23] These discrepancies may be attributed to differences in sample size, study population characteristics, and consideration of potential confounding factors such as medication use. To address these uncertainties, the present study evaluated the association between the TyG index and CAD severity in a cohort of patients newly diagnosed with CAD who underwent CAG at a single institution. In light of these findings, this study focused on patients undergoing their first coronary angiography at our hospital, newly diagnosed with CAD, minimizing drug interference. Results demonstrated a significant correlation between the TyG index and CAD severity in diabetic patients.

Chronic inflammation and lipid accumulation are central to the pathogenesis of atherosclerosis. Monocytes and monocyte-derived macrophages play a pivotal role in the development and progression of cardiovascular diseases and atherosclerosis. Monocytes infiltrate the subendothelial layer by adhering to adhesive molecules on the damaged vascular endothelium, differentiate into macrophages, accumulate lipids, and subsequently transform into foam cells, thereby contributing to the formation of atherosclerotic lesions. In contrast, HDL-C promotes endothelial repair and integrity by facilitating vasodilation and inhibiting cell adhesion and the release of pro-inflammatory mediators.[9,24] Furthermore, studies have demonstrated that the MHR is closely associated with the occurrence of atherosclerosis and multi-vessel coronary artery disease, and is considered a prognostic marker for cardiovascular diseases.[10,11,25,26]

This study elucidates the link between metabolic disorders and inflammatory lipids through the measurement of the TyG index and MHR, both of which are simple, cost-effective, and clinically feasible. Integrating these indicators offers a more comprehensive assessment of CAD risk and facilitates exploration of its multifactorial mechanisms.

This study has several limitations. First, as a single-center retrospective study with a small sample size and no randomized design, it may introduce bias. Second, the TyG index and MHR are based solely on baseline data, precluding dynamic monitoring and the assessment of their longitudinal association with cardiovascular disease risk. Third, the study did not account for the effects of secondary preventive drugs for CAD, antihypertensive drugs, and hypoglycemic drugs on blood glucose, blood lipids, and CAD occurrence. Lastly, while the Gensini score assessed coronary artery lesion severity, it did not fully consider lesion length and plaque characteristics, potentially underestimating lesion severity and affecting our results. Additionally, we acknowledge that while the Gensini score is widely used to quantify the severity of CAD by assessing both the degree of stenosis and the anatomical location of lesions, it may not always fully reflect the anatomical complexity of coronary artery disease. Anatomical complexity, such as the involvement of multiple vessels, the presence of complex plaques, or the distribution of lesions, might vary independently of the stenosis severity assessed by the Gensini score. Thus, while Gensini score is a valuable tool for assessing CAD burden, it does not necessarily capture all factors contributing to the severity of CAD. This should be considered when interpreting our findings, and future studies may benefit from combining Gensini score with other imaging modalities or scoring systems that take into account these anatomical complexities.

Conclusion

The TyG index and MHR are independent markers for assessing CAD severity. The TyG index is more predictive in diabetes patients, while MHR is more significant in those with normal glucose regulation. Combining both markers improves predictive accuracy, highlighting the role of metabolic and inflammatory factors in CAD progression.

Data Sharing Statement

The data supporting the results of this study are available from the corresponding author upon reasonable request.

Acknowledgments

The author gratefully acknowledges the valuable comments on the manuscript provided by colleagues who are not listed as authors.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This study did not receive any funding support.

Disclosure

The authors confirm that they have no conflicts of interest related to this work.

References

1. Townsend N, Nichols M, Scarborough P, et al. Cardiovascular disease in Europe—epidemiological update 2015. *Eur Heart J*. 2015;36(40):2696–2705. doi:10.1093/eurheartj/ehv428
2. Naser A. The gensini score system is a useful tool in assessing the burden and severity of coronary artery atherosclerotic lesions. *Int J Gene Med*. 2024:4227–4228.
3. Gensini GG. A more meaningful scoring system for determining the severity of coronary heart disease. *Am J Cardiol*. 1983;51:606. doi:10.1016/S0002-9149(83)80105-2
4. Mechanick JI, Farkouh ME, Newman JD, et al. Cardiometabolic-based chronic disease, adiposity and dysglycemia drivers: JACC state-of-the-art review. *J Am Coll Cardiol*. 2020;75(5):525–538. doi:10.1016/j.jacc.2019.11.044
5. Ormazabal V, Nair S, Elfeky O, et al. Association between insulin resistance and the development of cardiovascular disease. *Cardiovasc. Diabetol*. 2018;17:1–14. doi:10.1186/s12933-018-0762-4
6. Cai X, Xiang Y, Chen X, et al. Prognostic value of triglyceride glucose index in population at high cardiovascular disease risk. *Cardiovasc. Diabetoly*. 2023;22(1):198. doi:10.1186/s12933-023-01924-2
7. Liang S, Wang C, Zhang J, et al. Triglyceride-glucose index and coronary artery disease: a systematic review and meta-analysis of risk, severity, and prognosis. *Cardiovasc. Diabetol*. 2023;22(1):170. doi:10.1186/s12933-023-01906-4
8. Choi SH, Kim JH, Lim S, et al. Monocyte count as a predictor of cardiovascular mortality in older Korean people. *Age Ageing*. 2017;46(3):433–438. doi:10.1093/ageing/afw226
9. Tran-Dinh A, Diallo D, Delbosc S, et al. HDL and endothelial protection. *Br. J. Pharmacol*. 2013;169(3):493–511. doi:10.1111/bph.12174
10. Jiang M, Yang J, Zou H, et al. Monocyte-to-high-density lipoprotein-cholesterol ratio (MHR) and the risk of all-cause and cardiovascular mortality: a nationwide cohort study in the United States. *Lipids Health Dis*. 2022;21(1):30. doi:10.1186/s12944-022-01638-6
11. Villanueva DLE, Tiongson MD, Ramos JD, et al. Monocyte to High-Density Lipoprotein Ratio (MHR) as a predictor of mortality and Major Adverse Cardiovascular Events (MACE) among ST Elevation Myocardial Infarction (STEMI) patients undergoing primary percutaneous coronary intervention: a meta-analysis[J]. *Lipids Health Dis*. 2020;19:1–8. doi:10.1186/s12944-020-01242-6
12. Shu H, Han S, Qiu W, et al. Association of the monocyte to high-density lipoprotein cholesterol ratio and neutrophil to high-density lipoprotein cholesterol ratio with the severity of new-onset coronary artery disease. *J Inflamm Res*. 2025:463–476.
13. Rydén L, Grant PJ, Grant PJ, et al. ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD: the Task Force on diabetes, pre-diabetes, and cardiovascular diseases of the European Society of Cardiology (ESC) and developed in collaboration with the European Association for the Study of Diabetes (EASD). *Eur Heart J*. 2013;34(39):3035–3087. doi:10.1093/eurheartj/eht108
14. Laakso M, Kuusisto J. Insulin resistance and hyperglycaemia in cardiovascular disease development. *Nat Rev Endocrinol*. 2014;10(5):293–302. doi:10.1038/nrendo.2014.29

15. Li M, Chi X, Wang Y, et al. Trends in insulin resistance: insights into mechanisms and therapeutic strategy. *Signal Transduct Target Ther*. 2022;7(1):216. doi:10.1038/s41392-022-01073-0
16. Tam CS, Xie W, Johnson WD, et al. Defining insulin resistance from hyperinsulinemic-euglycemic clamps. *Diabetes Care*. 2012;35(7):1605–1610. doi:10.2337/dc11-2339
17. Vasques ACJ, Novaes FS, de Oliveira MS, et al. TyG index performs better than HOMA in a Brazilian population: a hyperglycemic clamp validated study. *Diabetes Res Clin Pract*. 2011;93(3):e98–e100. doi:10.1016/j.diabres.2011.05.030
18. Wang L, Cong H, Zhang J, et al. Triglyceride-glucose index predicts adverse cardiovascular events in patients with diabetes and acute coronary syndrome. *Cardiovasc. Diabetol*. 2020;19:1–11. doi:10.1186/s12933-020-01054-z
19. Wu S, Xu L, Wu M, et al. Association between triglyceride-glucose index and risk of arterial stiffness: a cohort study. *Cardiovasc. Diabetoly.* 2021;20:1–8. doi:10.1186/s12933-021-01342-2
20. Wang X, Xu W, Song Q, et al. Association between the triglyceride–glucose index and severity of coronary artery disease. *Cardiovasc. Diabetol*. 2022;21(1):168. doi:10.1186/s12933-022-01606-5
21. Su J, Li Z, Huang M, et al. Triglyceride glucose index for the detection of the severity of coronary artery disease in different glucose metabolic states in patients with coronary heart disease: a RCSCD-TCM study in China. *Cardiovasc. Diabetol*. 2022;21(1):96. doi:10.1186/s12933-022-01523-7
22. Wu X, Qiu W, Yang H, et al. Associations of the triglyceride-glucose index and atherogenic index of plasma with the severity of new-onset coronary artery disease in different glucose metabolic states. *Cardiovasc. Diabetoly.* 2024;23(1):76. doi:10.1186/s12933-024-02163-9
23. Zhao S, Wang Z, Qing P, et al. Comprehensive analysis of the association between triglyceride-glucose index and coronary artery disease severity across different glucose metabolism states: a large-scale cross-sectional study from an Asian cohort. *Cardiovasc. Diabetoly.* 2024;23(1):251. doi:10.1186/s12933-024-02355-3
24. Murphy AJ, Woollard KJ, Hoang A, et al. High-density lipoprotein reduces the human monocyte inflammatory response. *Arteriosclerosis Thrombosis Vasc Biol*. 2008;28(11):2071–2077. doi:10.1161/ATVBAHA.108.168690
25. Woollard KJ, Geissmann F. Monocytes in atherosclerosis: subsets and functions. *Nat Rev Cardiol*. 2010;7(2):77–86. doi:10.1038/nrcardio.2009.228
26. Chen J, Wu K, Cao W, et al. Association between monocyte to high-density lipoprotein cholesterol ratio and multi-vessel coronary artery disease: a cross-sectional study. *Lipids Health Dis*. 2023;22(1):121. doi:10.1186/s12944-023-01897-x