Balkan Med J 2025;42:339-46

Triglyceride-Glucose Index Predicts Major Adverse Cardiovascular and Cerebrovascular Events in Non-Diabetic Individuals

Cangtuo Li[1], Qi Qi[2], Wansong Li[2], Xuechao Zhang[3], Lei Li[3], Jie Deng[3], Quanle Han[3], Shouling Wu[4], Kangbo Li[5]

[1]Department of Vascular and Interventional Radiology, Tangshan Gongren Hospital, Tangshan, China
[2]Hebei Medical University, Shijiazhuang, China
[3]Department of Cardiology, Tangshan Gongren Hospital, Tangshan, China
[4]Department of Cardiology, Kailuan General Hospital, Tangshan, China
[5]School of Clinical Medicine, North China University of Science and Technology, Tangshan, China

Background: The association between the triglyceride-glucose (TyG) index and the occurrence of major adverse cardiovascular and cerebrovascular events (MACCEs) in individuals without diabetes has not been clearly established.

Aims: To investigate the potential of the TyG index to predict MACCEs in a non-diabetic population.

Study Design: Prospective cohort study.

Methods: This study analyzed data from 88,946 participants without diabetes, who were divided into four groups based on their TyG index values. The primary outcome was the occurrence of MACCEs, defined as myocardial infarction (MI) or stroke. Multivariable Cox proportional hazards regression models were used to assess the association between the TyG index and MACCEs.

Results: Participants in the higher TyG index quartiles exhibited a greater risk of MACCEs. Moreover, a significant interaction between the TyG index and sex was identified, with a stronger association observed in women than in men. A significant interaction was also found between the TyG index and age in relation to MI risk, indicating a stronger associations in individuals younger than 60 compared to those aged 60 or older.

Conclusion: The TyG index may serve as a useful prognostic marker for MACCEs among individuals without diabetes.

INTRODUCTION

Insulin resistance (IR) is defined by a diminished responsiveness of insulin-sensitive cells to insulin under normal physiological conditions. This dysfunction plays a central role in the onset of type 2 diabetes mellitus (T2DM)[1] and is also a major contributor to a range of cardiometabolic conditions, including myocardial infarction (MI) and stroke.[2,3] The triglyceride-glucose (TyG) index, derived from fasting triglyceride (TG) and glucose levels, has been identified as a practical surrogate marker for IR.[4] Recent research has demonstrated the TyG index's predictive value for major adverse cardiovascular and cerebrovascular events (MACCEs) among individuals with T2DM.[5-8] However, its association with MACCEs in people without diabetes remains insufficiently understood. Accordingly, this study aims to evaluate the TyG index as a potential predictor of MACCEs in non-diabetic individuals.

MATERIALS AND METHODS

Study Subjects

The study was approved by the Ethics Committee of Kailuan General Hospital (approval number: [2006]Yilunzi5Hao, date: 01.01.2006) and written informed consent was obtained from all participants.

Corresponding author: Quanle Han, Department of Cardiology, Tangshan Gongren Hospital, Tangshan, China

e-mail: quanle.han@outlook.com

Received: February 25, 2025 **Accepted:** May 08, 2025 **Available Online Date:** 01.07.2025 • **DOI:** 10.4274/balkanmedj.galenos.2025.2025-2-109

Available at www.balkanmedicaljournal.org

ORCID iDs of the authors: C.L. 0009-0003-8526-9593; Q.Q. 0009-0005-5107-7168; W.L. 0009-0000-8875-1615; X.Z. 0009-0002-7546-7425; L.L. 0009-0000-7420-5496; J.D. 0009-0004-4109-9075; Q.H. 0000-0002-3200-9224; S.W. 0000-0002-2921-7583; K.L. 0000-0003-0186-3265.

Cite this article as: Li C, Qi Q, Li W, Zhang X, Li L, Deng J, Han Q, Wu S, Li K. Triglyceride-Glucose Index Predicts Major Adverse Cardiovascular and Cerebrovascular Events in Non-Diabetic Individuals.. Balkan Med J.; 2025; 42(4):339-46.

The Kailuan study is a longitudinal cohort project designed to examine the mortality and mobility related to cardiovascular diseases (CVDs) in the city of Tangshan. The study initially enrolled 101,510 participants beginning in July 2006. For the current analysis, inclusion criteria required participants to be non-diabetic individuals aged over 18 years. Exclusion criteria encompassed individuals diagnosed with DM, MI, stroke, cancer, or other serious illnesses, as well as those with incomplete laboratory data. As a result, 12,564 individuals were excluded: 9,013 with DM, 90 with MI, 2,201 with stroke, and 1,260 with incomplete laboratory information. The final cohort for this study included 88,946 non-diabetic individuals (Figure 1).

Data collection

During the initial enrollment phase, all participants underwent comprehensive medical examinations and laboratory testing coordinated by the Kailuan General Hospital. The physical assessment included various components such as demographic information, anthropometric measurements, lifestyle factors, and medical history. A 6 ml sample of peripheral venous blood was collected to assess fasting TG and fasting blood glucose (FBG) levels. The TyG index was computed using the formula: ln [TG (mg/dl) × FBG (mg/dl)/2]. All clinical assessments and laboratory evaluations were conducted biennially for each participant from July 2006 through December 2021.

Clinical endpoint and follow-up

The primary clinical endpoint in this study was the incidence of MACCEs. For the purpose of this research, MACCEs were defined to include 1) MI (both ST-elevation and non-ST-elevation) and 2) stroke (including both ischemic and hemorrhagic types). Follow-up began on the date of participant enrollment and continued either until the occurrence of a defined clinical event or until December 2021.

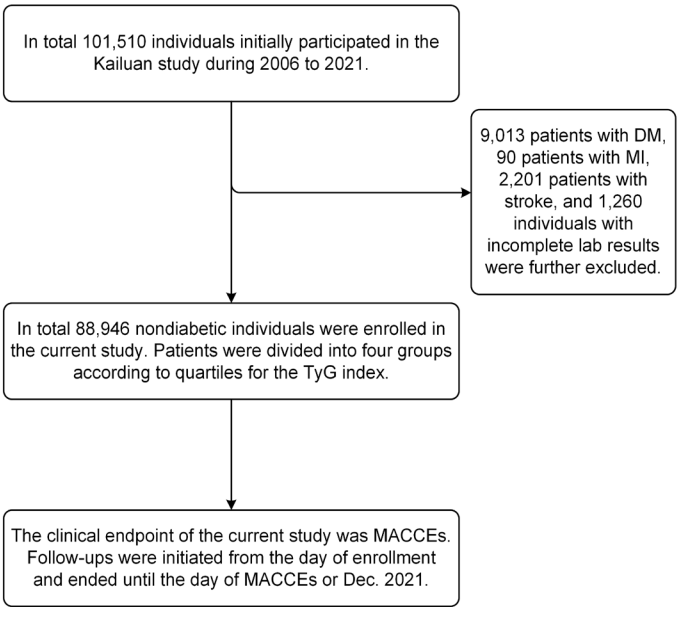

FIG. 1. Study flowchart.

DM, diabetes mellitus; MI, myocardial infarction; TyG index, triglyceride-glucose index; MACCEs, major adverse cardiovascular and cerebrovascular events.

Statistical analysis

All statistical analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, USA). Baseline characteristics were described as means with standard deviations for continuous variables and as frequencies with percentages for categorical variables. Comparisons across TyG index quartiles were carried out using one-way analysis of variance for continuous variables, and chi-square tests for categorical variables, where appropriate. The Kaplan-Meier method was applied to depict the cumulative incidence of time to MACCEs. Multivariable Cox proportional hazards regression models were used to examine the relationship between the TyG index and the risk of MACCEs. A p value of less than 0.05 was considered to indicate statistical significance.

RESULTS

Baseline characteristics

Table 1 presents the baseline characteristics of the 88,946 participants. The participants were divided into four equal groups according to their TyG index values: quartile 1 (3.61 ≤ TyG index < 8.15), quartile 2 (8.15 ≤ TyG index < 8.52), quartile 3 (8.52 ≤ TyG index < 9.45), and quartile 4 (9.45 ≤ TyG index < 11.50). Participants in quartile 4 had a higher proportion of men and showed increased levels of body mass index, blood pressure, FBG, and high-sensitivity C-reactive protein. This group also had a higher prevalence of smokers, alcohol users, individuals who reported snoring, and those diagnosed with hypertension and dyslipidemia.

Association between the TyG index and MACCEs

Over a median follow-up period of 14 years, a total of 6,999 MACCEs were documented, comprising 1,509 cases of MI and 5,658 cases of stroke. Participants in the higher TyG index quartiles demonstrated a greater cumulative incidence of MACCEs compared to those in the lower quartiles throughout the follow-up (log-rank test, $p < 0.01$). Specifically, the cumulative incidence of MACCEs in quartile 4 was markedly higher than in quartile 1 at multiple time points: 10.15% vs. 6.24% at 14 years, 6.34% vs. 3.95% at 10 years, and 2.84% vs. 1.83% at 5 years. Similarly, the cumulative incidence of MI in quartile 4 was significantly greater than in quartile 1 at the same intervals, with values of 2.57% vs. 1.13% at 14 years, 1.82% vs. 0.75% at 10 years, and 0.77% vs. 0.38% at 5 years. The cumulative incidence of stroke was also significantly higher in quartile 4 compared to quartile 1, reported as 7.91% vs. 5.27% at 14 years, 4.69% vs. 3.26% at 10 years, and 2.10% vs. 1.45% at 5 years (Figure 2).

Moreover, the findings indicated that participants in the highest TyG index quartile had a significantly greater risk of experiencing MACCEs compared to those in the lowest quartile [model 1, hazard ratio (HR), 1.657; 95% confidence interval (CI), 1.547-1.775; p for

trend = 0.0001; model 2, HR, 1.229; 95% CI, 1.135-1.331; p for trend = 0.0001). Similarly, the risk of MI was higher among individuals in the highest TyG quartile compared to those in the lowest (model 1, HR, 2.317, 95% CI, 1.988-2.699, p for trend = 0.0001), (model 2, HR, 1.695, 95% CI, 1.422-2.020, p for trend = 0.0001). The risk of stroke was higher among individuals in the highest TyG quartile compared to those in the lowest (model 1, HR, 1.513; 95% CI, 1.402-1.632; p for trend = 0.0001; model 2, HR, 1.123; 95% CI, 1.028-1.226; p for trend = 0.0001).

Furthermore, analysis of the TyG index as a continuous variable showed that each unit increase was linked to a higher risk of MACCEs (model 1, HR, 1.204; 95% CI, 1.176-1.232; $p < 0.0001$; model 2, HR, 1.140; 95% CI, 1.077-1.207; $p < 0.0001$). Each unit increase in the TyG index was also associated with an elevated risk of MI (model 1, HR, 1.330; 95% CI, 1.266-1.396; $p < 0.0001$; model 2, HR, 1.504; 95% CI, 1.315-1.721; $p < 0.0001$). Moreover, an increase of one unit in the TyG index was related to a greater risk of stroke (model 1, HR, 1.171; 95% CI, 1.141-1.202; $p < 0.0001$; model 2, HR, 1.063; 95% CI, 0.999-1.131; $p = 0.054$) (Table 2).

Subgroup analysis

Subgroup analysis identified a significant interaction between the TyG index and sex in relation to the risks of MACCEs, MI, and stroke, with stronger associations observed in women compared to men (p

TABLE 1. Baseline Characteristics.

Variables	Total (n=88,946)	Quartile 1 (n=22,257)	Quartile 2 (n=22,215)	Quartile 3 (n=22,238)	Quartile 4 (n=22,236)	*p*
Age, years	51.13 ± 12.67	50.24 ± 13.82	51.38 ± 12.85	51.88 ± 12.31	51.01 ± 11.55	< 0.0001
Male, n (%)	70.595 (79.37)	16.343 (73.43)	17.522 (78.87)	17.955 (80.74)	18.775 (84.44)	< 0.0001
BMI, kg/m^2	24.91 ± 3.47	23.34 ± 3.23	24.51 ± 3.29	25.45 ± 3.29	26.36 ± 3.35	< 0.0001
SBP, mmHg	129.90 ± 20.65	124.23 ± 19.91	129.17 ± 20.25	131.58 ± 20.55	134.64 ± 20.45	< 0.0001
DBP, mmHg	83.11 ± 11.69	79.50 ± 11.00	82.57 ± 11.34	84.17 ± 11.54	86.22 ± 11.80	< 0.0001
FBG, mmol/L	5.08 ± 0.69	4.76 ± 0.63	5.01 ± 0.63	5.20 ± 0.67	5.35 ± 0.71	< 0.0001
TC, mmol/L	4.92 ± 1.12	4.63 ± 0.92	4.90 ± 0.95	5.10 ± 1.01	5.04 ± 1.46	< 0.0001
TG, mmol/L	1.24 (0.88-1.87)	0.69 (0.57-0.80)	1.06 (0.95-1.18)	1.48 (1.31-1.67)	2.65 (2.14-3.75)	< 0.0001
HDL-C, mmol/L	1.55 ± 0.40	1.57 ± 0.41	1.56 ± 0.39	1.54 ± 0.39	1.52 ± 0.41	< 0.0001
LDL-C, mmol/L	2.34 ± 0.90	2.17 ± 0.92	2.38 ± 0.87	2.45 ± 0.87	2.36 ± 0.93	< 0.0001
hs-CRP, mg/L	0.80 (0.30-2.20)	0.62 (0.22-2.20)	0.73 (0.29-2.10)	0.88 (0.32-2.20)	0.98 (0.39-2.50)	< 0.0001
Hypertension, n (%)	37.237 (41.86)	6.380 (28.67)	8.869 (39.92)	10.266 (46.16)	11.722 (52.72)	< 0.0001
Dyslipidemia, n (%)	52.405 (58.92)	7.681 (34.51)	9.215 (41.48)	13.590 (61.11)	21.919 (98.57)	< 0.0001
Smoking, n (%)	30.649 (34.46)	7.369 (33.11)	7.161 (32.23)	7.507 (33.76)	8.612 (38.73)	< 0.0001
Drinking, n (%)	33.592 (37.77)	8.285 (37.22)	7.751 (34.89)	8.154 (36.67)	9.402 (42.28)	< 0.0001
Snoring, n (%)	32.175 (36.17)	7.793 (35.01)	7.540 (33.94)	7.988 (35.92)	8.854 (39.82)	< 0.0001

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; hs-CRP, high sensitivity-C-reactive protein.

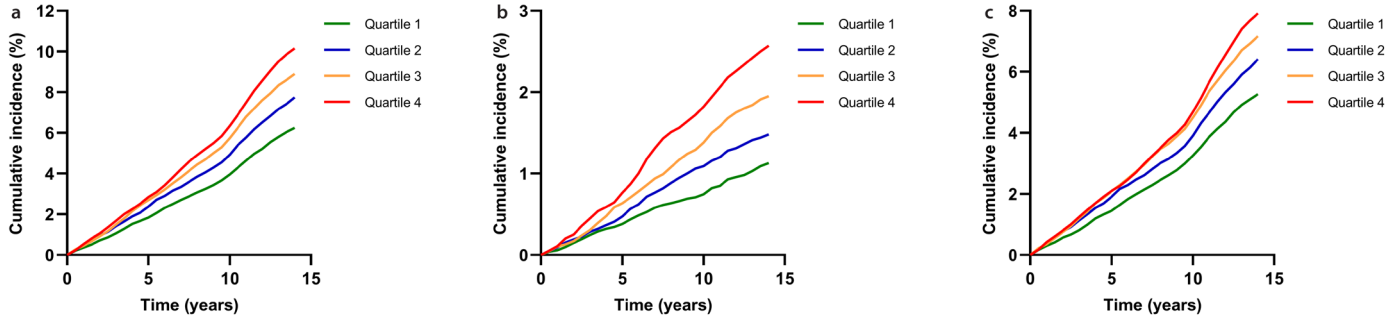

FIG. 2. Cumulative incidence of (a) MACCEs, (b) MI, and (c) stroke.
MACCEs, major adverse cardiovascular and cerebrovascular events; MI, myocardial infarction.

< 0.0001) (Tables 3-5). Furthermore, a significant interaction was found between the TyG index and age concerning the risk of MI (p = 0.030), showing that the association between the TyG index and MI risk was more pronounced in individuals younger than 60 years compared to those aged 60 and above (Table 4).

DISCUSSION

The primary finding of this study is a higher TyG index is linked to an increased risk of MACCEs in individuals without diabetes. Thus, the TyG index holds clinical importance and could be used as a prognostic indicator for MACCEs in the non-diabetic population. It is

TABLE 2. Adjusted HR and 95% CI for MACCEs.

	β	SE	χ^2	p	HR	95% CI	p for trend
MACCEs							
Model 1							< 0.0001
Quartile 2	0.185	0.037	25.024	< 0.0001	1.203	1.119-1.294	
Quartile 3	0.325	0.036	82.183	< 0.0001	1.384	1.290-1.485	
Quartile 4	0.505	0.035	207.662	< 0.0001	1.657	1.547-1.775	
Per unit increase	0.186	0.012	245.145	< 0.0001	1.204	1.176-1.232	
Model 2							< 0.0001
Quartile 2	0.076	0.037	4.101	0.043	1.079	1.002-1.161	
Quartile 3	0.128	0.038	11.671	0.001	1.137	1.056-1.223	
Quartile 4	0.206	0.041	25.857	< 0.0001	1.229	1.135-1.331	
Per unit increase	0.131	0.029	20.182	< 0.0001	1.140	1.077-1.207	
MI							
Model 1							< 0.0001
Quartile 2	0.247	0.086	8.296	0.004	1.281	1.082-1.516	
Quartile 3	0.515	0.081	40.045	< 0.0001	1.674	1.427-1.964	
Quartile 4	0.840	0.078	116.028	< 0.0001	2.317	1.988-2.699	
Per unit increase	0.285	0.025	130.071	< 0.0001	1.330	1.266-1.396	
Model 2							< 0.0001
Quartile 2	0.123	0.087	2.020	0.155	1.131	0.954-1.341	
Quartile 3	0.290	0.085	11.694	0.001	1.337	1.132-1.579	
Quartile 4	0.528	0.089	34.775	< 0.0001	1.695	1.422-2.020	
Per unit increase	0.408	0.069	35.303	< 0.0001	1.504	1.315-1.721	
Stroke							
Model 1							< 0.0001
Quartile 2	0.164	0.040	16.503	< 0.0001	1.179	1.089-1.276	
Quartile 3	0.275	0.039	48.500	< 0.0001	1.316	1.218-1.422	
Quartile 4	0.414	0.039	114.003	< 0.0001	1.513	1.402-1.632	
Per unit increase	0.158	0.013	141.328	< 0.0001	1.171	1.141-1.202	
Model 2							< 0.0001
Quartile 2	0.059	0.041	2.087	0.149	1.061	0.979-1.149	
Quartile 3	0.084	0.041	4.149	0.042	1.088	1.003-1.179	
Quartile 4	0.116	0.045	6.617	0.010	1.123	1.028-1.226	
Per unit increase	0.061	0.032	3.728	0.054	1.063	0.999-1.131	

Model 1, adjusted for age and sex; Model 2, further adjusted body mass index, systolic blood pressure, diastolic blood pressure, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, hypersensitive C-reactive protein, hypertension, dyslipidemia, smoking, drinking, snoring; MACCEs, major adverse cardiovascular and cerebrovascular events; β, beta coefficient; S.E., standard error; χ^2, chi-square statistic; HR, hazard ratio; CI, confidence interval; MI, myocardial infarction.

TABLE 3. Subgroup Analysis of Between the TyG Index and MACCEs.

Subgroup	Total number	Case number	*p*	HR	95% CI	*p* for interaction
Age						0.124
≥ 60						
Quartile 1	4,895	615	-	-	-	
Quartile 2	4,899	663	0.971	0.998	0.893-1.115	
Quartile 3	4,998	710	0.936	1.005	0.897-1.126	
Quartile 4	4,193	715	0.016	1.167	1.029-1.323	
< 60						
Quartile 1	17,362	707	-	-	-	
Quartile 2	17,316	974	0.007	1.144	1.037-1.262	
Quartile 3	17,240	1,178	< 0.0001	1.228	1.115-1.353	
Quartile 4	18,043	1,437	< 0.0001	1.268	1.143-1.406	
Sex						< 0.0001
Men						
Quartile 1	16,343	1,207	-	-	-	
Quartile 2	17,522	1,472	0.191	1.053	0.975-1.137	
Quartile 3	17,955	1,665	0.018	1.098	1.016-1.186	
Quartile 4	18,775	1,922	< 0.001	1.180	1.085-1.283	
Women						
Quartile 1	5,914	115	-	-	-	
Quartile 2	4,693	165	0.108	1.220	0.958-1.554	
Quartile 3	4,283	223	0.005	1.405	0.106-1.785	
Quartile 4	3,461	230	0.003	1.485	1.146-1.923	

MACCEs, major adverse cardiovascular and cerebrovascular events; TyG index, triglyceride-glucose index; HR, hazard ratio; CI, confidence interval.

worth noting that research on the predictive value of the TyG index for MACCEs in non-diabetic individuals is limited. In this context, Zhang et al.[9] conducted a study with 1,650 non-diabetic patients who had acute coronary syndrome (ACS) and underwent percutaneous coronary intervention (PCI). Their aim was to determine the relationship between the TyG index and clinical outcomes in ACS. The study found a positive association between the TyG index and MACCEs (HR, 1.493; 95% CI, 1.230-1.812). Moreover, their findings also demonstrated a positive correlation between the TyG index and revascularization (HR, 1.67; 95% CI, 1.02-2.75).[9] In contrast, Yang et al.[10] analyzed data from 5,489 non-diabetic patients with coronary artery disease (CAD) who underwent PCI to assess the predictive value of the TyG index for adverse cardiovascular outcomes. This study, however, did not find a significant association between the TyG index and MACCEs (HR, 0.77; 95% CI, 0.56-1.16).[10] Similarly, Drwiła et al.[11] examined data from 1,340 non-diabetic patients with acute MI to assess the relationship between the TyG index and MACE. Their results also showed no significant correlation between the TyG index and MACE.[11]

In summary, the predictive value of the TyG index in non-diabetic individuals remains controversial. A major difference between previous studies and ours is the criteria used to select the study populations. Our study focused on non-diabetic individuals without complications, whereas Yang et al.[10] investigated non-diabetic patients with CAD who underwent PCI, and Drwiła et al.[11] examined non-diabetic patients who had acute MI.[11] Furthermore, the definitions of MACCE (or MACE) differed across studies. In our research, MACCEs included MI and stroke, while Yang et al.'s[10] study covered all-cause mortality, non-fatal MI, non-fatal stroke, and target vessel revascularization. Drwiła et al.'s[11] study defined MACCEs as MI, in-stent restenosis, unstable angina, stroke or transient ischemic attack, and hospitalization due to heart failure. Although numerous studies have confirmed the TyG index's role in predicting CVDs,[12] its relationship with restenosis and revascularization remains uncertain.

Additionally, our findings showed a significant interaction between the TyG index and sex in relation to the risk of MACCEs, with the association being stronger in females than in males. Traditionally, CVDs have been conditions that primarily affect men, who generally have more risk factors than women.[13,14] However, CVD remains the leading cause of death among women globally, and the challenges women face regarding this condition are often underestimated.

TABLE 4. Subgroup Analysis of Between the TyG index and MI.

Subgroup	Total number	Case number	*p*	HR	95% CI	*p* for interaction
Age						0.030
≥ 60						
Quartile 1	4,895	120	-	-	-	
Quartile 2	4,899	132	0.859	0.978	0.761-1.255	
Quartile 3	4,998	157	0.548	1.080	0.841-1.386	
Quartile 4	4,193	189	0.003	1.497	1.148-1.952	
< 60						
Quartile 1	17,362	118	-	-	-	
Quartile 2	17,316	183	0.042	1.274	1.009-1.610	
Quartile 3	17,240	256	< 0.0001	1.567	1.250-1.965	
Quartile 4	18,043	354	< 0.0001	1.874	1.479-2.375	
Sex						< 0.0001
Men						
Quartile 1	16,343	227	-	-	-	
Quartile 2	17,522	291	0.387	1.080	0.907-1.287	
Quartile 3	17,955	378	0.006	1.270	1.070-1.508	
Quartile 4	18,775	495	< 0.0001	1.560	1.301-1.870	
Women						
Quartile 1	5,914	11	-	-	-	
Quartile 2	4,693	24	0.091	1.865	0.905-3.842	
Quartile 3	4,283	35	0.015	2.410	1.184-4.906	
Quartile 4	3,461	48	0.001	3.781	1.794-7.972	

TyG index, triglyceride-glucose index; MI, myocardial infarction; HR, hazard ratio; CI, confidence interval.

Studies show that women receive less treatment for both primary and secondary prevention compared to men. Furthermore, women tend to experience heart disease differently than men, and overlooking these differences can lead to poorer outcomes.[15] Prior to menopause, women exhibit a lower prevalence of IR than age-matched men; however, this protective effect diminishes after menopause, resulting in similar IR rates between sexes, which suggests a possible protective role of estrogen.[16]

Furthermore, a significant correlation was found between the TyG index and age in relation to the risk of MI. The association between the TyG index and MI occurrence was notably stronger in younger individuals (under 60 years) compared to older adults (60 years and above). Statistically, from 1990 to 2019, there was a concerning 25% rise in global annual deaths due to premature CVDs. Importantly, metabolic disorders have been identified as the main risk factors driving mortality from premature CVDs.[17] Cardiometabolic factors, such as DM and dyslipidemias, can initiate or worsen the onset of MI at a younger age.[18] In a study involving 108 patients who experienced an MI before age 45, none had DM, yet 65% showed impaired glucose response during an oral glucose tolerance test.[19]

Moreover, research shows that the accuracy of the TyG index may differ significantly across ethnic groups. Differences in metabolic traits, genetic backgrounds, and lifestyle factors can affect body fat distribution and metabolic rates, which in turn may influence the performance of the TyG index. These variations highlight the lack of standardization in using the TyG index and emphasize the need for additional research to verify its applicability in diverse demographic and clinical contexts. This necessitates validating the TyG index for each specific population and determining appropriate cut-off points. Evidence indicates that the optimal TyG index cut-off for diagnosing metabolic syndrome varies between ethnicities and populations. For instance, two comparable studies conducted in Türkiye and China reported different best cut-off values for predicting MACE, along with varying sensitivity and specificity levels.[20,21]

From another angle, investigating the relationship between the TyG index and MACCEs could greatly improve current knowledge, which is important for advancing artificial intelligence and machine learning (ML) approaches in managing MACCEs.[22] In this context, Mirjalili et al.[23] studied 2,000 individuals from a community-based Iranian cohort and found that a support vector machine (SVM) model that included the TyG index outperformed a diabetes-based SVM in predicting coronary heart disease. Furthermore, Chen et al.[24] examined data from 3,374 patients who experienced their first stroke and found that the TyG index, with an optimal cut-off value of 9,265, was an independent risk factor for both intensive care unit

TABLE 5. Subgroup Analysis of Between the TyG Index and Stroke.

Subgroup	Total number	Case number	*p*	HR	95% CI	*p* for interaction
Age						0.536
≥ 60						
Quartile 1	4,895	510	-	-	-	
Quartile 2	4,899	546	1.000	1.000	0.885-1.130	
Quartile 3	4,998	578	0.922	0.994	0.876-1.127	
Quartile 4	4,193	552	0.273	1.082	0.940-1.244	
< 60						
Quartile 1	17,362	604	-	-	-	
Quartile 2	17,316	807	0.055	1.110	0.998-1.235	
Quartile 3	17,240	942	0.011	1.148	1.032-1.277	
Quartile 4	18,043	1,119	0.022	1.143	1.019-1.281	
Sex						< 0.0001
Men						
Quartile 1	16,343	1,009	-	-	-	
Quartile 2	17,522	1,212	0.341	1.042	0.957-1.134	
Quartile 3	17,955	1,329	0.227	1.054	0.968-1.148	
Quartile 4	18,775	1,488	0.068	1.091	0.994-1.198	
Women						
Quartile 1	5,914	105	-	-	-	
Quartile 2	4,693	141	0.324	1.138	0.880-1.472	
Quartile 3	4,283	191	0.048	1.293	1.003-1.666	
Quartile 4	3,461	183	0.132	1.237	0.938-1.632	

TyG index, triglyceride-glucose index; HR, hazard ratio; CI, confidence interval.

and overall hospital mortality. The ML model that incorporated the TyG index demonstrated strong predictive ability.[24]

The TyG index may function as a predictor of MACCEs in individuals without diabetes. Understanding the link between the TyG index and MACCEs could improve risk evaluation and help inform treatment strategies targeting lipid and glucose metabolism in the non-diabetic population.

Ethics Committee Approval: The study was approved by the Ethics Committee of Kailuan General Hospital (approval number: [2006] Yilunzi5Hao, date: 01.01.2006).

Informed Consent: Written informed consent was obtained from all participants.

Data Sharing Statement: The datasets analyzed during the current study are available from the corresponding author upon reasonable request.

Authorship Contributions: Concept- C.L., Q.Q., W.L., X.Z., L.L., J.D., Q.H., S.W., K.L.; Design- C.L., Q.Q., W.L., X.Z., L.L., J.D., Q.H., S.W., K.L.; Supervision- Q.H.; Fundings- Q.H.; Materials- C.L., Q.Q., W.L., X.Z., L.L., J.D., Q.H., S.W., K.L.; Data Collection or Processing- C.L., Q.Q., W.L., X.Z., L.L., J.D., Q.H., S.W., K.L.; Analysis or Interpretation- C.L., Q.Q., W.L., X.Z., L.L., J.D., Q.H., S.W., K.L.; Literature Review- C.L., Q.Q., W.L., X.Z., L.L., J.D., Q.H., S.W., K.L.; Writing- C.L., Q.Q., W.L., X.Z., L.L., J.D., Q.H., S.W., K.L.; Critical Review- C.L., Q.Q., W.L., X.Z., L.L., J.D., Q.H., S.W., K.L.

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

Funding: This work was supported by the key scientific research project of the Health Commission of Hebei province .

REFERENCES

1. Lee SH, Park SY, Choi CS. Insulin resistance: from mechanisms to therapeutic strategies. *Diabetes Metab J*. 2022;46:15-37. [CrossRef]
2. Hill MA, Yang Y, Zhang L, et al. Insulin resistance, cardiovascular stiffening and cardiovascular disease. *Metabolism*. 2021;119:154766. [CrossRef]
3. Kernan WN, Inzucchi SE, Viscoli CM, Brass LM, Bravata DM, Horwitz RI. Insulin resistance and risk for stroke. *Neurology*. 2002;59:809-815. [CrossRef]
4. Simental-Mendía LE, Rodríguez-Morán M, Guerrero-Romero F. The product of fasting glucose and triglycerides as surrogate for identifying insulin resistance in apparently healthy subjects. *Metab Syndr Relat Disord*. 2008;6:299-304. [CrossRef]
5. Tai S, Fu L, Zhang N, Zhou Y, Xing Z, Wang Y. Impact of baseline and trajectory of triglyceride-glucose index on cardiovascular outcomes in patients with type 2 diabetes mellitus. *Front Endocrinol (Lausanne)*. 2022;13:858209. [CrossRef]
6. Zhang Y, Ding X, Hua B, et al. Predictive effect of triglyceride glucose index on clinical events in patients with type 2 diabetes mellitus and acute myocardial infarction: results from an observational cohort study in China. *Cardiovasc Diabetol*. 2021;20:43. [CrossRef]
7. Tai S, Fu L, Zhang N, et al. Association of the cumulative triglyceride-glucose index with major adverse cardiovascular events in patients with type 2 diabetes. *Cardiovasc Diabetol*. 2022;21:161. [CrossRef]
8. Xiong S, Chen Q, Zhang Z, et al. A synergistic effect of the triglyceride-glucose index and the residual SYNTAX score on the prediction of intermediate-term major adverse cardiac events in patients with type 2 diabetes mellitus undergoing percutaneous coronary intervention. *Cardiovasc Diabetol*. 2022;21:115. [CrossRef]
9. Zhang Y, Chu C, Zhong Z, Luo YB, Ning FF, Guo N. High triglyceride-glucose index is associated with poor cardiovascular outcomes in Chinese acute coronary syndrome patients without diabetes mellitus who underwent emergency percutaneous coronary

intervention with drug-eluting stents. *Front Endocrinol (Lausanne).* 2023;14:1101952. [CrossRef]

10. Yang J, Tang YD, Zheng Y, et al. The impact of the triglyceride-glucose index on poor prognosis in nondiabetic patients undergoing percutaneous coronary intervention. *Front Endocrinol (Lausanne).* 2021;12:710240. [CrossRef]
11. Drwiła D, Rostoff P, Gajos G, Nessler J, Konduracka E. Prognostic value of the triglyceride-glucose index among non-diabetic patients with acute myocardial infarction at one-year follow-up. *Kardiol Pol*. 2021;79:1116-1123. [CrossRef]
12. Sánchez-Íñigo L, Navarro-González D, Fernández-Montero A, Pastrana-Delgado J, Martínez JA. The TyG index may predict the development of cardiovascular events. *Eur J Clin Invest.* 2016;46:189-197. [CrossRef]
13. Möller-Leimkühler AM. Gender differences in cardiovascular disease and comorbid depression. *Dialogues Clin Neurosci.* 2007;9:71-83. [CrossRef]
14. Weidner G. Why do men get more heart disease than women? An international perspective. *J Am Coll Health.* 2000;48:291-294. [CrossRef]
15. Woodward M. Cardiovascular disease and the female disadvantage. *Int J Environ Res Public Health.* 2019;16:1165. [CrossRef]
16. Greenhill C. Obesity: sex differences in insulin resistance. *Nat Rev Endocrinol*. 2018;14:65. [CrossRef]
17. Lababidi H, Salerno PR, Wass SY, Shafiabadi Hasani N, Bourges-Sevenier B, Al-Kindi S. The global burden of premature cardiovascular disease, 1990-2019. *Int J Cardiol Cardiovasc Risk Prev.* 2023;19:200212. [CrossRef]
18. Kayikcioglu M, Ozkan HS, Yagmur B. Kayikcioglu M, Ozkan HS, Yagmur B. Premature myocardial infarction: a rising threat. *Balkan Med J.* 2022;39:83-95. [CrossRef]
19. Malmberg K, Båvenholm P, Hamsten A. Clinical and biochemical factors associated with prognosis after myocardial infarction at a young age. *J Am Coll Cardiol.* 1994;24:592-599. [CrossRef]
20. Hayıroğlu Mİ, Çınar T, Çiçek V, Palice A, Ayhan G, Tekkeşin Aİ. The triglyceride-glucose index can predict long-term major adverse cardiovascular events in Turkish patients with high cardiovascular risk. *J Lipid Atheroscler*. 2022;11:280-287. [CrossRef]
21. Wang L, Cong HL, Zhang JX, et al. Triglyceride-glucose index predicts adverse cardiovascular events in patients with diabetes and acute coronary syndrome. *Cardiovasc Diabetol*. 2020;19:80. [CrossRef]
22. Hayıroğlu Mİ, Altay S. The role of artificial intelligence in coronary artery disease and atrial fibrillation. *Balkan Med J.* 2023;40:151-152. [CrossRef]
23. Mirjalili SR, Soltani S, Heidari Meybodi Z, Marques-Vidal P, Kraemer A, Sarebanhassanabadi M. An innovative model for predicting coronary heart disease using triglyceride-glucose index: a machine learning-based cohort study. *Cardiovasc Diabetol.* 2023;22:200. [CrossRef]
24. Chen Y, Yang Z, Liu Y, et al. Exploring the prognostic impact of triglyceride-glucose index in critically ill patients with first-ever stroke: insights from traditional methods and machine learning-based mortality prediction. *Cardiovasc Diabetol.* 2024;23:443. [CrossRef]