scientific reports

Check for updates

OPEN

Association of body mass index combined with triglyceride-glucose index in cardiovascular disease risk: a prospective cohort study

Yu Cheng[1,2], Shouling Wu[2], Shuohua Chen[2] & Yuntao Wu[2]✉

Previous studies have mainly explored the effects of body mass index (BMI) and triglyceride-glucose index (TyG index) on cardiovascular disease (CVD) separately or by examining the composite parameter (TyG-BMI) formed by multiplying the two and its association with CVD. However, few studies have investigated the combined effect of BMI categories and the TyG index on CVD. This study aimed to determine the association of BMI categories combined with the TyG index in new-onset CVD. A total of 94,002 participants were included from the Kailuan study. Their BMI combined with the TyG index was categorized into six groups: Low-BMI/Low-TyG, Middle-BMI/Low-TyG, High-BMI/Low-TyG, Low-BMI/High-TyG, Middle-BMI/High-TyG, and High-BMI/High-TyG. A multifactorial Cox proportional hazards model was used to analyze the longitudinal association between BMI combined with the TyG index and new-onset CVD events. During a follow-up period of 15.95 ± 3.59 years, 9791 new CVD events were recorded. After adjusting for confounding factors such as sex, age, smoking, drinking, physical activity, systolic blood pressure, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, uric acid, high-sensitivity C-reactive protein, antihypertensive drugs, hypoglycemic drugs, and lipid-lowering drugs, Cox regression analysis showed that the risk of CVD events was 52% higher in the High-BMI/High-TyG group (HR: 1.52; 95% CI 1.42–1.64) compared to the Low-BMI/Low-TyG group. The combination of high BMI (≥ 28.0) and high TyG index (> 8.58) significantly increases individual CVD risk. This study suggests that the combination of BMI and the TyG index may better help identify individuals at risk of developing CVD.

Keywords Body mass index, Triglyceride-glucose index, Cardiovascular disease, Combined effect, Cohort study

Abbreviations

CVD	Cardiovascular disease
BMI	Body mass index
TyG index	Triglyceride-glucose index
HOMA-IR	Homeostatic model assessment of insulin resistance
TyG-BMI	Triglyceride glucose-body mass index
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
FBG	Fasting blood glucose
TG	Triglyceride
HDL-C	High-density lipoprotein cholesterol
LDL-C	Low-density lipoprotein cholesterol
TC	Total cholesterol
UA	Uric acid
Hs-CRP	High-sensitivity C-reactive protein
ICD-10	International Classification of Diseases, 10th revision
SD	Standard deviation

[1]School of Public Health, North China University of Science and Technology, Tangshan 063210, China. [2]Kailuan General Hospital, Tangshan 063000, China. ✉email: wyt0086@163.com

ANOVA	One-way analysis of variance
M	Median
HR	Hazard ratio
CI	Confidence interval

Cardiovascular disease (CVD) is among the leading causes of premature death and rising healthcare costs globally[1], and therefore prevention of CVD has become particularly important, especially in high-risk groups (e.g., the elderly, hypertensive patients, etc.)[2–4].

In addition to hypertension and dyslipidemia, overweight/obesity and insulin resistance are also major risk factors for developing CVD[5,6]. Body mass index (BMI), a commonly used measure of overweight/obesity, has been confirmed to be associated with increased CVD risk[7,8]. A longitudinal cohort study suggests that overweight/obese adults have a higher risk of CVD compared to those with normal BMI[9]. Meanwhile, the triglyceride-glucose (TyG) index has been recognized as a cost-effective and reliable marker of insulin resistance, demonstrating superiority over homeostatic model assessment of insulin resistance (HOMA-IR) in population studies because of its independence from insulin assays and its enhanced reproducibility[10]. Several cohort studies have verified that a higher TyG index is conspicuously correlated with an augmented risk of CVD[11–13].

However, current research evidence demonstrates that BMI inaccurately reflects body fat content, as elevated muscle mass may also contribute to increased BMI[14–16]. Thus, Korean scholars proposed the triglyceride glucose-body mass index (TyG-BMI) in 2016, a composite metric constructed through a multiplicative model integrating TyG and BMI, aiming to holistically characterize the synergistic effects of adipose accumulation and insulin resistance[17]. While prior studies have validated the applicability of TyG-BMI in evaluating CVD risk, it fails to account for nonlinear interactions and may obscure threshold effects within specific BMI categories. To address these limitations, this study leverages longitudinal cohort data from the Kailuan Study to investigate the joint association and multiplicative interactions between BMI categories (normal weight, overweight, obesity) and the TyG index in relation to CVD risk. Therefore, we can provide evidence for precision risk stratification of CVD, thereby optimizing the efficiency of clinical screening and reducing associated healthcare costs.

Methods

Study population

Participants in this study were drawn from the Kailuan Study (registration number: ChiCTR-TNRC-11001489), a large-scale prospective cohort study conducted in Tangshan City, China. Details of the study design and methodology have been published elsewhere[18]. The initial health check-ups for current and retired employees of Kailuan Group were conducted by 11 hospitals, including the Kailuan General Hospital, in 2006–2007 (referred to as 2006), with follow-up visits every two years thereafter. A total of 101,510 participants underwent health check-ups in 2006. After excluding 2052 participants with missing BMI and TyG data, 3372 participants with a history of cardiovascular disease, 332 participants with a history of cancer, and 1752 participants with BMI < 18.5, a total of 94,002 participants were included in the study (Fig. 1). The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Kailuan General Hospital, with all participants provided informed consent. This study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for cohort studies.

Data collection and related definitions

Trained professionals collected epidemiologic study content through questionnaires that included comprehensive information on age, sex, smoking, alcohol use, physical activity, medication use (e.g., hypoglycemic,

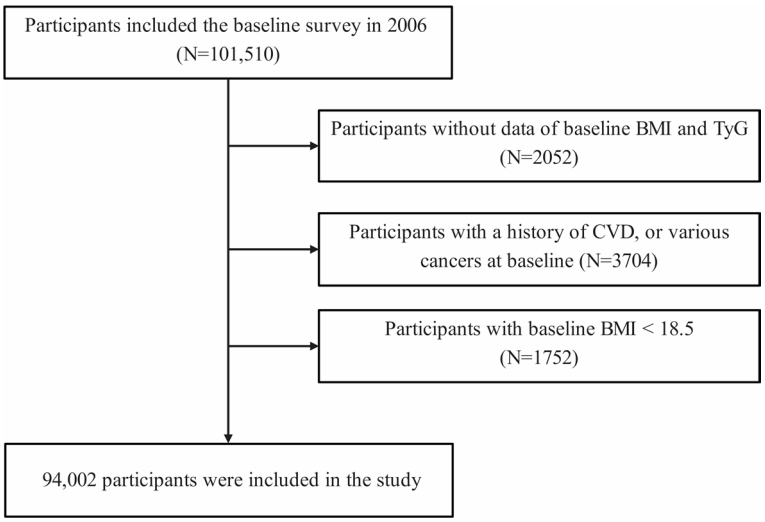

Fig. 1. Flow chart of study participants. Abbreviations: BMI, body mass index; TyG, triglyceride-glucose; CVD, cardiovascular disease.

antihypertensive, and lipid-lowering medications), and self-reported past medical history (e.g., hypertension and diabetes). Smoking was categorized as current smoking and current non-smoking, with current non-smoking including quitters. Alcohol consumption was categorized as current alcohol consumption and current non-alcohol consumption, with current non-alcohol consumption including abstainers. Active physical activity was defined as a frequency of at least three times per week and a duration of at least 30 min per session. Physical activity was divided into two categories: active and inactive.

Participants' height, weight, systolic blood pressure (SBP), and diastolic blood pressure (DBP) were measured by trained physicians or nurse practitioners. Height and body mass were measured using calibrated RGZ-120 body mass scales, accurate to 0.1 cm for height and 0.1 kg for body mass. BMI was calculated as weight (kg) divided by height squared (m^2). Hypertension was defined as SBP ≥ 140 mmHg or DBP ≥ 90 mmHg, or the presence of a history of clearly diagnosed hypertension, or the use of antihypertensive medication, even if SBP < 140 mmHg and DBP < 90 mmHg[19].

For biochemical markers, fasting blood glucose (FBG), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC), uric acid (UA), and high-sensitivity C-reactive protein (Hs-CRP) were measured using the Hitachi Autoanalyzer 747. FBG was measured by the hexokinase/glucose-6-phosphate dehydrogenase method with a coefficient of variation < 2.0%; TG was measured by the enzyme colorimetric method. Diabetes mellitus was defined as FBG ≥ 7.0 mmol/L or, in cases with FBG < 7.0 mmol/L, a history of diabetes mellitus or the use of hypoglycemic medication[20].

Calculation formula and grouping

According to previous studies[21], TyG index was calculated as TyG = ln [TG (mg/dl) × FBG (mg/dl)/2]. We divided BMI categories into three groups according to the recommendations of the Chinese Obesity Working Group[22], Low-BMI: normal weight (18.5 ≤ BMI < 24.0); Middle-BMI: overweight (24.0 ≤ BMI < 28.0); and High-BMI: obesity (BMI ≥ 28.0). Like previous studies[23,24], TyG index was divided into two groups according to the median: Low-TyG (≤ 8.58) and High-TyG (> 8.58). BMI combined with TyG index was categorized into six groups: Low-BMI/Low-TyG; Middle-BMI/Low-TyG; High-BMI/Low-TyG; Low-BMI/High-TyG; Middle-BMI/High-TyG; High-BMI/High-TyG.

Outcomes

The follow-up period began with the 2006 physical examination, and the endpoint events were defined as new-onset CVD events, including myocardial infarction and stroke (both cerebral infarction and cerebral hemorrhage). For participants who experienced two or more events, the time of the first event was recorded as the follow-up endpoint. The final follow-up date was December 31, 2022. For participants who did not experience an endpoint event but died during the study, the follow-up endpoint was recorded as the date of death. The definitions of endpoint events are provided in published literature[25], and the diagnostic criteria followed the World Health Organization standards[26,27]. Like previous studies[28,29], we used the International Classification of Diseases, 10th Revision (ICD-10), myocardial infarction was coded as I21, and stroke was coded as I63 or I60-I61. Each year, trained medical personnel reviewed the hospitalization diagnoses of the study participants at hospitals affiliated with Kailuan Group and designated medical insurance hospitals in Tangshan City, documenting the occurrence of endpoint events. All diagnoses were confirmed by specialist physicians based on the hospitalization medical records.

Statistical analysis

The 2006 physical examination data were used as baseline data. Normally distributed continuous variables were expressed as mean ± standard deviation (SD) and compared between groups using one-way analysis of variance (ANOVA). Skewed continuous variables were expressed as median (M) with interquartile range and compared using the Kruskal–Wallis test. Categorical variables were expressed as percentages (%), and comparisons between groups were made using the chi-square test.

The Schoenfeld residual test showed that all variables met the proportional hazards assumption ($P > 0.05$). The Cox proportional hazards model was used to analyze the hazard ratio (HR) and 95% confidence interval (CI) for the risk of endpoint events in groups based on BMI and TyG, both separately and jointly.

Three progressively adjusted Cox proportional hazards models were constructed: Model 1: Adjusted for sex (male/female) and age (continuous). Model 2: Additionally adjusted for smoking (current smoking/current non-smoking), drinking (current drinking/current non-drinking), physical activity (active/inactive), SBP (continuous), LDL-C (continuous), HDL-C (continuous), UA (continuous), and Hs-CRP (continuous). Model 3: Further adjusted for antihypertensive drugs (taking/not taking), hypoglycemic drugs (taking/not taking), and lipid-lowering therapies (taking/not taking). Meanwhile, We evaluated the multiplicative interactions between BMI and TyG index on CVD risk in Model 3 of the multivariate Cox regression by including their product term (BMI × TyG). Statistical significance was determined using the likelihood ratio test (P for interaction < 0.05). Additionally, Subgroup analyses were also conducted based on sex, age, and the presence of diabetes. Lastly, several sensitivity analyses were conducted to assess robustness: First, we excluded participants who developed CVD within 2 years of follow-up to avoid reverse causality; Second, we excluded patients who were using antihypertensive, hypoglycemic, or lipid-lowering drugs at baseline, respectively, to reduce treatment confounding factors; At last, we conducted the Fine-Grey subdistribution hazard model to account for death as a competing risk.

All statistical analyses were conducted using SAS software (version 9.4; SAS Institute, Cary, NC, USA), with a P-value of less than 0.05 (two-tailed) considered statistically significant.

Results

Baseline characteristics of the participants

The mean age of the participants was 51.5 ± 12.4 years, with 75,040 (79.8%) of them being male. Significant differences in baseline characteristics were observed among the groups classified by BMI combined with the TyG index ($P < 0.05$) (Table 1).

Cox proportional risk modeling of BMI combined with TyG index groups affecting endpoint events

During a follow-up period of 15.95 ± 3.59 years, a total of 9791 new CVD events were recorded. After adjusting for confounding factors such as sex, age, smoking, drinking, physical activity, SBP, LDL-C, HDL-C, UA, Hs-CRP, and the use of antihypertensive, hypoglycemic, and lipid-lowering medications, Cox regression analysis showed that, compared to the Low-BMI/Low-TyG group, the HR (95% CI) of CVD, stroke and myocardial infarction in H-BMI/H-TyG group were 1.52 (1.42–1.64), 1.44 (1.33–1.55) and 1.89 (1.60–2.24), respectively. (Tables 2, 3).

Subgroup analysis

Subgroup analyses revealed that the risk of CVD associated with the High-BMI/High-TyG group was more pronounced among females, younger individuals (under 60 years), and non-diabetic populations compared to the Low-BMI/Low-TyG group. The HR with 95% CI for these groups were 2.05 (1.65–2.52), 1.46 (1.34–1.60), and 1.47 (1.36–1.58), respectively. It was observed that BMI combined with TyG index in CVD risk were influenced by sex, age, and diabetes ($P < 0.05$ for interaction) (Table 4).

Sensitivity analysis

We repeated the Cox proportional hazard models analysis after excluding participants who had a CVD event within the first two years of follow-up and those who were taking medications at baseline, respectively. In addition, 11,850 deaths from any cause occurred during follow-up. Due to the competing risk of death, the traditional Cox model may have a bias in the risk of CVD. Therefore, death was regarded as a competing event, and the Fine-Gray model was used to analyze the difference of CVD risk in different groups. The results of the above sensitivity analyses all showed a higher CVD risk in the high BMI/ high TyG group, which was consistent with the results of the previous main analysis (Table 5).

Discussion

In this prospective cohort study of 94,002 participants, we found that BMI and TyG index had a joint effect on the risk of CVD development. Those with High-BMI/High-TyG had the highest risk of CVD development. This

Variables	Total (n = 94,002)	L-BMI/L-TyG (n = 23,945)	M-BMI/L-TyG (n = 17,710)	H-BMI/L-TyG (n = 5398)	L-BMI/H-TyG (n = 12,439)	M-BMI/H-TyG (n = 22,300)	H-BMI/H-TyG (n = 12,210)	*P* value
Age, years	51.5 ± 12.4	50.3 ± 13.7	51.7 ± 12.3	51.1 ± 12.7	52.4 ± 12.5	52.3 ± 11.3	51.3 ± 11.8	< 0.001
Male, n (%)	75,040 (79.8)	17,705 (73.9)	14,269 (80.6)	4155 (77.0)	9995 (80.4)	18,800 (84.3)	10,116 (82.9)	< 0.001
SBP, (mmHg)	130.8 ± 20.7	123.4 ± 19.2	130.2 ± 20.1	135.5 ± 20.9	129.4 ± 20.1	134.5 ± 20.5	139.2 ± 20.5	< 0.001
TC, (mmol/L)	4.9 ± 1.1	4.8 ± 0.9	4.8 ± 0.9	4.8 ± 0.9	5.0 ± 1.3	5.1 ± 1.2	5.1 ± 1.2	< 0.001
TG, (mmol/L)	1.3 (0.9–1.9)	0.9 (0.7–1.1)	1.0 (0.8–1.1)	1.0 (0.8–1.2)	1.8 (1.5–2.5)	2.0 (1.5–2.8)	2.1 (1.6–3.0)	< 0.001
LDL-C, (mmol/L)	2.3 (1.8–2.8)	2.2 (1.7–2.7)	2.4 (1.8–2.8)	2.4 (1.9–2.9)	2.4 (1.9–2.8)	2.4 (1.9–2.9)	2.4 (1.9–2.9)	< 0.001
HDL-C, (mmol/L)	1.5 ± 0.4	1.6 ± 0.4	1.5 ± 0.4	1.5 ± 0.4	1.6 ± 0.4	1.5 ± 0.4	1.5 ± 0.4	< 0.001
FBG, (mmol/L)	5.5 ± 1.6	4.9 ± 0.7	5.0 ± 0.7	5.0 ± 0.7	6.0 ± 2.2	6.0 ± 2.0	6.0 ± 1.9	< 0.001
UA, (μmol/L)	289.4 ± 82.8	266.2 ± 72.8	282.6 ± 76.6	296.2 ± 83.8	286.0 ± 81.8	303.5 ± 86.0	319.2 ± 89.9	< 0.001
Hs-CRP, (mg/L)	0.8 (0.3–2.3)	0.6 (0.2–1.8)	0.8 (0.3–2.2)	1.2 (0.5–3.0)	0.7 (0.3–2.0)	1.0 (0.4–2.4)	1.3 (0.6–3.1)	< 0.001
BMI, (kg/m^2)	25.2 ± 3.4	21.8 ± 1.4	25.7 ± 1.1	30.2 ± 2.3	22.3 ± 1.3	25.9 ± 1.1	30.3 ± 2.2	< 0.001
TyG index	8.7 ± 0.7	8.1 ± 0.3	8.2 ± 0.3	8.2 ± 0.3	9.1 ± 0.5	9.2 ± 0.5	9.3 ± 0.5	< 0.001
Current smoking, n (%)	32,138 (34.2)	7983 (33.3)	5685 (32.1)	1585 (29.4)	4590 (36.9)	8111 (36.4)	4184 (34.3)	< 0.001
Current drinking, n (%)	35,193 (37.4)	8674 (36.2)	6487 (36.6)	1817 (33.7)	4673 (37.6)	8858 (39.7)	4684 (38.4)	< 0.001
Active Physical activity, n (%)	14,256 (15.2)	3555 (14.8)	2779 (15.7)	863 (16.0)	1801 (14.5)	3376 (15.1)	1882 (15.4)	< 0.001
Hypertension, n (%)	41,262 (43.9)	6572 (27.4)	7298 (41.2)	2893 (53.6)	5051 (40.6)	11,688 (52.4)	7760 (63.6)	< 0.001
Diabetes, n (%)	8605 (9.2)	375 (1.6)	395 (2.2)	117 (2.2)	1816 (14.6)	3717 (16.7)	2185 (17.9)	< 0.001
Taking antihypertensive drugs, n (%)	9447 (10.0)	1079 (4.5)	1591 (9.0)	730 (13.5)	944 (7.6)	2828 (12.7)	2275 (18.6)	< 0.001
Taking hypoglycemic drugs, n (%)	2038 (2.2)	130 (0.5)	165 (0.9)	47 (0.9)	406 (3.3)	818 (3.7)	472 (3.9)	< 0.001
Taking lipid-lowering drugs, n (%)	708 (0.8)	82 (0.3)	84 (0.5)	50 (0.9)	82 (0.7)	243 (1.1)	167 (1.4)	< 0.001

Table 1. Baseline characteristics of participants grouped by BMI and TyG index levels. *SBP* systolic blood pressure, *TC* total cholesterol, *TG* triglyceride, *LDL-C* low-density lipoprotein cholesterol, *HDL-C* high density lipoprotein cholesterol, *FBG* fasting blood glucose, *BMI* body mass index, *TyG index* triglyceride-glucose index, *UA* uric acid, *Hs-CRP* high-sensitivity C-reactive protein, *L-BMI* low-BMI, *M-BMI* middle-BMI, *H-BMI* high-BMI, *L-TyG* low-TyG, *H-TyG* high-TyG.

Groups	Events/n	Incident rate (per 1000 person-years)	HR (95% CI)		
			Model 1	Model 2	Model 3
BMI category					
18.5 ≤ BMI < 24 (Low)	3049/36,384	5.75	Ref	Ref	Ref
24 ≤ BMI < 28 (Middle)	4469/40,010	7.73	1.30 (1.23–1.36)	1.17 (1.11–1.22)	1.15 (1.10–1.21)
≥ 28 (High)	2273/17,608	9.05	1.60 (1.51–1.68)	1.30 (1.23–1.38)	1.27 (1.20–1.35)
TyG index category					
≤ 8.58 (Low)	3934/47,053	5.71	Ref	Ref	Ref
> 8.58 (High)	5857/46,949	8.74	1.49 (1.43–1.55)	1.35 (1.29–1.40)	1.32 (1.26–1.37)
Combined variables					
P for interaction = 0.011					
L-BMI/L-TyG	1712/23,945	4.85	Ref	Ref	Ref
M-BMI/L-TyG	1635/17,710	6.32	1.24 (1.15–1.32)	1.13 (1.06–1.21)	1.12 (1.05–1.20)
H-BMI/L-TyG	587/5,398	7.53	1.55 (1.41–1.70)	1.29 (1.17–1.41)	1.28 (1.16–1.40)
L-BMI/H-TyG	1337/12,439	7.55	1.47 (1.36–1.57)	1.36 (1.26–1.46)	1.34 (1.24–1.44)
M-BMI/H-TyG	2834/22,300	8.87	1.72 (1.62–1.83)	1.48 (1.39–1.57)	1.44 (1.35–1.53)
H-BMI/H-TyG	1686/12,210	9.73	1.99 (1.86–2.13)	1.58 (1.47–1.69)	1.52 (1.42–1.64)

Table 2. Multivariate Cox regression analysis of the combined association of BMI and TyG index with CVD. Model 1: adjusted for sex (male/female) and age (continuous); Model 2: adjusted for variables in Model 1 plus smoking (current smoking/current non-smoking), drinking (current drinking/current non-drinking), physical activity (active/inactive), SBP (continuous), LDL-C (continuous), HDL-C (continuous), UA (continuous), Hs-CRP (continuous); Model 3: adjusted for variables in Model 2 plus antihypertensive drugs (taking/not taking), hypoglycemic drugs (taking/not taking), lipid-lowering therapies (taking/not taking). *TyG index* triglyceride-glucose index, *BMI* body mass index, *L-BMI* low-BMI, *M-BMI* middle-BMI, *H-BMI* high-BMI, *L-TyG* low-TyG, *H-TyG* high-TyG.

Groups	Events/n	Incident rate (per 1000 person-years)	HR (95% CI)		
			Model 1	Model 2	Model 3
Myocardial infarction					
L-BMI/L-TyG	277/23,945	0.77	Ref	Ref	Ref
M-BMI/L-TyG	261/17,710	0.98	1.21 (1.02–1.43)	1.12 (0.94–1.33)	1.11 (0.94–1.31)
H-BMI/L-TyG	98/5398	1.22	1.58 (1.26–1.99)	1.33 (1.05–1.68)	1.32 (1.04–1.66)
L-BMI/H-TyG	292/12,439	1.60	1.96 (1.66–2.31)	1.82 (1.55–2.15)	1.79 (1.51–2.11)
M-BMI/H-TyG	542/22,300	1.63	2.00 (1.73–2.31)	1.74 (1.50–2.02)	1.69 (1.46–1.96)
H-BMI/H-TyG	344/12,210	1.90	2.45 (2.09–2.87)	1.97 (1.67–2.32)	1.89 (1.60–2.24)
Stroke					
L-BMI/L-TyG	1439/23,945	4.06	Ref	Ref	Ref
M-BMI/L-TyG	1375/17,710	5.28	1.23 (1.15–1.33)	1.13 (1.05–1.22)	1.12 (1.04–1.21)
H-BMI/L-TyG	490/5398	6.24	1.53 (1.38–1.70)	1.27 (1.15–1.41)	1.26 (1.14–1.40)
L-BMI/H-TyG	1048/12,439	5.86	1.36 (1.25–1.47)	1.26 (1.16–1.36)	1.24 (1.14–1.34)
M-BMI/H-TyG	2300/22,300	7.13	1.65 (1.55–1.77)	1.42 (1.33–1.52)	1.38 (1.29–1.48)
H-BMI/H-TyG	1348/12,210	7.68	1.87 (1.74–2.01)	1.49 (1.38–1.61)	1.44 (1.33–1.55)

Table 3. Multivariate Cox regression analysis of the combined association of BMI and TyG index with CVD subtypes. Model 1: adjusted for sex (male/female) and age (continuous); Model 2: adjusted for variables in Model 1 plus smoking (current smoking/current non-smoking), drinking (current drinking/current non-drinking), physical activity (active/inactive), SBP (continuous), LDL-C (continuous), HDL-C (continuous), UA (continuous), Hs-CRP (continuous); Model 3: adjusted for variables in Model 2 plus antihypertensive drugs (taking/not taking), hypoglycemic drugs (taking/not taking), lipid-lowering therapies (taking/not taking). *TyG index* triglyceride-glucose index, *BMI* body mass index, *L-BMI* low-BMI, *M-BMI* middle-BMI, *H-BMI* high-BMI, *L-TyG* low-TyG, *H-TyG* high-TyG.

Subgroups	Events/n	Incident rate (per 1000 person-years)	HR (95% CI)	*P* value	*P* for interaction
Gender					0.002
Male					
L-BMI/L-TyG	1542/17,705	6.04	Ref		
M-BMI/L-TyG	1484/14,269	7.21	1.10 (1.03–1.19)	0.007	
H-BMI/L-TyG	507/4155	8.61	1.24 (1.12–1.38)	< 0.001	
L-BMI/H-TyG	1162/9995	8.28	1.29 (1.20–1.39)	< 0.001	
M-BMI/H-TyG	2535/18,800	9.50	1.41 (1.32–1.50)	< 0.001	
H-BMI/H-TyG	1453/10,116	10.18	1.45 (1.35–1.57)	< 0.001	
Female					
L-BMI/L-TyG	170/6240	1.75	Ref		
M-BMI/L-TyG	151/3441	2.85	1.23 (0.99–1.54)	0.062	
H-BMI/L-TyG	80/1243	4.20	1.49 (1.14–1.95)	0.004	
L-BMI/H-TyG	175/2444	4.76	1.62 (1.30–2.01)	< 0.001	
M-BMI/H-TyG	299/3500	5.70	1.61 (1.32–1.97)	< 0.001	
H-BMI/H-TyG	233/2094	7.62	2.05 (1.65–2.52)	< 0.001	
Age					< 0.001
< 60 years					
L-BMI/L-TyG	991/18,769	3.45	Ref		
M-BMI/L-TyG	1030/13,884	4.89	1.15 (1.05–1.26)	0.002	
H-BMI/L-TyG	375/4210	5.92	1.24 (1.10–1.40)	< 0.001	
L-BMI/H-TyG	858/9490	6.06	1.43 (1.30–1.56)	< 0.001	
M-BMI/H-TyG	1875/17,415	7.24	1.46 (1.35–1.58)	< 0.001	
H-BMI/H-TyG	1173/9684	8.22	1.46 (1.34–1.60)	< 0.001	
60 ≤ ~ < 70 years					
L-BMI/L-TyG	449/3111	10.60	Ref		
M-BMI/L-TyG	392/2471	11.89	1.03 (0.90–1.19)	0.640	
H-BMI/L-TyG	144/802	13.72	1.12 (0.93–1.36)	0.237	
L-BMI/H-TyG	317/1831	13.61	1.23 (1.07–1.42)	0.005	
M-BMI/H-TyG	688/3335	15.95	1.34 (1.21–1.52)	< 0.001	
H-BMI/H-TyG	373/1772	16.35	1.28 (1.11–1.48)	< 0.001	
70 ≤ ~ < 80 years					
L-BMI/L-TyG	224/1581	12.72	Ref		
M-BMI/L-TyG	183/1093	14.78	1.12 (0.92–1.36)	0.266	
H-BMI/L-TyG	60/314	17.58	1.29 (0.97–1.72)	0.085	
L-BMI/H-TyG	142/891	14.23	1.11 (0.90–1.37)	0.332	
M-BMI/H-TyG	243/1343	16.15	1.21 (1.00–1.46)	0.046	
H-BMI/H-TyG	120/646	17.55	1.29 (1.02–1.62)	0.032	
≥ 80 years					
L-BMI/L-TyG	48/484	9.32	Ref		
M-BMI/L-TyG	30/262	11.05	1.09 (0.69–1.73)	0.711	
H-BMI/L-TyG	8/72	11.69	1.13 (0.53–2.39)	0.759	
L-BMI/H-TyG	20/227	8.93	0.88 (0.52–1.48)	0.618	
M-BMI/H-TyG	28/207	13.21	1.20 (0.74–1.95)	0.466	
H-BMI/H-TyG	20/108	19.58	1.69 (0.98–2.93)	0.061	
Diabetes					0.021
Yes					
L-BMI/L-TyG	54/375	10.82	Ref		
M-BMI/L-TyG	67/395	12.78	1.09 (0.76–1.58)	0.624	
H-BMI/L-TyG	18/117	12.10	1.05 (0.63–1.83)	0.808	
L-BMI/H-TyG	338/1816	14.74	1.35 (1.01–1.81)	0.040	
M-BMI/H-TyG	697/3717	14.25	1.27 (1.01–1.81)	0.088	
H-BMI/H-TyG	401/2185	13.87	1.22 (0.91–1.62)	0.186	
No					
L-BMI/L-TyG	1658/23,570	4.77	Ref		
M-BMI/L-TyG	1568/17,315	6.18	1.12 (1.04–1.20)	0.002	
H-BMI/L-TyG	569/5281	7.44	1.27 (1.15–1.40)	< 0.001	
Continued					

Subgroups	Events/n	Incident rate (per 1000 person-years)	HR (95% CI)	*P* value	*P* for interaction
L-BMI/H-TyG	999/10,623	6.48	1.22 (1.13–1.32)	< 0.001	
M-BMI/H-TyG	2137/18,583	7.90	1.35 (1.27–1.45)	< 0.001	
H-BMI/H-TyG	1285/10,025	8.90	1.47 (1.36–1.58)	< 0.001	

Table 4. Multivariate Cox proportional hazards models affecting CVD in different subgroups. Models were adjusted for sex (male/female), age (continuous), smoking (current smoking/current non-smoking), drinking (current drinking/current non-drinking), physical activity (active/inactive), SBP (continuous), LDL-C (continuous), HDL-C (continuous), UA (continuous), Hs-CRP (continuous), antihypertensive drugs (taking/not taking), hypoglycemic drugs (taking/not taking), lipid-lowering therapies (taking/not taking). *TyG index* triglyceride-glucose index, *BMI* body mass index, *L-BMI* low-BMI, *M-BMI* middle-BMI, *H-BMI* high-BMI, *L-TyG* low-TyG, *H-TyG* high-TyG.

risk may be sex- and age-dependent. In addition, the risk of CVD due to high TyG index was more substantial than the risk of CVD due to high BMI in people with inconsistent BMI and TyG index.

Our critical finding is that obesity combined with a high TyG index significantly increases the risk of CVD. Specifically, the High-BMI/High-TyG group had a 1.52-fold higher risk of CVD compared to the Low-BMI/Low-TyG group. Although there are no directly comparable studies, an Italian study with a 15-year follow-up reported a 1.4-fold increase in all-cause mortality risk and a 1.61-fold increase in CVD mortality risk among obese, insulin-resistant individuals compared to non-obese, insulin-sensitive individuals[30]. Additionally, a cross-sectional study of 13,239 adults[31] found that metabolically abnormal non-obese and metabolically abnormal obese individuals had higher CVD risks than metabolically healthy non-obese individuals, with odds ratios (OR) of 2.34 (95% CI 1.89–2.89) and 3.45 (95% CI 2.50–4.75), respectively. A cohort study in Xinjiang, China, also demonstrated that metabolically obese individuals had the highest CVD risk, being 3.8 times higher than that of metabolically healthy, normal-weight individuals[32]. These studies on metabolic obesity phenotypes indirectly support our findings.

Furthermore, the risk of CVD increased by 1.28-fold in the High-BMI/Low-TyG group and by 1.33-fold in the Low-BMI/High-TyG group, compared to the Low-BMI/Low-TyG group. This suggests that a high TyG index poses a more substantial risk for CVD than a high BMI in individuals with inconsistent BMI and TyG index values. The TyG index may thus be more valuable than BMI for identifying cardiovascular risk. Previous studies have indicated that elevated TyG levels are indicative of insulin resistance, which can impair the cardiovascular system and increase the risk of CVD[33]. A study by Liu et al.[34] confirmed the association between a high TyG index and an increased risk of CVD. Therefore, effective cardiovascular risk prevention should include both reasonable weight control and the maintenance of metabolic health.

The results of our subgroup analyses suggest that the risk of CVD associated with the combination of high BMI and a high TyG index may depend on sex and age. Specifically, the risk of CVD was higher in women than in men when comparing the High-BMI/High-TyG group to the Low-BMI/Low-TyG group, with HR of 2.05 (95% CI 1.65–2.52) for women and 1.45 (95% CI 1.35–1.57) for men. This indicates that the coexistence of overweight/obesity and insulin resistance might be more detrimental for women. However, current studies show inconsistent results regarding gender differences in the TyG index, the composite TyG-BMI parameter, and CVD-related events. For instance, a cross-sectional study of 11,937 adults by Dang et al.[35] found that the correlation between the TyG index, TyG-BMI, and CVD was stronger in men than in women. Conversely, a Mendelian randomization analysis involving two independent cohorts suggested that the association between the TyG index and heart failure risk was stronger in women than in men[36]. Additionally, the risk of CVD associated with the High-BMI/High-TyG combination decreased progressively with age. This finding may reflect survivor bias or elevated competing risks in older adults; alternatively, it could stem from the synergistic effects of physiological particularities in elderly populations (such as the obesity paradox and metabolic adaptation), thereby contributing to the attenuation of risk associations. A prospective cohort study with a median follow-up of 9.59 years showed that the HR for CVD among metabolically unhealthy, obese individuals was 2.68 (95% CI 2.02–3.55) for those under 55 years of age and 1.55 (95% CI 1.09–2.10) for those aged 75 years and older[37]. These findings align with our study, suggesting that the risk of CVD linked to obesity and metabolic abnormalities decreases with advancing age. Another study on the association between TyG-BMI and CVD in U.S. adults confirmed that additional cardiovascular risk factors in older adults might weaken the effect of TyG-BMI on CVD. In contrast, TyG-BMI may more accurately reflect cardiovascular risk in younger adults[38]. These findings underscore the importance of early and targeted CVD prevention strategies, such as enhancing insulin sensitivity through a balanced diet, moderate exercise, limiting tobacco and alcohol use, and monitoring blood pressure, blood glucose, and lipid levels.

Lastly, it is noteworthy that the combined effect of BMI and the TyG index appeared more sensitive for assessing CVD risk in non-diabetic populations. Studies by Liu et al.[34] and Dang et al.[35] support this observation, consistent with our findings. This may be because individuals diagnosed with diabetes often engage in health management practices, such as taking glucose-lowering medications, which alter blood glucose levels and potentially reduce CVD risk.

Our study has several strengths. It was a prospective cohort study with a long follow-up period, a large sample size, and a wide age range. We adjusted for numerous confounding factors and conducted sensitivity analyses. Additionally, we collected longitudinal data on BMI and the TyG index before the onset of CVD, allowing for a direct assessment of the long-term effects of combined exposure to these factors on CVD risk. Moreover,

Groups	Events/n	Incident rate (per 1000 person-years)	HR (95% CI)
Participants with CVD events in the two years prior to follow-up were excluded*			
L-BMI/L-TyG	1565/23,798	4.44	Ref
M-BMI/L-TyG	1467/17,542	5.67	1.11 (1.03–1.19)
H-BMI/L-TyG	521/5,332	6.69	1.25 (1.13–1.38)
L-BMI/H-TyG	1222/12,324	6.90	1.35 (1.25–1.45)
M-BMI/H-TyG	2585/22,051	8.10	1.45 (1.36–1.55)
H-BMI/H-TyG	1529/12,053	8.83	1.54 (1.43–1.65)
Participants with taking antihypertensive drugs at baseline were excluded*			
L-BMI/L-TyG	1536/22,866	4.54	Ref
M-BMI/L-TyG	1350/16,119	5.68	1.11 (1.03–1.19)
H-BMI/L-TyG	462/4668	6.77	1.28 (1.16–1.43)
L-BMI/H-TyG	1172/11,495	7.10	1.36 (1.26–1.47)
M-BMI/H-TyG	2315/19,472	8.22	1.48 (1.39–1.59)
H-BMI/H-TyG	1239/9935	8.74	1.57 (1.45–1.70)
Participants with taking hypoglycemic drugs at baseline were excluded*			
L-BMI/L-TyG	1696/23,815	4.84	Ref
M-BMI/L-TyG	1597/17,545	6.22	1.11 (1.04–1.19)
H-BMI/L-TyG	576/5351	7.44	1.26 (1.15–1.39)
L-BMI/H-TyG	1254/12,033	7.27	1.32 (1.23–1.42)
M-BMI/H-TyG	2659/21,482	8.60	1.44 (1.35–1.53)
H-BMI/H-TyG	1592/11,738	9.52	1.54 (1.43–1.65)
Participants taking lipid-lowering drugs at baseline were excluded*			
L-BMI/L-TyG	1700/23,863	4.84	Ref
M-BMI/L-TyG	1621/17,626	6.29	1.12 (1.05–1.20)
H-BMI/L-TyG	578/5348	7.48	1.27 (1.15–1.40)
L-BMI/H-TyG	1326/12,357	7.53	1.34 (1.25–1.44)
M-BMI/H-TyG	2799/22,057	8.86	1.45 (1.36–1.54)
H-BMI/H-TyG	1656/12,043	9.68	1.52 (1.42–1.64)
Consider deaths as competing risk events**			
L-BMI/L-TyG	1712/23,945	4.85	Ref
M-BMI/L-TyG	1635/17,710	6.32	1.15 (1.07–1.23)
H-BMI/L-TyG	587/5398	7.53	1.30 (1.18–1.43)
L-BMI/H-TyG	1337/12,439	7.55	1.32 (1.23–1.42)
M-BMI/H-TyG	2834/22,300	8.87	1.47 (1.39–1.57)
H-BMI/H-TyG	1686/12,210	9.73	1.55 (1.44–1.67)

Table 5. Sensitivity analysis of the combined association of BMI and TyG index with CVD. Models were adjusted for sex (male/female), age (continuous), smoking (current smoking/current non-smoking), drinking (current drinking/current non-drinking), physical activity (active/inactive), SBP (continuous), LDL-C (continuous), HDL-C (continuous), UA (continuous), Hs-CRP (continuous), antihypertensive drugs (taking/not taking), hypoglycemic drugs (taking/not taking), lipid-lowering therapies (taking/not taking). *Cox proportional hazards model was used for analysis. **Fine-Grey subdistribution hazard model was used for analysis. *TyG index* triglyceride-glucose index, *BMI* body mass index, *L-BMI* low-BMI, *M-BMI* middle-BMI, *H-BMI* high-BMI, *L-TyG* low-TyG, *H-TyG* high-TyG.

BMI and the TyG index are simple indicators of obesity and metabolism, making them easy to generalize and apply. However, our study also has limitations. Although we used multivariate regression models to adjust for confounding factors, residual confounding cannot be entirely ruled out. The study was conducted in a northern Chinese population, which may limit its generalizability to other regions. Finally, the lack of fasting insulin data prevented a comparison of the TyG index with other indices used to evaluate insulin resistance.

Conclusions

Combining BMI with the TyG index increases the risk of developing CVD. This combined effect is particularly pronounced in women, young adults (under 60 years), and non-diabetic populations. Therefore, this study suggests that using BMI categories in combination with the TyG index in clinical practice could effectively stratify cardiovascular risk and enhance primary prevention efforts.

Data availability

Data used and analyzed are available from the corresponding author on reasonable request.

Received: 21 January 2025; Accepted: 13 May 2025
Published online: 21 May 2025

References

1. Roth, G. A. et al. Global burden of cardiovascular diseases and risk factors, 1990–2019: Update from the GBD 2019 study. *J. Am. Coll. Cardiol.* **76**, 2982–3021 (2020).
2. Zhao, J. et al. J-shaped relationship between weight-adjusted-waist index and cardiovascular disease risk in hypertensive patients with obstructive sleep apnea: A cohort study. *Diabet. Metab. Syndr. Obes.* **17**, 823–833 (2024).
3. Hu, J. et al. Association between weight-adjusted waist index with incident stroke in the elderly with hypertension: A cohort study. *Sci. Rep.* **14**, 1–13 (2024).
4. Cai, X. et al. Association of the trajectory of plasma aldosterone concentration with the risk of cardiovascular disease in patients with hypertension: A cohort study. *Sci. Rep.* **14**, 4906 (2024).
5. Hubert, H. B., Feinleib, M., McNamara, P. M. & Castelli, W. P. Obesity as an independent risk factor for cardiovascular disease: A 26-year follow-up of participants in the Framingham Heart Study. *Circulation* **67**, 968–977 (1983).
6. Laakso, M. & Kuusisto, J. Insulin resistance and hyperglycaemia in cardiovascular disease development. *Nat. Rev. Endocrinol.* **10**, 293–302 (2014).
7. Dikaiou, P. et al. Obesity, overweight and risk for cardiovascular disease and mortality in young women. *Eur. J. Prev. Cardiol.* **28**, 1351–1359 (2021).
8. Wang, L. et al. Associations of obesity indices change with cardiovascular outcomes: A dose-response meta-analysis. *Int. J. Obes.* **48**, 635–645 (2024).
9. Khan, S. S. et al. Association of body mass index with lifetime risk of cardiovascular disease and compression of morbidity. *JAMA Cardiol.* **3**, 280–287 (2018).
10. Simental-Mendía, L. E., 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.* **6**, 299–304 (2008).
11. Liu, C. & Liang, D. The association between the triglyceride-glucose index and the risk of cardiovascular disease in US population aged ≤65 years with prediabetes or diabetes: A population-based study. *Cardiovasc. Diabetol.* **23**, 168 (2024).
12. Liu, Q. et al. Triglyceride-glucose index associated with the risk of cardiovascular disease: The Kailuan study. *Endocrine* **75**, 392–399 (2022).
13. Wan, Y. et al. Association of triglyceride-glucose index with cardiovascular disease among a general population: A prospective cohort study. *Diabetol. Metab. Syndr.* **15**, 204 (2023).
14. Kok, P., Seidell, J. C. & Meinders, A. E. The value and limitations of the body mass index (BMI) in the assessment of the health risks of overweight and obesity. *Ned. Tijdschr. Geneeskd.* **148**, 2379–2382 (2004).
15. Romero-Corral, A. et al. Diagnostic performance of body mass index to detect obesity in patients with coronary artery disease. *Eur. Heart J.* **28**, 2087–2093 (2007).
16. Romero-Corral, A. et al. Accuracy of body mass index in diagnosing obesity in the adult general population. *Int. J. Obes.* **32**, 959–966 (2008).
17. Er, L. K. et al. Triglyceride glucose-body mass index is a simple and clinically useful surrogate marker for insulin resistance in nondiabetic individuals. *PLoS ONE* **11**, e0149731 (2016).
18. Wu, S. et al. Aging, arterial stiffness, and blood pressure association in Chinese adults. *Hypertension* **73**, 893–899 (2019).
19. Chobanian, A. V. et al. The seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood Pressure: The JNC 7 report. *JAMA* **289**, 2560–2572 (2003).
20. Genuth, S. et al. Follow-up report on the diagnosis of diabetes mellitus. *Diabet. Care* **26**, 3160–3167 (2003).
21. Wang, A. et al. Change in triglyceride-glucose index predicts the risk of cardiovascular disease in the general population: a prospective cohort study. *Cardiovasc. Diabetol.* **20**, 113 (2021).
22. Zhou, B. F. Predictive values of body mass index and waist circumference for risk factors of certain related diseases in Chinese adults—Study on optimal cut-off points of body mass index and waist circumference in Chinese adults. *Biomed. Environ. Sci.* **15**, 83–96 (2002).
23. Cui, C. et al. Triglyceride-glucose index, renal function and cardiovascular disease: A national cohort study. *Cardiovasc. Diabetol.* **22**, 1–12 (2023).
24. Yang, Y. et al. The interaction between triglyceride-glucose index and visceral adiposity in cardiovascular disease risk: Findings from a nationwide Chinese cohort. *Cardiovasc. Diabetol.* **23**, 1–13 (2024).
25. Wu, S. et al. Association of trajectory of cardiovascular health score and incident cardiovascular disease. *JAMA Netw. Open* **2**, e194758 (2019).
26. Tunstall-Pedoe, H. et al. Myocardial infarction and coronary deaths in the World Health Organization MONICA Project. *Circulation* **90**, 583–612 (1994).
27. WHO Task Force on Stroke. Recommendations on stroke prevention, diagnosis, and therapy. *Stroke* **20**, 1407–1431 (1989).
28. Li, W. et al. Blood pressure trajectories and the risk of intracerebral hemorrhage and cerebral infarction: A prospective study. *Hypertension* **70**, 508–514 (2017).
29. Jin, C. et al. Longitudinal change in fasting blood glucose and myocardial infarction risk in a population without diabetes. *Diabet. Care* **40**, 1565–1572 (2017).
30. Calori, G. et al. Prevalence, metabolic features, and prognosis of metabolically healthy obese Italian individuals. *Diabet. Care* **34**, 210–215 (2011).
31. Liu, J. T. et al. Joint association of metabolic health and obesity with ten-year risk of cardiovascular disease among Chinese adults. *Biomed. Environ. Sci.* **35**, 13–21 (2022).
32. Wang, W. et al. Comparison of the incidence of cardiovascular diseases in weight groups with healthy and unhealthy metabolism. *Diabet. Metab. Syndr. Obes.* **14**, 4155–4163 (2021).
33. Yu, X. et al. Fasting triglycerides and glucose index is more suitable for the identification of metabolically unhealthy individuals in the Chinese adult population: A nationwide study. *J. Diabet. Investig.* **10**, 1050–1058 (2019).
34. Liu, L. et al. Association of triglyceride-glucose index and traditional risk factors with cardiovascular disease among non-diabetic population: A 10-year prospective cohort study. *Cardiovasc. Diabetol.* **21**, 256 (2022).
35. Dang, K. et al. The association between triglyceride-glucose index and its combination with obesity indicators and cardiovascular disease: NHANES 2003–2018. *Cardiovasc. Diabetol.* **23**, 8 (2024).
36. Li, X. et al. Triglyceride-glucose index and the risk of heart failure: Evidence from two large cohorts and a Mendelian randomization analysis. *Cardiovasc. Diabetol.* **21**, 229 (2022).
37. Zhao, M. et al. Transitions in metabolic health and onset age of cardiovascular diseases. *Am. J. Prev. Med.* **65**, 1059–1068 (2023).
38. Wang, R., Cheng, X. & Tao, W. Association between triglyceride glucose body mass index and cardiovascular disease in adults: Evidence from NHANES 2011–2020. *Front. Endocrinol.* **15**, 1362667 (2024).

Acknowledgements
We appreciate all the participants involved in this study and members of the Kailuan Research Group for their contributions.

Author contributions
Y.C. designed this study, conducted the main analysis and drafted the manuscript. S.L.W., S.H.C. and Y.T.W. contributed to acquisition of data, analysis and interpretation of data. The manuscript was reviewed by S.L.W. and Y.T.W.

Funding
This study is not supported by any funding projects.

Declarations

Competing interest
The authors declare no competing interests.

Ethical approval and consent to participate
The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Kailuan General Hospital. All participants provided their written informed consent to participate in this study.

Additional information
Correspondence and requests for materials should be addressed to Y.W.