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ORIGINAL RESEARCH

The Impact of Triglyceride-Glucose Index Trajectories on Incidence and Recurrent Cardiovascular Events: Evidence from a Retrospective Cohort Study

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Patients and Methods: The study retrospectively collected 8086 clinical data from 2019 to 2021. Latent Class Trajectory Modeling (LCTM) was utilized to identify the longitudinal trajectories of the triglyceride-glucose index, and logistic regression was employed to analyze the relationship between different triglyceride-glucose trajectories and the incidence and recurrence of cardiovascular diseases.

Results: During the study period, 1484 patients in the cohort experienced cardiovascular events. Using LCTM, three distinct triglyceride-glucose index trajectories were identified. In the overall cohort of recurrent patients, as well as among those with higher triglyceride-glucose levels (triglyceride-glucose > 8.309) within it, a high-gradual-increase trajectory was found to be significantly associated with cardiovascular disease risk compared to a low-stable trajectory. Similar observations were seen in incidence patients with higher triglyceride-glucose levels (OR 1.179; 95% CI 1.017–1.368), which adjusted the demographic characteristics and the test indicators.

Conclusion: A high baseline level of triglyceride-glucose index with a high-gradual-increasing trajectory was significantly associated with incidence and recurrence of cardiovascular disease. Early identification of such populations can aid in the prevention of both incidence and recurrent cardiovascular diseases in the future.

Purpose: The triglyceride-glucose index is related to the cerebrovascular diseases. This study aimed to investigate the relationship between different triglyceride-glucose index trajectories and incidence and recurrence of cardiovascular disease.

Keywords: cardiovascular diseases, triglyceride-glucose index, trajectory, incidence, recurrence

Introduction

Cardiovascular diseases (CVDs) have imposed a significant burden on the Chinese population. In response to this situation, China has implemented strategies for preventing and controlling CVDs, which have shown initial effectiveness. For instance, China has implemented nationwide strategies under initiatives such as "Implementation Plan for the Prevention and Control of Cardiovascular and Cerebrovascular Diseases under the Healthy China Initiative (2023–2030)", which emphasize community-based screening programs and public health campaigns targeting key CVD risk factors, including hypertension and diabetes. Evidence suggests these measures have yielded positive outcomes: the age-standardized incidence rate of coronary heart disease decreased from 203.7 per 100,000 person-years in 2010 to 197.4 per 100,000 person-years in 2019, reflecting a consistent downward trend. However, the country still faces formidable challenges. The prevalence and mortality rates of CVDs continue to show an upward trend overall. According to the 2022 Cardiovascular Disease Report in China, there are

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290 million patients with CVDs, including 11 million with coronary heart disease (CHD), 13 million with stroke, 5 million with pulmonary heart disease, 4.5 million with heart failure, 2.5 million with rheumatic heart disease, 2 million with congenital heart disease, and 270 million with hypertension (HBP).[1] CVDs account for over 40% of the disease-related deaths among residents, ranking first and surpassing cancer and other diseases. Two out of every five deaths are due to CVDs. In 2020, CVDs accounted for 48% of rural deaths and 45.86% of urban deaths. Since 2009, the CVDs mortality rate in rural areas has exceeded that in urban areas and has remained higher. The increasing economic and social burden caused by CVDs has become a significant public health issue, necessitating urgent reinforcement of prevention and control efforts.

Numerous studies have shown that insulin resistance (IR) is a crucial pathological pathway in developing CVDs.[2] High-dose insulin euglycemic clamp (HIEC) is the gold standard for assessing insulin resistance. However, due to its complexity and high cost, it is not widely used in clinical settings or large-scale population studies. In this context, the triglyceride-glucose (TyG) index has emerged as a simple, accessible, and reliable indicator and is widely considered a reliable alternative marker for insulin resistance.[3–6] CVDs is the most common complication in patients with chronic kidney disease (CKD) and a significant cause of death in patients with CKD. The TyG index is associated with coronary artery disease and the severity of coronary artery stenosis in those patients with CKD who have not undergone dialysis. A higher TyG index is an independent factor for CHD and severe coronary artery stenosis.[7] A multicenter retrospective study also found that the TyG index is associated with the severity of coronary artery stenosis and the all-cause in-hospital mortality rate in patients with acute ST-segment elevation myocardial infarction after percutaneous coronary intervention.[8] This finding may help doctors to stratify patient risk and implement personalized treatment strategies accurately. Diabetic eye disease has become a global burden, with markers of glucose intolerance and IR being significantly, independently, and negatively correlated with the outer nuclear layer and the muscle-like zone of the retina.[9] IR is typical in patients with cholelithiasis, and the TyG index is positively correlated with the homeostasis model assessment of insulin resistance (HOMA-IR).[10] Research by W. Huang et al found that in critically ill patients with hemorrhagic stroke, the TyG index is significantly associated with all-cause mortality.[11–13] While there have been studies evaluating the association between the TyG index and CVDs,[14] there is currently a lack of research on the impact of the TyG index and its trajectory on the incidence and recurrence of CVDs. Dynamic trajectory analysis of medical biomarkers provides crucial insights into disease risk prediction that surpass those obtained from single measurements. Long-term trajectory models can identify high-risk subpopulations characterized by persistent high-level biomarker exposure, a condition that significantly exacerbates disease risk. For instance, Wang et al found that sustained high mean arterial pressure (MAP) substantially increased the risk of acute kidney injury (AKI). Similarly, Zhang et al identified that a stable trajectory of high serum phosphate levels was a significant risk factor for short-term mortality in sepsis patients.[15,16] Given the severe situation of cardiovascular diseases in China and the various applications of the TyG index, this study aimed to better predict and alert the incidence and recurrence of CVDs in patients by combining the baseline predictive trajectory of the TyG index with other clinical indicators.

Materials and Methods

Study Population

This longitudinal retrospective cohort study collected data from individuals who underwent five measurements of triglycerides and fasting blood glucose at the Second Affiliated Hospital of Nanchang University between January 2019 and December 2021. Initially, the study included 16,336 participants >18 years who underwent general medical examinations. The main exclusion criteria included a diagnosis of cancer or tumor, intervals between two measurements of <30 days, and more than two missing values for either triglyceride or fasting blood glucose data. Ultimately, a total of 8086 cases were included in the study. The study flowchart is depicted in Figure 1. This study strictly adhered to the Helsinki Declaration and was approved by the local institutional ethics committee.

Characteristics and Measurement

Demographic characteristics, clinical histories, laboratory findings, and medical information were extracted from electronic medical records. Basic patient information was analyzed, encompassing variables such as gender, age, diastolic and systolic blood pressures, smoking status, and alcohol consumption. Additional covariates included HBP, cerebral

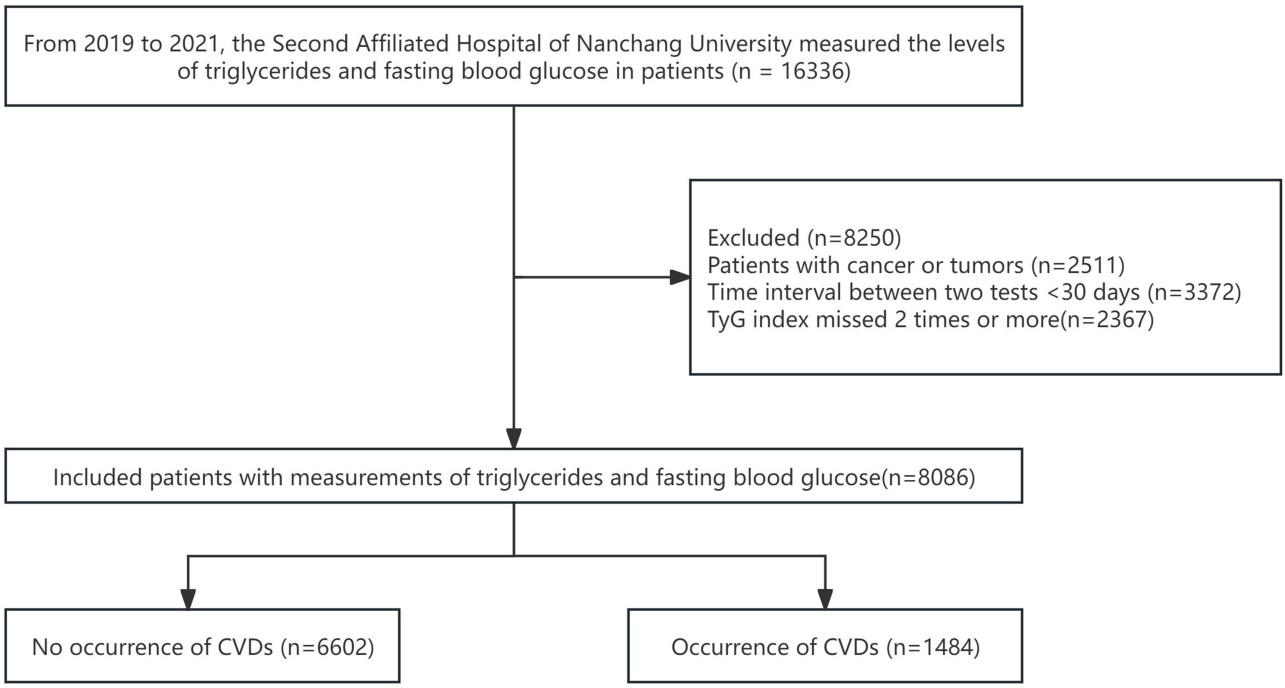

Figure 1 Flowchart of the case selection process.

infarction (CeI), diabetes (DM), hyperlipidemia (HL), baseline TyG index, TC, high-density lipoprotein cholesterol (HDL-C), lipoprotein(a), albumin, white blood cell count, red blood cell count, lymphocyte count, lymphocyte ratio, neutrophil count, neutrophil ratio, platelet count, apolipoproteins A and B, serum sodium, serum potassium, fibrinogen, homocysteine, and the use of medications such as statins, antiplatelet medication (APD), anticoagulants, and lipid-lowering medications (LLD). For research purposes, we defined hyper-low-density-lipoproteinemia (HLDL) as low-density lipoprotein cholesterol (LDL-C) levels exceeding 2.6 mmol/L. This threshold aligns with the AHA/ACC/MS guidelines, where LDL-C > 2.6 mmol/L (100 mg/dL) serves as a key therapeutic indicator for intensifying lipid-lowering therapy in high-risk patients, specifically through the addition of non-statin medications.[17]

Definitions

The TyG index is calculated using fasting blood glucose and triglyceride levels through the formula: TyG = Ln{(triglycerides [mg/dL] * fasting blood glucose [mg/dL]) / 2}. All CVDs events were coded using the International Statistical Classification of Diseases and Related Health Problems, 10th Edition (ICD-10). Coronary artery disease (ICD-10 code: I20 - I25).[18]

Recurrence was defined as patients who had a documented history of cardiovascular disease diagnosis or hospitalization within the five years preceding the baseline date (January 1, 2018), and who had at least two laboratory records of triglycerides and glucose levels during the study period (2018–2021), followed by subsequent hospitalization for cardiovascular disease.

Incidence was defined as patients who had no documented history of cardiovascular disease diagnosis or hospitalization within the five years preceding the baseline date (January 1, 2018), and who had at least two laboratory records of triglycerides and glucose levels during the study period (2018–2021), followed by subsequent hospitalization for cardiovascular disease.

Statistical Analysis

Baseline demographic data were categorized based on TyG index trajectories. Given the skewed distribution, continuous variables were represented by the median with the interquartile range (IQR). Categorical variables were presented as absolute numbers with percentages (%). Analysis of variance (ANOVA) and Mann–Whitney *U*-test were employed for group comparisons of continuous variables, while the chi-square test was used for categorical variables. Univariate and

multivariable logistic regression (MASS 7.3.60) models were employed to calculate CIs and ORs for each independent risk factor. ROC curves were used to determine the TyG index threshold for stratified analysis.

Latent Class Trajectory Modeling (LCTM) was employed to identify the trajectories of the TyG index over time. LCTM is based on a finite mixture model framework, which assumes that the overall population consists of multiple unobserved latent classes, each with a unique temporal change trajectory. It handles the fuzziness and uncertainty of individual trajectories more naturally through probabilistic assignment. LCTM addresses the limitations of GBTM's hard classification bias and predetermined trajectory shapes via probabilistic soft classification, flexible latent class modeling, and rigorous statistical inference mechanisms, achieving more precise characterization of heterogeneous population trajectories.[19,20] The optimal number of trajectories was determined based on the Bayesian Information Criterion (BIC), ensuring each class's average posterior probability exceeded 70%, with the class size being ≥2% of the sample size.[21] In epidemiology, LCTM is a relatively new method to describe exposures over the life course. This type of finite mixture model enables us to simplify the heterogeneous longitudinal processes of the lipid profile into homogeneous classes and investigate the comparable trajectories of these latent classes over time.[22] The clinical characteristics and plausibility of trajectory classes were accounted for. Finally, three different trajectories of the TyG index were chosen for the best-fitting model. The trajectories were labeled as class 1, class 2, and class 3 based on the visual patterns of the trajectories and clinical features to facilitate interpretation. Moreover, various potential confounding factors were considered. Subsequently, comparative analyses were conducted before and after adjusting the model for covariates such as gender, age, HL, TC, HDL, and AC. The study design is shown in Figure 2.

All statistical analyses were conducted using R 4.3.1 (R Statistical Computing Base) and plotted using the ggplot package (version 3.4.1), along with Xsmart software (https://www.xsmartanalysis.com/). We implemented trajectory modeling to identify distinct trajectories of the TyG index values, calculated from blood glucose and triglyceride measurements each time by LCMM package (v2.1.0). For all tests, a two-tailed $P < 0.05$ was considered statistically significant.

Results

Baseline Analysis

A comprehensive baseline analysis examined the significance of differences between various indicators in different outcome groups. There were 8086 valid samples, with 6602 cases without occurrences and 1484 cases with CVDs occurrences. (Comprehensive baseline analysis will intelligently select the analytical methods based on sample distribution, homogeneity of variance, and sample size): Using chi-square tests, significant differences ($P < 0.05$) were observed among the groups for gender, HLDL, smoking status, alcohol consumption, AC, APD, LLD, HL, HBP, and DM. Moreover, using the Mann–Whitney *U*-test, significant differences ($P < 0.05$) were observed among the groups for baseline TyG index, TC, low-density lipoprotein cholesterol (LDL-C), HDL-C, and age (Table 1).

Multivariable Stratified Analysis for Baseline TYG

The TyG threshold of 8.309 was determined using the Youden index derived from the ROC curve. Subsequently, the TyG index was stratified into low (T1) and high levels (T2) based on this threshold. Multivariable stratified analysis was conducted to observe variations in the impact of high TyG levels on CVDs occurrence across different CVDs strata. Statistical analysis revealed that women, those aged ≤60 years, non-smokers, non-alcohol, those with HLDL, individuals not taking APD, those with DM, and those without HBP exhibited a significant impact on CVDs occurrence ($P < 0.05$). Conversely, among men, those aged >60 years, smokers, drinkers, those taking APD, individuals without DM, and those with HBP did not show a significant impact on CVDs occurrence ($P > 0.05$) (Figure 3).

Trajectories of TYG

The trajectory data of the TyG index was classified into three categories using HLME: class 1 (n=3469), representing low-stable trajectories, with CVDs occurring in 15.21% of cases; class 2 (n=621), representing high-decrease trajectories, with CVDs occurring in 20.29% of cases; and class 3 (n=3996), representing high-gradual-increase trajectories, with CVDs occurring in 19.44% of cases (Figure 4). The incidence of CVDs was similar in class 2 and class 3, while it was lower in class 1 compared to both. Trajectory classification was conducted on the overall samples, distinguishing between

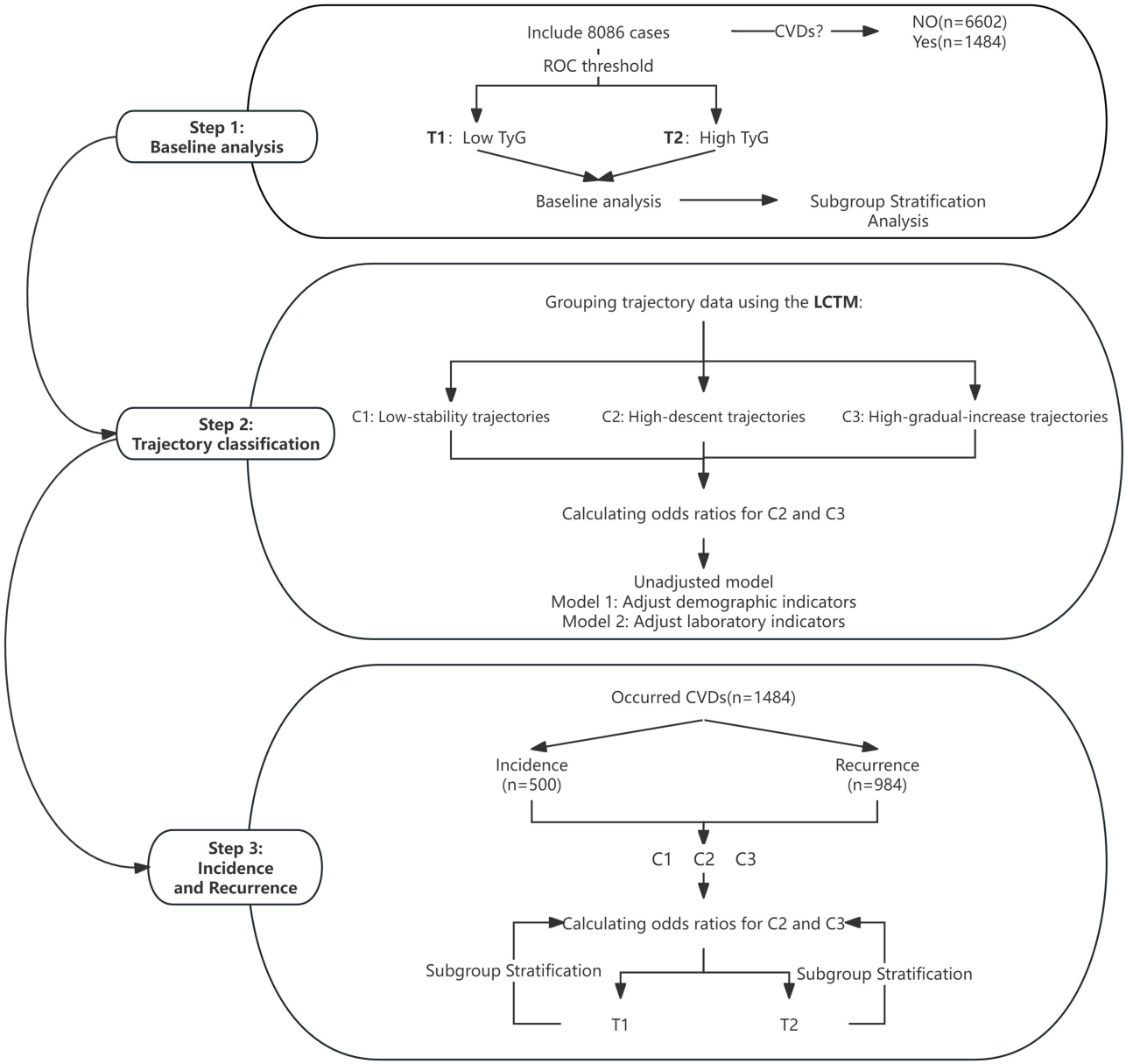

Figure 2 Schematic diagram of the Research design process.
Notes: Unadjusted model: No variable adjustments; Model 1: Adjusted for baseline TyG index, age, and gender; Model 2: Adjusted for baseline TyG index, gender, age, HL, TC, high-density lipoprotein, and AC.
Abbreviations: TyG index, Triglyceride-Glucose index; CVDs, cardiovascular disease; ROC, receiver operating characteristic; LCTM, Latent Class Trajectory Modeling.

individuals who experienced CVDs and those who did not. Among the 1484 cases in the CVDs group, there were 581 cases with low-stable TyG trajectories, 126 cases with high-decrease TyG trajectories, and 777 cases with high-gradual-increase TyG trajectories. In the 6602 cases without CVDs group, there were 2888 cases with low-stable TyG trajectories, 495 cases with high-decrease TyG trajectories, and 3219 cases with high-gradual-increase TyG trajectories (Table 2).

Associations Between TYG Trajectories and CVDs

Logistic regression analysis was conducted on the classified trajectory results of the entire sample, with class 1 serving as the reference group. In the unadjusted model, a considerable difference existed between class 3 and class 1 (OR, 1.2; 95% CI, 1.066–1.351; $P = 0.003$). Similarly, the difference between class 2 and class 1 was also significant (OR, 1.265; 95% CI, 1.017–1.564; $P = 0.032$). Following adjustments for baseline TyG index, age, and gender, logistic regression

Table 1 Baseline Analysis of the Entire Dataset

Variables	Total (n=8086)	No Occurred CVDs (n=6602)	Occurred CVDs (n=1484)	*P*
Men gender[a]	4439(54.9)	3543(53.7)	896(60.4)	<0.001
Smoking[a]	296(3.7)	164(2.5)	132(8.9)	<0.001
Alcohol consumption[a]	272(3.4)	150(2.3)	122(8.2)	<0.001
HLDL[a]	4783(59.2)	4087(61.9)	696(46.9)	<0.001
AC[a]	108(1.3)	28(0.4)	80(5.4)	<0.001
APD[a]	939(11.6)	269(4.1)	670(45.1)	<0.001
LLD[a]	1506(18.6)	629(9.5)	877(59.1)	<0.001
HL[a]	905(11.19)	517(7.83)	388(26.1)	<0.001
HBP[a]	1697(21.0)	837(12.7)	860(58.0)	<0.001
DM[a]	1094(13.5)	657(10.0)	437(29.4)	<0.001
TyG[b]	8.68[8.28,9.13]	8.67[8.27,9.12]	8.71[8.33,9.18]	<0.001
TC[b]	4.94[4.25,5.69]	5.01[4.36,5.72]	4.56[3.78,5.47]	<0.001
LDL-C[b]	2.79[2.25,3.39]	2.83[2.32,3.41]	2.53[1.93,3.27]	<0.001
HDL-C[b]	1.24[1.02,1.51]	1.26[1.040,1.54]	1.16[0.95,1.41]	<0.001
Age[b]	53[42,63]	50[39,59]	64[56,72]	<0.001

Notes: a: n(%); b: median[interquartile range].
Abbreviations: HLDL, hyper-low-density lipoproteinemia; AC, anticoagulant medication; APD, antiplatelet medication; LLD, lipid-lowering medication; HL, hyperlipidemia; HBP, hypertension; DM, diabetes mellitus; TyG, triglyceride-glucose index; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; TyG, triglyceride-glucose index.

analysis revealed a significant difference between class 3 and class 1 (OR, 1.207; 95% CI, 1.061–1.374; $P = 0.004$). Subsequent adjustments for laboratory indicators, including HDL-C, LDL-C, and TC, indicated that the difference between class 3 and class 1 remained substantial (OR, 1.206; 95% CI, 1.053–1.382; $P = 0.007$).

Through logistic regression analysis of the baseline stratified trajectory classification results, it was found that in the unadjusted model, there was no significant difference between trajectory class 2 ($P = 0.218$) and class 3 ($P = 0.645$) compared to class 1 ($P > 0.05$). Similarly, in Model 1 and Model 2, the results remained consistent.

Through logistic regression analysis of the baseline stratified T2 trajectory classification results, it was found that in the unadjusted model, there was a significant difference between trajectory class 3 and class 1 (OR, 1.247; 95% CI, 1.088–1.429; $P = 0.002$). In Model 1, a significant difference was still present between class 3 and class 1 (OR, 1.257; 95% CI, 1.085–1.457; $P = 0.020$). Similarly, in Model 2, a significant difference persisted between class 3 and class 1 (OR, 1.272; 95% CI, 1.089–1.487; $P = 0.002$) (Table 3). The interaction effect between baseline TyG stratification and TyG trajectory had *P*-values of 0.243 in the Unadjusted Model, 0.224 in Model 1, and 0.169 in Model 2, all of which were non-significant. This indicates that baseline TyG stratification and TyG trajectory do not influence each other. Additionally, multivariate stratified analyses were performed to assess the association between the TyG index and cardiovascular diseases in the overall sample (Table S1).

Associations Between TyG Trajectories and Recurrent CVDs

The logistic regression analysis of recurrent data determined that in the unadjusted model, there existed a significant difference between class 3 and class 1 (OR, 1.441; 95% CI, 1.091–1.906; $P = 0.010$). In Model 1, a significant difference was observed between class 3 and class 1 (OR, 1.488; 95% CI, 1.121–1.977; $P = 0.006$). Similarly, in Model 2, a significant difference remained between class 3 and class 1 (OR, 1.492; 95% CI, 1.120–1.988; $P = 0.006$). Among the recurrent data, the interaction effect between baseline TyG and TyG trajectories was non-significant in all three models (Unadjusted Model, Model 1, Model 2), indicating no significant mutual interaction between these factors. Similarly, multivariate stratified analyses were performed to assess the association between the TyG index and cardiovascular diseases in the recurrent sample (Table S2). There was a significant difference between TyG and cardiovascular diseases in the recurrence (OR, 1.200; 95% CI, 1.043–1.380; $P = 0.011$). Among them, the differences in the female group, the

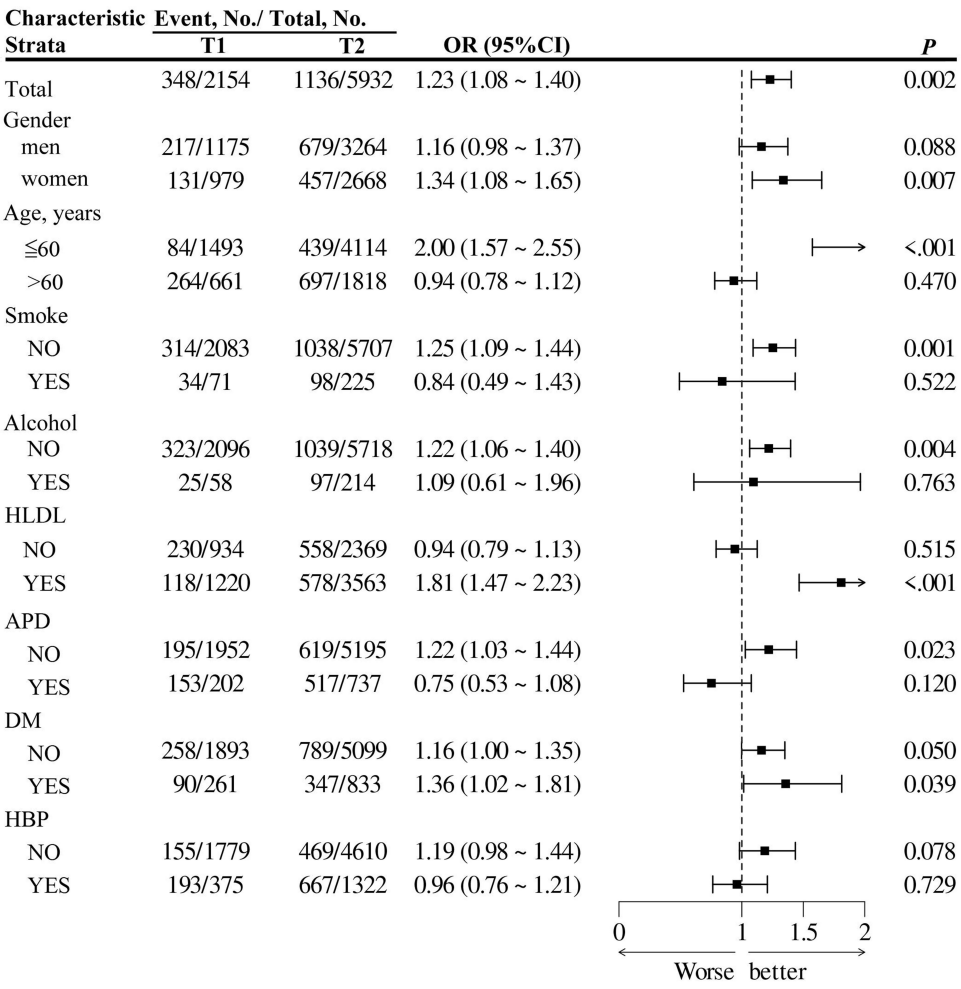

Figure 3 Multivariable Stratified Analyses of the Association Between TYG Baseline Level and CVDs Development.
Abbreviations: OR, Odds Ratio; CI, Confidence Interval; HLDL, hyper-low-density lipoproteinemia; APD, antiplatelet medication; DM, diabetes mellitus; HBP, hypertension.

age ≤60 group, the non-smoking group, the non-drinking group, the HLDL group, the group not APD, and the group with HBP were statistically significant ($P < 0.05$).

The logistic regression analysis of recurrent data revealed no substantial difference between class 2 and class 3 compared to class 1 ($P > 0.05$) in the T1 trajectory classification results across the three models.

Similarly, in the logistic regression analysis of recurrent data in the T2 trajectory classification results, it was found that in the unadjusted model, a significant difference existed between class 3 and class 1 (OR, 1.532; 95% CI, 1.120–2.096; $P = 0.008$). In Model 1, a significant difference persisted between class 3 and class 1 (OR, 1.593; 95% CI, 1.160–2.188; $P = 0.004$). Furthermore, in Model 2, a significant difference persisted between class 3 and class 1 (OR, 1.623; 95% CI, 1.178–2.239; $P = 0.003$) (Table 4).

Associations Between TyG Trajectories and Incident CVDs

Among 8086 samples analyzed, we identified 6824 incidence, of which 500 still exhibited CVD. Logistic regression analysis of the incidence revealed no significant differences between class 2 and class 3 compared to class 1 across all three models ($P > 0.05$). The analysis of interaction terms in the incidence shows no significance. Hierarchical analysis was also carried out.

Similarly, analyzing the T1 trajectory classification results for incidence showed no significant differences between class 2 and class 3 compared to class 1 in any of the three models ($P > 0.05$).

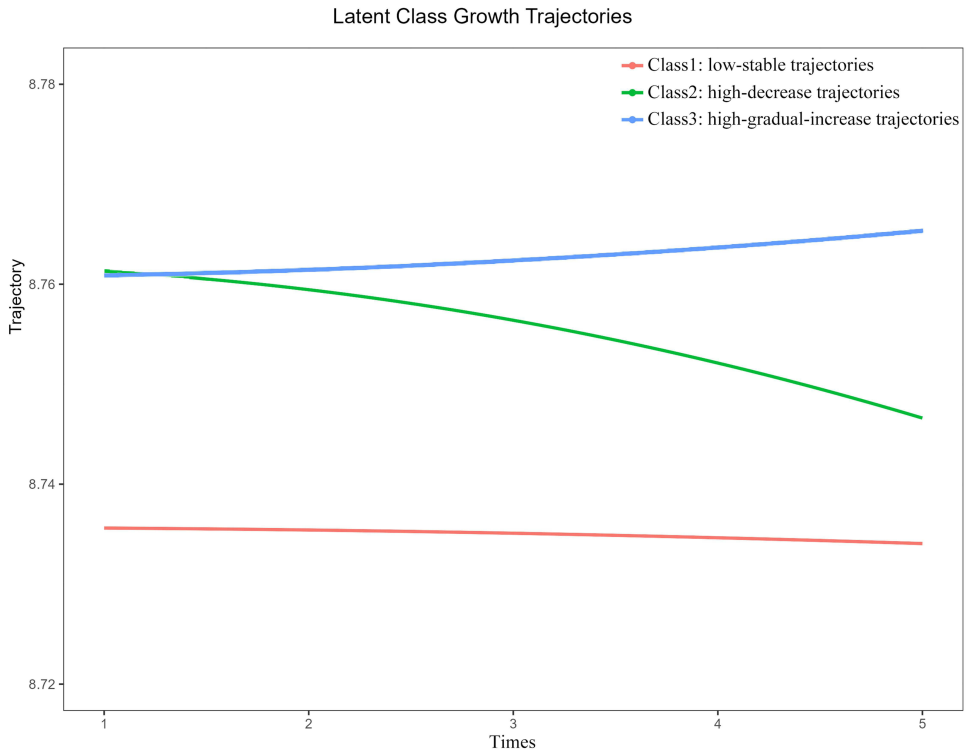

Figure 4 The HLME classification of the trajectory data.
Abbreviations: Class 1, representing low-stable trajectories; Class 2, representing a high-decrease trajectories; Class 3, representing high-gradual-increase trajectories; HLME, Hierarchical Latent Class Mixed Effects.

Furthermore, the T2 trajectory classification results demonstrated significant findings. In the unadjusted model, there was a substantial difference between class 3 and class 1 (OR, 1.176; 95% CI, 1.035–1.336; $P = 0.013$). Model 1 showed no significant differences between class 2 and class 3 compared to class 1 ($P > 0.05$). In Model 2, a considerable difference was found between class 3 and class 1 (OR, 1.017; 95% CI, 1.017–1.368; $P = 0.029$) (Table 5). Similarly, we performed multivariate stratified analyses to assess how the TyG index relates to incident sample (Table S3).

This section may be divided by subheadings. It should provide a concise and precise description of the experimental results, their interpretation, as well as the experimental conclusions that can be drawn.

Discussion

This study suggested a significant association between high-gradual-increase TyG trajectories and the occurrence of CVDs. Even after adjusting for various CVDs risk factors, the relationship of high-gradual-increase TyG trajectories and CVDs persisted. Considering the incidence and recurrent CVDs, logistic regression analysis was conducted on models representing three different TyG trajectories. The study revealed the relationship persisted in the recurrent cohort. Although this relationship was not observed in the entire cohort of incidence patients, it was also observed in incidence patients with higher TyG levels, with a higher risk of disease associated with a high-gradual-increase trajectories compared to a low-stable trajectories. Notably, this relationship remained true for higher TyG levels in both the overall cohort and the recurrent cohort, underscoring the predictive and alerting role of higher TyG levels and high-gradual-increase trajectories in the incidence and recurrence of CVDs.

Our study utilized ROC analysis to determine a threshold (8.309) for stratifying the TyG index, revealing that high TyG levels are positively associated with CVDs, HLDL, HBP, DM, and other conditions. Compared to low TyG levels, high TyG levels can increase the risk of developing CVDs by 8% to 40%. This study indicates that the TyG index can serve as an alert for individuals at high risk of CVDs, with attention warranted for individuals having a TyG index above 8.309; this observation is consistent with numerous previous studies.[23–27] For example, research on the TyG index and

Table 2 Baseline Analysis of Each Trajectory with and without CVDs

CVDs		Trajectories			No-CVDs		Trajectories		
Characteristics	**Total (n=1484)**	**Class 1 (n=581)**	**Class 2 (n=126)**	**Class 3 (n=777)**	**Characteristics**	**Total (n=6602)**	**Class 1 (n=2888)**	**Class 2 (n=495)**	**Class 3 (n=3219)**
Men gender[a]	896(60.4)	360(62.0)	76(60.3)	460(59.2)	Men gender[a]	3543(53.7)	1545(53.5)	251(50.7)	1747(54.3)
Smoking[a]	132(8.9)	43(7.4)	8(6.3)	81(10.4)	Smoking[a]	164(2.5)	58(2.0)	16(3.2)	90(2.8)
Alcohol consumption[a]	122(8.2)	37(6.4)	9(7.1)	76(9.8)	Alcohol consumption[a]	150(2.3)	56(1.9)	12(2.4)	82(2.5)
HLDL[a]	696(46.9)	264(45.4)	55(43.7)	377(48.5)	HLDL[a]	4087(61.9)	1780(61.6)	302(61.0)	2005(62.3)
AC[a]	80(5.4)	30(5.2)	9(7.1)	41(5.3)	AC[a]	28(0.4)	11(0.4)	3(0.6)	14(0.4)
APD[a]	670(45.1)	245(42.2)	57(45.2)	368(47.4)	APD[a]	269(4.1)	119(4.1)	23(4.6)	127(3.9)
LLD[a]	877(59.1)	334(57.5)	78(61.9)	465(59.8)	LLD[a]	629(9.5)	260(9.0)	48(9.7)	321(10.0)
HL[a]	388(26.1)	162(27.9)	40(31.7)	186(23.9)	HL[a]	517(7.8)	207(7.2)	32(6.5)	278(8.6)
HBPa	860(58.0)	327(56.3)	75(59.5)	458(58.9)	HBPa	837(12.7)	355(12.3)	71(14.3)	411(12.8)
DM[a]	437(29.4)	165(28.4)	37(29.4)	235(30.2)	DM[a]	657(10.0)	271(9.4)	44(8.9)	342(10.6)
TyG[b]	8.71[8.33,9.18]	8.73[8.31,9.18]	8.59[8.31,9.10]	8.71[8.34,9.20]	TyG[b]	8.67[8.27,9.12]	8.67[8.26,9.12]	8.69[8.27,9.12]	8.66[8.27,9.12]
TC[b]	4.56[3.78,5.47]	4.54[3.75,5.52]	4.52[3.56,5.35]	4.58[3.86,5.45]	TC[b]	5.01[4.36,5.72]	5.01[4.36,5.70]	5.00[4.34,5.68]	5.01[4.35,5.76]
LDL-C[b]	2.53[1.93,3.27]	2.50[1.91,3.26]	2.40[1.84,3.37]	2.56[1.98,3.27]	LDL-C[b]	2.83[2.32,3.41]	2.82[2.33,3.40]	2.840[2.25,3.42]	2.84[2.31,3.44]
HDL-C[b]	1.16[0.95,1.41]	1.15[0.95,1.41]	1.16[0.96,1.36]	1.17[0.96,1.42]	HDL-C[b]	1.26[1.04,1.54]	1.270[1.04,1.55]	1.27[1.03,1.53]	1.25[1.03,1.53]
Age[b]	64[56,72]	65[57,73]	64[58,73]	64[56,72]	Age[b]	50[39,59]	50[39,59]	50[39,60]	50[39,59]

Notes: Class 1, representing low-stable trajectories; Class 2, representing high-decrease trajectories; Class 3, representing high-gradual-increase trajectories. a: n(%); b: median[interquartile range].

Abbreviations: HLDL, hyper-low-density lipoproteinemia; AC, anticoagulant medication; APD, antiplatelet medication; LLD, lipid-lowering medication; HL, hyperlipidemia; HBP, hypertension; DM, diabetes mellitus; TyG, triglyceride-glucose index; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; TyG, triglyceride-glucose index.

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Table 3 Odds Ratios (with 95% CI) for the Overall Samples, Stratified by Baseline and Trajectory Classes of the TyG Index

Baseline TyG	TyG-Traj	Events/N	Unadjusted Model		Model 1		Model 2	
			OR	*P*	OR	*P*	OR	*P*
Total	Class 1	581/3469	Ref		Ref		Ref	
	Class 2	126/621	**1.265[1.017,1.564]**	**0.032**	1.251[0.987,1.582]	0.061	1.201[0.933,1.539]	0.151
	Class 3	777/3996	**1.200[1.066,1.351]**	**0.003**	**1.207[1.061,1.374]**	**0.004**	**1.206[1.053,1.382]**	**0.007**
	P-interaction			0.243		0.224		0.169
T1	Class 1	146/942	Ref		Ref		Ref	
	Class 2	31/160	1.310[0.841,1.991]	0.218	1.153[0.691,1.885]	0.577	1.118[0.643,1.899]	0.686
	Class 3	171/1052	1.058[0.832,1.347]	0.645	1.031[0.785,1.355]	0.827	1.309[0.776,1.392]	0.796
T2	Class 1	435/2527	Ref		Ref		Ref	
	Class 2	95/461	1.248[0.970,1.594]	0.080	1.258[0.958,1.64]	0.094	1.21[0.906,1.604]	0.190
	Class 3	606/2944	**1.247[1.088,1.429]**	**0.002**	**1.257[1.085,1.457]**	**0.002**	**1.272[1.089,1.487]**	**0.002**

Notes: Bold values denote significant differences between the groups; TyG-Traj, Trajectories of TyG; Model 1, Adjusted for baseline TyG index, gender, and age; Model 2, Adjusted for baseline TyG index, gender, age, HL, TC, HDL, and AC; OR, Odds Ratio; ref, reference group; T1, low-level TyG population; T2, high-level TyG population; *P*-interaction, p-value testing the statistical interaction of baseline TyG and TyG trajectory patterns.

Table 4 Odds Ratios (with 95% CI) for the Recurrence Samples, Stratified by Baseline and Trajectory Classes of the TyG Index

Baseline TyG	TyG-Traj	Events/N	Unadjusted Model		Model 1		Model 2	
			OR	*P*	OR	*P*	OR	*P*
Total	Class 1	367/495	Ref		Ref		Ref	
	Class 2	88/110	1.395[0.852,2.368]	0.200	1.369[0.829,2.339]	0.233	1.321[0.804,2.283]	0.281
	Class 3	529/657	**1.441[1.091,1.906]**	**0.010**	**1.488[1.121,1.977]**	**0.006**	**1.492[1.12,1.988]**	**0.006**
	P-interaction			0.595		0.607		0.614
T1	Class 1	91/117	Ref		Ref		Ref	
	Class 2	20/23	1.905[0.593,8.527]	0.327	1.435[0.429,6.565]	0.592	1.517[0.416,7.464]	0.561
	Class 3	102/127	1.166[0.628,2.169]	0.626	1.098[0.577,2.089]	0.774	1.00[0.508,1.957]	0.999
T2	Class 1	276/378	Ref		Ref		Ref	
	Class 2	68/87	1.323[0.771,2.361]	0.325	1.348[0.779,2.424]	0.301	1.31[0.754,2.363]	0.352
	Class 3	427/530	**1.532[1.12,2.096]**	**0.008**	**1.593[1.16,2.188]**	**0.004**	**1.623[1.178,2.239]**	**0.003**

Notes: Bold values denote significant differences between the groups; TyG-Traj, Trajectories of TyG; Model 1, Adjusted for baseline TyG index, gender, and age; Model 2, Adjusted for baseline TyG index, gender, age, HL, TC, HDL, and AC; OR, Odds Ratio; ref, reference group; T1, low-level TyG population; T2, high-level TyG population; *P*-interaction, p-value testing the statistical interaction of baseline TyG and TyG trajectory patterns.

Table 5 Odds Ratios (with 95% CI) for the Incidence, Stratified by Baseline and Trajectory Classes of the TyG Index

Baseline TyG	TyG-Traj	Events/N	Unadjusted Model		Model 1		Model 2	
			OR	*P*	OR	*P*	OR	*P*
Total	Class 1	214/2974	Ref		Ref		Ref	
	Class 2	38/511	1.036[0.714,1.466]	0.846	1.040[0.707,1.494]	0.838	1.035[0.697,1.501]	0.859
	Class 3	248/3339	1.035[0.856,1.252]	0.724	1.019[0.836,1.242]	0.855	1.003[0.818,1.230]	0.979
	P-interaction			0.445		0.607		0.614
T1	Class 1	55/825	Ref		Ref		Ref	
	Class 2	11/137	1.208[0.789,1.808]	0.370	1.162[0.545,2.290]	0.680	1.056[0.481,2.148]	0.886
	Class 3	69/925	1.025[0.817,1.287]	0.831	1.096[0.743,1.623]	0.646	1.063[0.709,1.600]	0.767
T2	Class 1	159/2149	Ref		Ref		Ref	
	Class 2	27/374	1.217[0.962,1.531]	0.097	0.990[0.627,1.512]	0.965	1.180[0.896,1.545]	0.234
	Class 3	179/2414	**1.176[1.035,1.336]**	**0.013**	0.990[0.786,1.247]	0.929	**1.179[1.017,1.368]**	**0.029**

Notes: Bold values denote significant differences between the groups; TyG-Traj, Trajectories of TyG; Model 1, Adjusted for baseline TyG index, gender, and age; Model 2, Adjusted for baseline TyG index, gender, age, HL, TC, HDL, and AC; OR, Odds Ratio; ref, reference group; T1, low-level TyG population; T2, high-level TyG population; *P*-interaction, p-value testing the statistical interaction of baseline TyG and TyG trajectory patterns.

CHD has found a positive correlation between the severity of CHD and increasing TyG index values.[28] The TyG index has been identified as a prognostic indicator in patients undergoing percutaneous coronary intervention,[29] and aids in blood sugar management in patients with diabetes and CHD.[30] Research by Yang et al demonstrated a significant association between the TyG index and the risk of HBP in the general population.[31] Jiao et al's study on the TyG index revealed its effectiveness in predicting diabetes and HL.[32] These findings align with our research, collectively demonstrating the efficacy of the TyG index in cardiovascular prediction.

This study, which classified TyG index trajectory data, found that individuals in the high-gradual-increase trajectory group had a greater risk of developing CVDs than those in the low-stable trajectory group. The high-gradual-increase trajectories of the TyG index increased the risk of CVDs by 6.6% to 35.1% compared to the low-stable trajectories. Even after adjusting for specific demographic and laboratory indicators, the results remained consistent, showing that individuals in the high-gradual-increase trajectories of the TyG index were more likely to develop CVDs than those in the low-stable trajectories. These findings align with several current studies.[33–35] For instance, a prospective cohort study found a link between long-term increases in the TyG index in patients with HBP and an increased risk of stroke.[36] These studies, consistent with our findings, suggest that TyG index trajectories can effectively indicate the risk of developing CVDs.

The association between different TyG trajectories and the incidence and recurrence of CVDs is also investigated. In cases of CVDs recurrence with high TyG levels, without adjusting for model variables, individuals in the high-gradual-increase trajectory group had a 12% to 109.6% increased risk of developing CVDs compared to those in the low-stable trajectory group. After adjusting for specific demographic and laboratory indicators, individuals in the high-gradual-increase trajectories group had a 17.8% to 123.9% higher risk of developing CVDs than those in the low-stable trajectories group. In incidence cases with elevated TyG levels, without adjusting model variables, the high-gradual-increase trajectories group had a 3.5% to 33.6% higher risk of developing CVDs than the low-stable trajectories group. After adjustments, the high-gradual-increase trajectories group was found to have a 1.7% to 36.8% increased risk of developing CVDs compared to the low-stable trajectories group. These results indicate that high levels of TyG index and high-gradual-increase trajectories are adequate risk predictors for incidence and recurrent CVDs. Furthermore, within this trajectory group, the risk of recurrence was higher than that of incidence cases, underscoring the need for vigilance regarding the possibility of recurrence.

CVDs refer to diseases affecting the heart and vascular system, including CHD, stroke, and CeI. IR is a common chronic condition where cells in the body have a reduced response to insulin, leading to increased insulin concentration in the blood and affecting blood sugar regulation. A review study on the association between CVDs and IR indicated[37] that the mechanisms linking the two include the following. Firstly, insulin resistance can lead to abnormal blood sugar and lipid levels, increasing the risk of CVDs such as atherosclerosis.[38] Secondly, insulin resistance can also increase inflammatory responses,[39] promoting endothelial inflammation and plaque formation, and accelerating the progression of atherosclerosis. Lastly, insulin resistance can cause endothelial dysfunction,[40] raising the risk of thrombosis and vasoconstriction, further exacerbating the development of cardiovascular diseases. The TyG index is an indicator used to assess the degree of IR, calculated by measuring fasting triglycerides and blood glucose levels. The TyG index is positively correlated with the degree of insulin resistance and can serve as an alternative marker for IR.[41]

In comparison with prior research, this study demonstrated several innovations: Firstly, utilizing LCTM, the three types of TyG index trajectories were differentiated: high-gradual-increase, high-decrease, and low-stable trajectory groups. Secondly, multiple models were constructed by adjusting for demographic and laboratory indicators to delve into the association between various TyG index trajectories and CVDs. Lastly, this study separately analyzed incidence and recurrent CVDs, revealing that changes in TyG index trajectories significantly impact the occurrence of CVDs, particularly among patients with higher baseline TyG index levels, with the influence of TyG index trajectories being particularly pronounced in the population experiencing recurrent CVDs.

However, this study also presents several limitations. Firstly, being a retrospective study in a real-world setting, interventions regarding treatment methods and medications were not implemented, potentially introducing unaccounted confounding factors that could influence the analysis results. Secondly, the study's duration is relatively short, spanning data collection only from 2019 to 2021, thereby failing to observe longer-term trajectory changes and outcomes. Finally, our research was a central study and did not undergo external validation. Therefore, the adaptability for non-Chinese individuals remains undetermined. Our future research endeavors are aimed to involve

longitudinal prospective studies with stricter control over treatment modalities to address these limitations, minimize the impact of confounding factors, and collect a more significant number of outcome events. Moreover, retrospective data is intended to be used with prospective studies to develop more precise and effective clinical predictive models. This approach will assist clinical researchers in early risk warning for CVDs and in gaining a better understanding of the potential impact of the TyG index trajectory on cardiovascular diseases and other illnesses.

Conclusion

Conclusively, our research indicates that a high baseline TyG with a high-gradual-increasing trajectory are significantly associated with the risk of incidence and recurrent cardiovascular diseases. While the TyG index trajectory serves as a clinically valuable biomarker for cardiovascular risk stratification, its predictive power is optimally realized when integrated within multifactorial risk assessment frameworks rather than as an independent diagnostic tool. This approach enhances identification of individuals at elevated risk for subclinical atherosclerotic progression. Therefore, it is recommended that people continuously monitor their TyG levels every year to identify individuals with a high risk of new or recurrent cardiovascular diseases.

Abbreviations

95% CIs, 95% confidence intervals; AC, Anticoagulant medication; ANOVA, Analysis of variance; APD, Antiplatelet medication; BIC, Bayesian Information Criterion; CeI, Cerebral infarction; CHD, Coronary heart disease; CKD, Chronic kidney disease; CVDs, Cardiovascular disease; DM, Diabetes; HBP, Hypertension; HDL, High-density lipoprotein; HDL-C, High-density lipoprotein cholesterol; HIEC, High-dose insulin euglycemic clamp; HL, Hyperlipidemia; HLDL, Hyper-low-density lipoproteinemia; HLME, Hierarchical latent class mixed-effects; HOMA-IR, Homeostasis model assessment of insulin resistance; IQR, Interquartile range; IR, Insulin resistance; LCTM, Latent Class Trajectory Modeling; LDL-C, Low-density lipoprotein cholesterol; LLD, Lipid-lowering medication; ORs, Odds ratios; TC, Total cholesterol; TyG, Triglyceride-glucose.

Data Sharing Statement

The data presented in this study are available on request from the corresponding author.

Ethics Approval and Consent to Participate

The authors take responsibility for all aspects of the work, ensuring that questions regarding the accuracy or integrity of any part are thoroughly investigated and resolved. The study adhered to the Declaration of Helsinki (revised in 2013), approved by the ethics board of the Second Affiliated Hospital of Nanchang University (No. [2024] 046), with informed consent obtained from all participants.

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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.

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Disclosure

The authors declare no competing interests in this work.

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