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ORIGINAL RESEARCH

Interaction of Triglyceride-Glucose Index and Metabolic Syndrome with Risk of Incident Stroke Among Middle-Aged and Older Chinese Adults

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Objective: The triglyceride-glucose (TyG) index, a reliable surrogate marker of insulin resistance, has been shown as an independent risk factor for stroke. Still, the interaction between metabolic syndrome (MetS) and the TyG index in determining stroke risk remains to be clarified, which may help optimize stroke prevention strategies. This study aims to explore whether metabolic syndrome (MetS) influences the association between the TyG index and the risk of stroke.

Methods: A total of 7770 middle-aged and older participants free of stroke at baseline were enrolled from the China Health and Retirement Longitudinal Study. The TyG index was calculated as ln (triglyceride [mg/dL] × fasting glucose [mg/dL]/2). MetS was defined following the modified International Diabetes Federation criteria. The outcome was self-reported, physician-diagnosed, incident stroke during follow-up. Cox proportional hazard models were used to examine whether MetS influences the associations between the TyG index and the risk of incident stroke.

Results: A total of 568 (7.3%) incident stroke cases occurred after a median observation time of 7.0 years. After adjusting for potential confounders, a higher TyG level was associated with an increased risk of incident stroke (hazard ratio (HR) 1.19, 95% CI 1.05–1.33, P = 0.016). The association was significant in participants without MetS (HR 1.69, 95% CI 1.40–1.97, P < 0.001), but not in those with MetS (HR 1.05, 95% CI 0.88–1.21, P = 0.599). The interaction between the TyG index and MetS on the risk of incident stroke was significant (P = 0.004).

Conclusion: MetS influenced the association of the TyG index with the risk of incident stroke among middle-aged and older Chinese adults. The TyG index may be more effective for stroke risk stratification in populations without MetS compared to those with MetS.

Keywords: triglyceride-glucose index, stroke, metabolic syndrome, risk

Introduction

Stroke is the second-leading cause of death and the third-leading cause of disability globally, with a substantial impact on health and social economic costs worldwide.[1] Despite advances in prevention, diagnosis, and treatment in recent years, the global burden of stroke is still increasing. In 2021, there were 93.8 million prevalent and 11.9 million incident strokes.[2] Evidence from the Global Burden of Disease, Injuries, and Risk Factors Study shows that the majority of this burden is due to modifiable risk factors, suggesting the enormous potential to reduce the burden of stroke through effective prevention.[3] Consequently, identifying high-risk stroke populations is of paramount importance in public health and clinical practice.

Insulin resistance, defined as the failure of cells responding to the normal actions of insulin, has been shown to facilitate stroke by accelerating atherosclerosis, promoting platelet dysfunction, and inducing hypercoagulable state of the blood.[4] The triglyceride-glucose (TyG) index, calculated using triglyceride (TG) and fasting blood glucose (FBG), is a simple, accessible, and reliable clinical surrogate marker of insulin resistance.[5] Several studies have investigated the

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association of the TyG index with the risk of stroke. A prospective cohort study involving 97,653 participants revealed that individuals with a higher TyG index faced a 1.32-fold increased risk of stroke within the general population.[6] This association was similarly observed in a large-scale national observational cohort study in Korea, which included 5,593,134 participants.[7] A recent meta-analysis further confirmed that the TyG index is an independent risk factor for stroke.[8] These findings suggest that the TyG index can serve as a cost-effective and important indicator for stroke risk stratification.[6] Utilizing the TyG index in clinical practice may provide a more effective means of identifying individuals at high risk for stroke and implementing targeted preventive measures, ultimately contributing to improved patient outcomes.

Metabolic syndrome (MetS) is a cluster of clinical, metabolic, and biochemical abnormalities, such as central adiposity, hypertension, and insulin resistance.[9] It has become a global public health challenge, affecting over 1 billion individuals worldwide.[10] Studies have demonstrated that the presence of metabolic syndrome significantly increases the risk of stroke.[11] While insulin resistance represents a cornerstone of its pathophysiological changes and is a contributor to stroke risk among patients with MetS, other components of MetS, such as central obesity and hypertension, also play significant roles in elevating stroke risk.[9,12] Therefore, the TyG index, as an indicator of insulin resistance, may only capture a partial aspect of the comprehensive vascular risk profile in MetS patients, and its ability to predict stroke risk within this specific population may be inherently limited. Notably, no studies to date have assessed the TyG index's predictive value for stroke risk in MetS patients. This highlights a critical research gap, offering an opportunity to enhance stroke prevention strategies. We therefore aimed to use data from a nationally representative longitudinal survey to explore whether MetS influences the association of the TyG index with the risk of incident stroke among middle-aged and older Chinese adults.

Materials and Methods

Study Design and Participants

The China Health and Retirement Longitudinal Study (CHARLS) is a nationally representative longitudinal survey of the middle-aged and older population (≥45 years) conducted by the National School of Development at Peking University. Descriptions of the study design and methods have been reported in detail elsewhere.[13] In brief, all participants were assessed by one-to-one interviews with a standardized questionnaire. Participants were followed up every 2 years by a face-to-face interview. Physical measurements were conducted at every follow-up and blood sample collection was performed in every two follow-up cycles (4 years). The nationwide baseline survey (Wave 1) was conducted in 2011, with Wave 2 in 2013, Wave 3 in 2015 and Wave 4 in 2018.

This prospective cohort study was conducted using data from these four waves of the CHARLS. Of the 11,847 participants with blood samples collected at Wave 1, we excluded participants less than 45 years old (N = 430), without fasting blood glucose or triglyceride (N = 1330), with incomplete information on MetS (N = 1750), with a stroke diagnosis (N = 239), and with missing data on stroke information in Wave 2–4 (N = 241) or baseline characteristic (N = 87). The final analyses therefore included 7770 participants (Figure 1). All data was extracted from publicly available databases and was deidentified, therefore, this study was exempt from ethics approval based on Measures for Ethical Review of Life Science and Medical Research Involving Human Subjects (February 18, 2023, China). The data and study materials that support the findings of this study will be available at the CHARLS project website (http://charls.pku.edu.cn/).

Exposure Assessment and Definition

Blood pressure was measured 3 times with Omron™ HEM-7200 Monitor in the seating position after a short rest. The mean of the second and third measurements was used for the analysis. Waist circumference (WC) was measured at the level of the umbilicus. The Chinese Center for Disease Control and Prevention in Beijing promptly received venous blood samples within two weeks of their departure from the Centers for Disease Control and Prevention station. These samples were immediately stored and frozen at −20°C before delivery. After completing necessary assays at the Chinese Medical University laboratory, they were transferred to a deep freezer and maintained at −80 °C. At the Youanmen Clinical Laboratory of Capital Medical University, TG, high-density lipoprotein cholesterol (HDL-C), and FBG
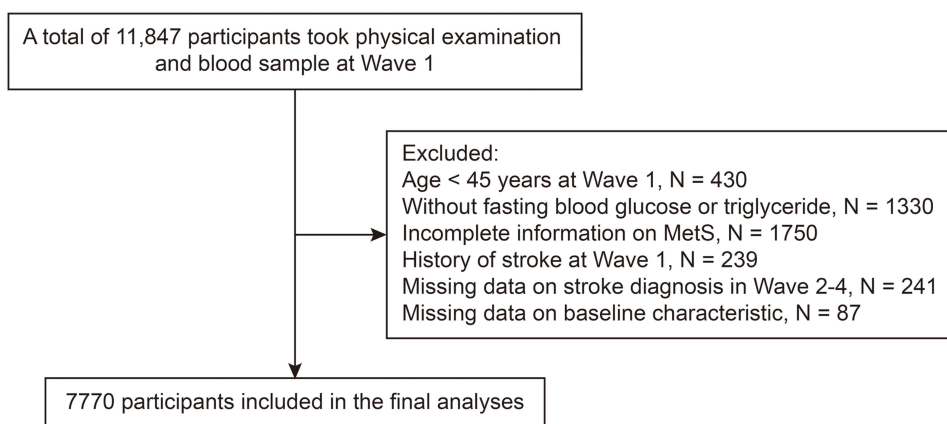
Figure 1 Flowchart of the study inclusion/exclusion and grouping process.
Abbreviations: MetS, metabolic syndrome; TyG, triglyceride-glucose.

concentrations were determined using the enzyme colorimetric assay. The laboratory used quality control samples daily during the testing of the study samples. The TyG index was calculated by the formula ln [TG (mg/dl) × FBG (mg/dl)/2].[5]

In our main analysis, we used a modified definition of MetS for Chinese in accordance with recommendations from the International Diabetes Federation.[14] MetS was defined as having 3 or more following criteria: (1) elevated WC (≥85 cm for men, ≥80 cm for women), (2) elevated fasting triglycerides (≥150 mg/dL), (3) reduced HDL-C (<40 mg/dL for men, <50 mg/dL for women), (4) elevated blood pressure (≥130/85 mmHg), or receiving antihypertensive treatment, (5) elevated fasting glucose (≥100 mg/dL), or receiving hypoglycemic treatment. To enhance the generalizability of our findings, we used an alternative definition of MetS for Caucasian in the sensitivity analysis, which applied a stricter criterion for increased waist circumference (≥102 cm for men and ≥88 cm for women).

Covariates

Information on age, gender, residential area (rural, urban), educational level (primary school or below, middle school and above), married status (married, unmarried), smoking status (yes, no), drinking status (yes, no), body mass index (BMI), and heart disease was obtained from the standard questionnaires. BMI was defined as weight in kilograms divided by the square of the height in meter. Heart disease was defined as a self-reported history of heart disease.

Outcome Assessment

The primary outcome was incident, self-reported, physician-diagnosed stroke, which was defined as answering "yes" to the question: "Have you been diagnosed with stroke by a doctor?" in Wave 2–4. For participants suffering incident stroke, the middle date between this and the nearest survey before was used to calculate the follow-up time. For those free of stroke in all following surveys, the last survey date was used to calculate the follow-up time.[15]

Statistical Analysis

The Kolmogorov–Smirnov test was used to test the data distribution. Continuous variables were presented as mean ± standard deviation or median (interquartile range) according to their distribution, and categorical variables were expressed as frequencies and percentages.

At first, the level of TyG index was dichotomized into low (<8.60 mg/dL) and high (≥8.60 mg/dL) levels based on the Youden index. Kaplan–Meier analysis was employed to assess the incidence rate of incident stroke in all participants and stratified by metabolic status based on the categorized TyG index, and their differences were assessed through Log rank tests. The proportional hazards assumption was checked by scaled Schoenfeld residuals. Then, the associations of the TyG index (continuous, categorized) with the risk of incident stroke were estimated using Cox proportional hazards models (hazard ratios [HRs] and 95% confidence intervals [CIs]) with and without adjustments for age, sex, body mass

index, marriage status, smoking status, heart disease, and MetS in all participants and stratified by metabolic status. These confounders were chosen based on their statistical significance (P < 0.10) in the univariable analysis and their potential influence on stroke risk based on existing literature.[8] Furthermore, we also analyzed the nonlinear association between the TyG index and the risk of incident stroke using a restricted cubic spline regression model with four knots. Finally, interaction analyses were performed to examine whether MetS influences the associations between the TyG index and the risk of incident stroke by adding an interaction term (MetS × TyG index) to the multivariable Cox proportional hazards model. P value for interaction was calculated using the Wald-test of the interaction term. Multicollinearity between explanatory variables was assessed using the variance inflation factor.

Moreover, we conducted 3 sensitivity analyses. First, we repeated our analysis using the alternative definition of MetS as described above. Second, we replaced MetS with its criteria (elevated WC, reduced HDL-C, and elevated blood pressure) in the adjusted models to more directly eliminate the influence of other common stroke risk factors. Third, we divided the TyG index into two groups based on its median value to examine the impact of different dichotomization criteria on the results. A two-tailed P < 0.05 was considered to be statistically significant in all analyses. Statistical analyses were conducted using R software (version 4.4.1, http://www.R-project.org/).

Results
Baseline Characteristics
Of 7770 enrolled participants, the median age was 58 (52, 65) years, and 3592 (46.2%) were male. The median TyG index was 8.6 (8.2, 9.0), and 3276 participants (42.2%) had MetS. Participants with MetS were older, had a higher BMI, and were prone to have heart disease. They were also less likely to be male, live in rural areas, have completed middle school or above, and be current smokers or drinkers (Table S1). In participants without MetS, those with high TyG levels had less reduction in HDL-C, and similar elevation in WC or blood pressure. When comparing within participants with MetS, those with high TyG levels had less elevation in WC or blood pressure, but a more significant reduction in HDL-C (Table 1).

Table 1 Baseline Characteristics of Participants by Categorized TyG Index and Metabolic Status

Characteristics	Participants without MetS			Participants with MetS		
	Low TyG (N = 3233)	High TyG (N = 1164)	P-value	Low TyG (N = 683)	High TyG (N = 2536)	P-value
Age, years	58 (51, 65)	57 (52, 64)	0.781	60 (53, 67)	58 (52, 65)	**0.004**
Male	1764 (53.7)	593 (49.0)	**0.005**	254 (37.0)	981 (37.9)	0.716
BMI, kg/m2	21.7 (19.9, 23.8)	21.8 (20.1, 24.1)	**0.013**	24.8 (23.0, 27.1)	25.4 (23.2, 27.7)	**0.001**
Residence in rural village	2318 (70.6)	825 (68.1)	0.116	412 (60.1)	1461 (56.4)	0.094
Graduate from middle school or above	2357 (71.8)	857 (70.8)	0.523	472 (68.8)	1801 (69.5)	0.746
Married	2783 (84.8)	1014 (83.7)	0.420	570 (83.1)	2196 (84.8)	0.303
Current smoker	1188 (36.2)	418 (34.5)	0.317	136 (19.8)	598 (23.1)	0.076
Current drinker	1237 (37.7)	428 (35.3)	0.160	188 (27.4)	727 (28.1)	0.767
Heart disease	279 (8.5)	123 (10.2)	0.095	97 (14.1)	409 (15.8)	0.315
MetS evaluation indicators						
Elevated waist circumference	1157 (35.2)	447 (36.9)	0.317	650 (94.8)	2269 (87.6)	**<0.001**
Waist circumference, cm	80 (75, 86)	80 (75, 86)	0.446	90 (86, 96)	91 (86, 97)	0.194
Elevated triglycerides	3 (0.9)	220 (18.2)	**<0.001**	2 (0.3)	1741 (67.2)	**<0.001**
Triglycerides, mg/dL	74.3 (60.2, 90.3)	130.1 (115.0, 145.1)	**<0.001**	79.7 (66.4, 92.0)	174.3 (136.3, 235.4)	**<0.001**
Reduced HDL-C	425 (12.9)	254 (21.0)	**<0.001**	352 (51.3)	1947 (75.2)	**<0.001**
HDL-C, mg/dL	57.2 (49.5, 67.3)	52.2 (44.5, 59.5)	**<0.001**	47.6 (40.6, 59.5)	40.2 (34.0, 47.2)	**<0.001**
Elevated blood pressure	1047 (31.9)	355 (29.3)	0.106	601 (87.6)	1821 (70.3)	**<0.001**
Systolic blood pressure, mmHg	119.5 (109.5, 132.5)	120.0 (111.0, 130.0)	0.486	139.0 (130.5, 150.5)	134.0 (121.5, 148.0)	**<0.001**

(*Continued*)

Table 1 (Continued).

Characteristics	Participants without MetS			Participants with MetS		
	Low TyG (N = 3233)	High TyG (N = 1164)	P-value	Low TyG (N = 683)	High TyG (N = 2536)	P-value
Diastolic blood pressure, mmHg	71.0 (64.0, 79.0)	71.5 (65.5, 79.0)	0.182	81.0 (73.0, 87.9)	78.5 (70.5, 86.5)	**<0.001**
Antihypertensive treatment	296 (9.0)	109 (9.0)	>0.999	219 (31.9)	853 (32.9)	0.649
Elevated fasting glucose	1127 (34.3)	652 (53.8)	**<0.001**	547 (79.7)	2151 (83.1)	**0.049**
Glucose, mg/dL	96 (90, 103)	102 (95, 115)	**<0.001**	104 (101, 111)	111 (102, 127)	**<0.001**
Hypoglycemic treatment	29 (0.9)	44 (3.6)	**<0.001**	28 (4.1)	206 (8.0)	**0.001**
Number of MetS risk factors	1 (1, 2)	2 (1, 2)	**<0.001**	3 (3, 3)	4 (3, 4)	**<0.001**
TyG index, mg/dL	8.2 (8.0, 8.4)	8.8 (8.7, 9.0)	**<0.001**	8.4 (8.2, 8.5)	9.2 (8.9, 9.6)	**<0.001**
Follow-up time, year	7.0 (6.9, 7.0)	7.0 (6.9, 7.0)	0.191	7.0 (6.7, 7.0)	7.0 (6.7, 7.0)	0.341

Notes: Data are expressed as median (interquartile range), or n (%). P values of < 0.05 are shown in bold.
Abbreviations: TyG, triglyceride-glucose; MetS, metabolic syndrome; BMI, body mass index; HDL-C, high-density lipoprotein-cholesterol.

Clinical Outcomes

During a median observation time of 7.0 years, accounting for 49,122 person-years, 568 (7.3%) participants experienced an incident stroke. The proportional hazards assumption was checked and found to be met. Participants with a higher TyG index exhibited an increased risk of incident stroke among all participants (log-rank P < 0.001, Figure 2A) and those without MetS (log-rank P = 0.001, Figure 2B), while the risk of incident stroke did not significantly differ in participants with MetS (log-rank P = 0.900, Figure 2C).

When treated as a continuous variable, a higher TyG index was associated with an increased risk of incident stroke in all enrolled participants (HR 1.19, 95% CI 1.05–1.33, P = 0.016). The association was significant in participants without MetS (HR 1.69, 95% CI 1.40–1.97, P < 0.001), but not in those with MetS (HR 1.05, 95% CI 0.88–1.21, P = 0.599). The interaction between the TyG index and MetS on the risk of incident stroke was significant (P = 0.004; Table 2). When treated as a categorized variable, the association of the TyG index with the risk of incident stroke was also significant in participants without MetS (HR 1.55, 95% CI 1.28–1.81, P = 0.001), but not in those with MetS (HR 1.03, 95% CI 0.76–1.30, P = 0.832; Table 3). Furthermore, as the TyG levels increased, the risk of stroke showed a non-linear increase in the overall population (P
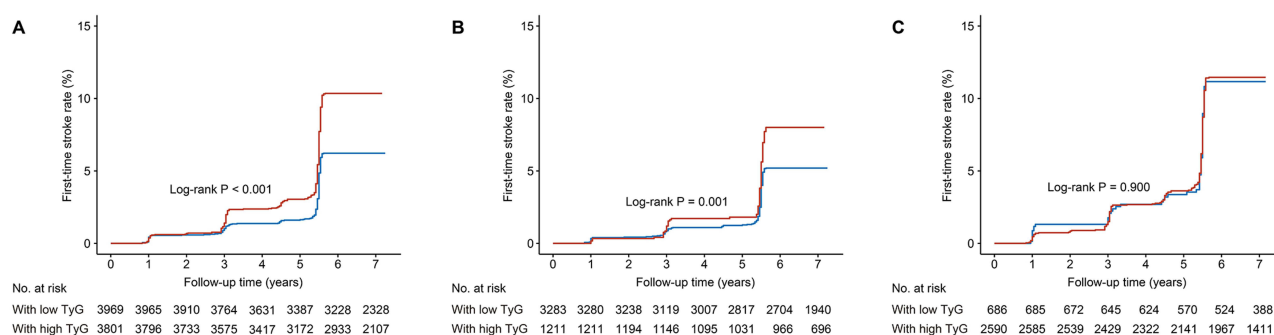

Figure 2 Kaplan-Meier analysis curve for (**A**) all participants, (**B**) participants without MetS, and (**C**) participants with MetS. Red line indicated participants with high TyG, and blue line indicated those with low TyG.
Abbreviations: MetS, metabolic syndrome; TyG, triglyceride-glucose.

Table 2 Association of Continuous TyG Index With Incident Stroke in All Participants and Stratified by Metabolic Status

	Stroke Incidence (n/N (%))	HR (95% CI)	P-value	HR (95% CI)[a]	P-value	P-value for Interaction
All participants	568/7770 (7.3)	1.44 (1.33, 1.55)	<0.001	1.19 (1.05, 1.33)	**0.016**	
Participants without MetS	238/4494 (5.3)	1.70 (1.41, 1.98)	<0.001	1.69 (1.40, 1.97)	**<0.001**	**0.004**
Participants with MetS	330/3276 (10.1)	1.03 (0.86, 1.19)	0.747	1.05 (0.88, 1.21)	0.599	

Notes: P values of < 0.05 are shown in bold. [a]adjusted for age, sex, body mass index, married status, smoking status, heart disease, and MetS.
Abbreviations: TyG, triglyceride-glucose; HR, hazard ratio; CI, confidence interval; aHR, adjusted hazard ratio; MetS, metabolic syndrome.

Table 3 Association of Categorized TyG Index With Incident Stroke in All Participants and Stratified by Metabolic Status

	Stroke Incidence (n/N (%))		HR (95% CI)	P-value	HR (95% CI)[a]	P-value	P-value for Interaction
	Low TyG	High TyG					
All participants	220/3969 (5.5)	348/3801 (9.2)	1.70 (1.53, 1.87)	<0.001	1.28 (1.08, 1.48)	**0.014**	
Participants without MetS	152/3283 (4.6)	86/1211 (7.1)	1.55 (1.29, 1.82)	0.001	1.55 (1.28, 1.81)	**0.001**	**0.031**
Participants with MetS	68/686 (9.9)	262/2590 (10.1)	1.02 (0.76, 1.29)	0.869	1.03 (0.76, 1.30)	0.832	

Notes: P values of < 0.05 are shown in bold. [a]Adjusted for age, sex, body mass index, married status, smoking status, heart disease, and MetS.
Abbreviations: TyG, triglyceride-glucose; HR, hazard ratio; CI, confidence interval; aHR, adjusted hazard ratio; MetS, metabolic syndrome.

for overall = 0.001, P for non-linearity = 0.002, Figure 3A), a linear increase in individuals without MetS (P for overall = 0.002, P for non-linearity = 0.091, Figure 3B), and no significant change in those with MetS (P for overall = 0.377, P for non-linearity = 0.269, Figure 3C) in the restricted cubic splines regression analyses. In the sensitivity analyses, the interaction between the continuous TyG index and MetS remained significant when using the alternative definition of MetS (P for interaction = 0.006) or replacing MetS with its criteria (P for interaction = 0.003) in the adjusted models (Table S2). Moreover, MetS also significantly influenced the association between the categorized TyG index and stroke risk when the TyG index was dichotomized by its median value (P for interaction = 0.034, Table S3). No collinearity was detected between the variables included in the models (variance inflation factor <2 in all of them).
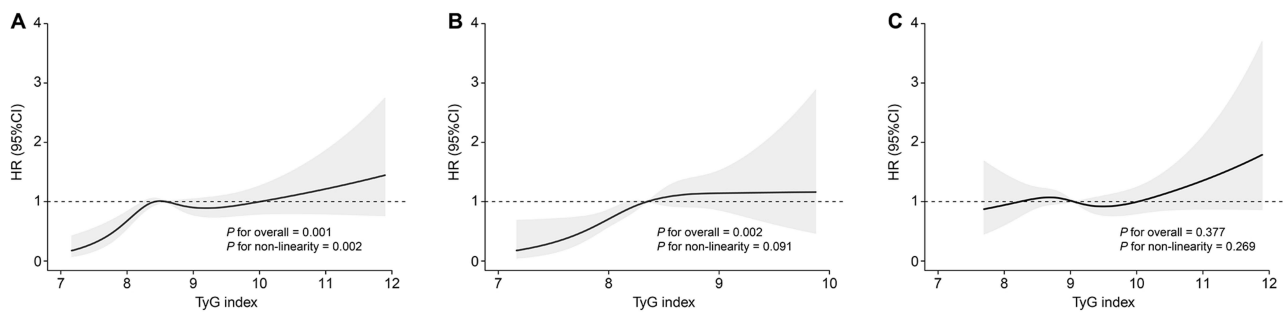

Figure 3 Restricted cubic spline curve adjusted for age, sex, body mass index, married status, smoking status, heart disease, and MetS for (**A**) all participants, (**B**) participants without MetS, and (**C**) participants with MetS.
Abbreviations: MetS, metabolic syndrome; TyG, triglyceride-glucose.

Discussion

In this prospective cohort study, we found that MetS influenced the association of the TyG index with the risk of incident stroke among middle-aged and older Chinese adults. A higher TyG index was related to an increased risk of incident stroke among adults without MetS, but not among those with MetS.

We first confirmed the previous observed findings that the TyG index was associated with the risk of incident stroke in the general population.[8,16] Several possible mechanisms behind this association have been suggested. First, the TyG index might be involved in the formation and development of atherosclerotic plaques in carotid and intracranial arteries.[17,18] Second, the TyG index has also been shown to be related to the occurrence of other common stroke risk factors, such as diabetes, hypertension, and hyperuricemia.[19–21] Third, the TyG index is considered an effective biomarker of insulin resistance, and therefore could lead to stroke through insulin resistance by promoting both atherogenesis and advanced plaque progression.[5]

Moreover, we revealed that the association between the TyG index and the risk of incident stroke was observed only in adults without MetS but not in those with MetS. Still, the exact mechanisms behind this finding have yet to be clarified. On the one hand, the TyG index, derived solely from triglyceride and fasting glucose levels, mainly reflects insulin resistance but does not incorporate other cerebrovascular risk factors associated with metabolic syndrome, such as blood pressure, HDL cholesterol, or central obesity.[5,22] Notably, the association between insulin resistance and stroke risk may be weakened when these additional cerebrovascular risk factors are taken into consideration.[12] Moreover, MetS is a highly heterogeneous condition, with patients exhibiting varying severities of its components.[23,24] This variability in clinical presentation may lead to differences in the extent of insulin resistance among MetS patients, potentially affecting the ability of the TyG index to predict stroke risk. On the other hand, glucose metabolism and lipid homeostasis can be affected to varying degrees by chronic inflammation in MetS.[9] Furthermore, the dysregulation of adipokines like adiponectin can further impact insulin sensitivity and other critical metabolic pathways.[25] These intricate and interrelated mechanisms can introduce significant complexity, which may limit the TyG index's ability to fully and accurately capture the true extent of insulin resistance in individuals with MetS. Future prospective studies are needed to clarify the underlying mechanisms.

Currently, along with the rising global stroke burden, the disparities between low-income and middle-income countries (LMICs) and high-income countries have been growing, with about 75% of deaths from stroke and more than 80% of disability now occurring in LMICs.[22] Due to their characteristics of inexpensive and easy-to-obtain, the laboratory tests (TG, FBG) used to calculate the TyG index have been widely utilized in clinical practice.[8] Thus, the TyG index has great potential value in assessing stroke risk and guiding stroke prevention, and might be especially suitable for LMICs. Meanwhile, our study further revealed that adults without MetS were more likely to benefit from the TyG index screening, which could potentially provide a basis for the allocation of scarce medical resources in LMICs. Conversely, for individuals with MetS, the TyG index might not effectively identify those at high risk for stroke. Therefore, future research should aim to develop other cost-effective indicators tailored for stroke risk stratification within the MetS population.

Strengths of the current study include the use of its prospective cohort design, large sample size, and a long follow-up for stroke events. However, our study had several limitations. First, the data reported here are observational, and causality cannot be claimed. Still, we strived to minimize the potential effect of reverse causality by excluding participants with a history of stroke. Second, the outcome measure in the CHARLS was self-reported, which might lead to a misclassification bias. Still, it has been reported that self-reported strokes were highly in agreement with medical records.[26] Third, the study only included general Chinese adults aged 45 years and older, and the findings may not be fully generalized to younger or other populations. Nevertheless, the consistency of our analysis results based on both Chinese and Caucasian criteria of MetS suggests the generalizability of our findings. Fourth, the definition of follow-up time may lead to a certain degree of margin of error, posing substantial limitations that may affect the feasibility and reliability of the results. Finally, there may be a survivor bias due to the exclusion of individuals without complete exposure and outcome data. Moreover, the inherent limitations of the public database included the omission of certain features, such as diet and physical activity, which made it impossible for us to control all potential confounders. Future prospective studies are warranted to minimize such biases and confirm the results obtained from this study.

Conclusion

Our results suggested that MetS influenced the relationship between the TyG index and the risk of incident stroke in middle-aged and older Chinese adults. Specifically, a higher TyG index is linked to an increased risk of incident stroke in adults without MetS, whereas this association is absent in those with MetS. This indicates that the TyG index may be more effective for stroke risk stratification in populations without MetS compared to those with MetS.

Data Sharing Statement

The data and study materials that support the findings of this study will be available at the CHARLS project website (http://charls.pku.edu.cn/).

Ethics Approval and Consent to Participate

All data was extracted from publicly available databases and was deidentified, therefore, this study was exempt from ethics approval based on Measures for Ethical Review of Life Science and Medical Research Involving Human Subjects (February 18, 2023, China).

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Disclosure

The authors declare that there are no conflicts of interest.

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