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Association between Cumulative Triglyceride Glucose-Body Mass Index and Diabetes Incidence in Middle-aged and Elderly Chinese Population: A Prospective Nationwide Cohort Study Based on the CHARLS Database

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Abstract

Purpose:The present study aimed to evaluate the association between cumulative TyG-BMI and the incidence of diabetes in a nationally representative sample of middle-aged and elderly Chinese adults.

Methods: This prospective cohort study utilized data from the China Health and Retirement Longitudinal Study (CHARLS), including participants aged ≥45 years. Cumulative TyG-BMI was calculated by integrating baseline and follow-up TyG-BMI values. The primary outcome was incident diabetes. Multivariable logistic regression models were used to estimate odds ratios (*OR*) and 95% confidence intervals (*CI*). In addition, restricted cubic splines (RCS), and subgroup analyses were used to explore the association between cumulative TyG-BMI and diabetes incidence.

Results: Among the 4,945 participants included in the final analysis, 547 (11.06%) developed diabetes. The average cumulative TyG-BMI was 810.27 ± 139.92. After adjusting for multiple covariates, participants in the second, third, and fourth quartiles of cumulative TyG-BMI had progressively higher odds of developing diabetes compared to those in the lowest quartile, with *OR* (95% *CI*) of 1.355 (0.973–1.886), 2.040 (1.453–2.864), and 3.391 (2.311–4.975), respectively ($P_{trend} < 0.001$). Furthermore, each standard deviation increase in cumulative TyG-BMI was associated with a 64.1% increase in diabetes risk (*OR*: 1.641; 95% *CI*: 1.439–1.873). RCS analysis revealed a positive linear association between cumulative TyG-BMI and diabetes incidence ($P_{overall} < 0.001$; $P_{nonlinearity} = 0.308$). Subgroup analysis showed that the association was significantly

modified by sleep duration ($P_{interaction}$ = 0.029).

Conclusion: Cumulative exposure to elevated TyG-BMI levels is independently associated with an increased risk of diabetes among middle-aged and elderly individuals in China.

Keywords: TyG-BMI; Diabetes Mellitus; CHARLS; Prospective Cohort Study;

Introduction

Diabetes is a chronic metabolic disorder and one of the most prevalent non-communicable diseases globally, posing a substantial threat to both quality of life and life expectancy. In China, the prevalence and incidence of diabetes have continued to rise in recent years, reflecting a growing public health challenge. According to national estimates, the number of individuals living with diabetes in China reached approximately 140 million in 2021, the highest reported worldwide, with a predominance among the middle-aged and elderly population [1]. Given this trend, early identification of high-risk individuals and targeted preventive strategies are essential to reduce the disease burden.

Although diabetes is a multifactorial disease, insulin resistance (IR) is widely recognized as a key precursor and a central pathogenic mechanism in its development [2]. However, conventional methods for assessing IR, such as the hyperinsulinemic-euglycemic clamp or homeostasis model assessment of IR (HOMA-IR), remain costly and technically demanding, thereby limiting their application in large-scale or routine clinical settings [3], which has led to increased interest in identifying simple and cost-effective surrogate markers for IR and diabetes risk prediction.

The triglyceride-glucose index (TyG), calculated from fasting triglyceride and glucose levels, has been validated as a reliable surrogate marker for IR and is readily accessible in clinical practice [4]. More recently, the triglyceride-glucose body mass index (TyG-BMI), which integrates BMI into the TyG index, has been reported to outperform other TyG-related indicators in predicting IR [5,6]. Several studies have further demonstrated a significant association between TyG-BMI and the risk of developing diabetes [7-9]. Despite these findings, existing evidence has largely been limited to single time-point measurements, and the influence of cumulative exposure to TyG-BMI over time on diabetes risk remains inadequately understood, particularly in the Chinese population aged ≥45 years.

Herein, we designed this study to investigate the association between cumulative TyG-BMI and the incidence of diabetes in a nationally representative cohort of middle-aged and elderly Chinese adults, using longitudinal data from the China Health and Retirement Longitudinal Study (CHARLS).

Methods

Data source and study population

This study utilized data from the China Health and Retirement Longitudinal Study (CHARLS), a nationally representative longitudinal survey initiated by the National School of Development at Peking University. The CHARLS project tracks the health and socioeconomic status of middle-aged and elderly individuals in China, with the baseline survey conducted in 2011 and subsequent follow-up waves carried out every two to three years. As of 2020, five waves of data collection had been completed [10]. The CHARLS dataset is freely accessible to researchers upon application and approval.

For the present analysis, participants were selected from the first wave (2011–2012), which initially included 14,728 individuals aged ≥45 years who did not have a diagnosis of diabetes at baseline. These individuals were followed up through the third wave (2015–2016). Participants were excluded if they were lost to follow-up (n = 2,490), had incomplete data on relevant variables (n = 7,219), or presented with outlier values for cumulative TyG-BMI (defined as values exceeding ±1.5 interquartile ranges, n = 74). After applying these exclusion criteria, a total of 4,945 participants were included in the final analysis (Figure 1). The CHARLS study protocol was approved by the Biomedical Ethics Review Committee of Peking University (Approval No: IRB00001052-11015). All participants provided written informed consent.

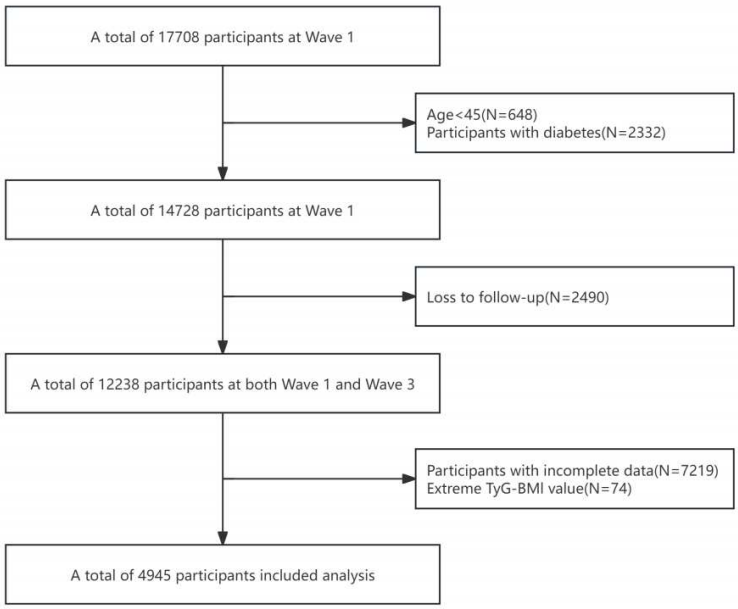


Figure 1. Flowchart of the study population

Relevant Variables and Indicators

Cumulative TyG-BMI Index

The TyG index was calculated using the formula: TyG = ln[TG (mg/dL) × FBG (mg/dL) / 2], where TG is fasting triglyceride and FBG is fasting blood glucose. The TyG-BMI index was then calculated as: TyG-BMI = TyG × BMI (kg/m²) [11].

To quantify long-term exposure, the cumulative TyG-BMI index was derived as follows: Cumulative TyG-BMI index = $(\text{TyG-BMI}_{\text{wave1}} + \text{TyG-BMI}_{\text{wave3}}) / 2 \times \text{time}_{(\text{wave3-wave1})}$ [12].

Diabetes Diagnosis

Diabetes was defined based on the diagnostic criteria outlined in the 2024 edition of the Chinese Guidelines for the Prevention and Treatment of Diabetes [13]. Participants were classified as having diabetes if they met any of the following conditions: FBG ≥ 7.0 mmol/L (126 mg/dL), glycated hemoglobin (HbA1c) ≥ 6.5%, self-reported diagnosis of diabetes, or current use of antidiabetic medications, as reported in the CHARLS questionnaire. Prediabetes was defined as an FBG level between 6.1 and 7.0 mmol/L. Individuals diagnosed with diabetes at baseline were excluded from the analysis.

Covariates

Various covariates were included in the analysis to account for potential confounding factors and were categorized as follows:

(1) Demographic characteristics: age, sex, educational level, and marital status.

(2) Physical condition and lifestyle factors: Waist measurement (M_{waist}), BMI, current smoking status (smoking), current alcohol consumption (drinking), and average sleep duration (sleep).

(3) Medical history: reported or self-reported history of hypertension (hypertension), liver disease (liver), kidney disease (kidney), gastrointestinal disorders (digest), and cancer.

(4) Biochemical parameters: white blood cell count (WBC), mean corpuscular volume (MCV), platelet count (PLT), blood urea nitrogen (BUN), FBG, serum creatinine (CREA), total cholesterol (CHO), triglycerides (TG), high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c), C-reactive protein (CRP), HbA1c, and uric acid (UA).

Anthropometric measurements and laboratory tests were performed by trained healthcare personnel following standardized procedures. Body weight was measured without shoes, and height was recorded with the

participant standing upright. Fasting venous blood samples were collected and transported via cold chain logistics to the Chinese Center for Disease Control and Prevention for centralized biochemical analysis. Information on sociodemographic characteristics, medical history, and treatment history was obtained through structured self-report questionnaires administered during the survey. Additional details regarding variable definitions and measurement protocols are provided in the Supplementary Materials (Table S1).

Statistical Analysis

All statistical analyses were performed using R software, version 4.4.3. Participants were categorized into quartiles (Q1–Q4) according to the distribution of cumulative TyG-BMI values. Continuous variables with a normal distribution were reported as mean ± standard deviation (SD) and compared across quartiles using analysis of variance (ANOVA). Categorical variables were presented as counts and percentages, with differences evaluated using the chi-square (χ^2) test.

To examine the association between cumulative TyG-BMI and incident diabetes, logistic regression models were constructed, and results were expressed as odds ratios (*OR*) with corresponding 95% confidence intervals (*CI*s). Three models with progressive adjustment for potential confounders were applied: Model 1 adjusted for age and sex; Model 2 further adjusted for education level, marital status, smoking status, alcohol consumption, gastrointestinal disorders, hypertension, M_{waist}, and sleep duration; and Model 3 additionally included biochemical markers such as WBC, MCV, PLT, BUN, CREA, CHO, HDL-c, LDL-c, CRP, HbA1c, and UA. Multicollinearity among covariates was assessed using variance inflation factors (VIF), with all variables demonstrating VIF values <10, indicating no significant multicollinearity (Supplementary Table S2).

To further evaluate the dose-response relationship and potential nonlinearity between cumulative TyG-BMI and diabetes incidence, a fully adjusted restricted cubic spline (RCS) model with four knots was constructed. Subgroup analyses were also performed to investigate potential effect modification by age, sex, smoking status, alcohol consumption, gastrointestinal disorders, hypertension, M_{waist}, and sleep duration. Statistical significance was defined as a two-sided *P*-value < 0.05.

Sensitivity Analysis

The robustness of the main findings was assessed through several sensitivity analyses. First, baseline characteristics of included and excluded participants were compared to evaluate potential selection bias. Second, the cumulative TyG-BMI index was reclassified into four categories using K-means cluster analysis,

and logistic regression models were re-estimated to assess the consistency of the association under an alternative grouping strategy. Third, a subgroup analysis restricted to participants aged >65 years was conducted to explore potential age-related heterogeneity in the observed associations.

Results

Baseline Characteristics of the Study Population

A total of 4,945 participants were included in the final analysis, with a mean age of 58.89 ± 8.72 years. Among them, 2,635 individuals (53.29%) were female, and the average cumulative TyG-BMI index was 810.27 ± 139.92. During the four-year follow-up period from 2011 to 2015, a total of 547 new cases of diabetes were identified, corresponding to an incidence rate of 11.06% (547/4,945).

To explore baseline differences, participants were stratified into quartiles based on their cumulative TyG-BMI index. Notably, individuals in the higher TyG-BMI quartiles were more likely to be younger and female. They also showed a significantly higher prevalence of diabetes (χ^2 = 131.772) and were more likely to report higher education levels (χ^2 = 40.049) and a higher likelihood of being married (χ^2 = 31.728). Moreover, participants in these groups tended to have longer sleep duration (F = 4.838) and exhibited elevated anthropometric and metabolic indicators, including M_{waist} (F = 774.154), PLT (F = 3.929), WBC (F = 6.214), CHO (F = 44.012), LDL-c (F = 28.590), HbA1c (F = 22.631), UA (F = 17.867), TyG index (F = 533.609), and TyG-BMI (F = 5970.361).

In contrast, participants with higher cumulative TyG-BMI values were less likely to be current smokers (χ^2 = 197.327) or alcohol consumers (χ^2 = 47.229), and they had lower prevalence of gastrointestinal disorders (χ^2 = 12.533) and hypertension (χ^2 = 209.709). Biochemical markers such as MCV (F = 3.523), BUN (F = 10.033), and HDL-c (F = 299.915) were also significantly lower in the higher TyG-BMI quartiles. All observed differences across quartile groups were statistically significant ($P < 0.05$), as summarized in Table 1.

Table 1. Baseline characteristics of the participants

Variable	Q1(n=1237)	Q2(n=1236)	Q3(n=1236)	Q4(n=1236)	F/χ^2	P
Age (years)	61.45 (9.18)	59.14 (8.55)	58.14 (8.42)	56.81 (8.04)	64.635	<0.001
Gender (male)	732 (59.17)	619 (50.08)	513 (41.50)	446 (36.08)	152.379	<0.001
Education					40.049	<0.001
Illiterate	650 (52.54)	596 (48.22)	580 (46.93)	539 (43.61)		
Junior school	297 (24.00)	290 (23.46)	276 (22.33)	285 (23.06)		
High schools and vocational school	210 (16.98)	253 (20.47)	248 (20.06)	280 (22.65)		
Higher education	80 (6.47)	97 (7.85)	132 (10.68)	132 (10.67)		
Marriage (yes)	1067 (86.25)	1086 (87.86)	1121 (90.69)	1145 (92.64)	31.728	<0.001

Cancer (yes)	7 (0.56)	8 (0.65)	9 (0.73)	11 (0.89)	1.010	0.799
Liver (yes)	49 (43.96)	35 (2.83)	38 (3.07)	38 (3.07)	2.929	0.403
Kidney (yes)	74 (5.98)	72 (5.83)	67 (5.42)	76 (6.15)	0.655	0.884
Digest (yes)	319 (25.81)	293 (23.71)	275 (22.25)	247 (19.98)	12.533	0.006
Hypertension (yes)	408 (32.98)	485 (39.24)	570 (46.12)	748 (60.52)	209.709	<0.001
Drinking (yes)	485 (39.21)	432 (34.95)	397 (32.12)	328 (26.54)	47.229	<0.001
Smoking (yes)	546 (44.17)	428 (34.63)	311 (25.16)	247 (19.98)	197.327	<0.001
M_{waist} (cm)	74.89 (8.47)	80.45 (9.90)	86.24 (9.37)	93.31 (11.87)	774.154	<0.001
BMI (kg/m2)	19.47 (1.66)	22.05 (1.37)	24.14 (1.59)	27.61 (2.79)	3914.490	<0.001
Sleep (h)	6.24 (2.00)	6.25 (1.87)	6.45 (1.86)	6.46 (1.77)	4.838	0.002
WBC (10^9/L)	6.11 (1.96)	6.08 (1.78)	6.23 (1.85)	6.37 (1.86)	6.214	<0.001
MCV (fl)	91.26 (9.21)	90.89 (8.64)	90.67 (8.22)	90.18 (7.49)	3.523	0.014
PLT (10^9/L)	209.06 (77.07)	209.56 (72.19)	215.40 (73.00)	218.01 (89.06)	3.929	0.008
BUN (mg/dl)	16.16 (4.67)	15.79 (4.36)	15.43 (4.36)	15.27 (4.14)	10.033	<0.001
FBG (mg/dl)	98.17 (12.96)	99.96 (13.55)	102.06 (15.50)	105.36 (16.51)	54.600	<0.001
CREA (mg/dl)	0.77 (0.18)	0.77 (0.19)	0.76 (0.17)	0.77 (0.18)	0.684	0.561
CHO (mg/dl)	184.42 (35.87)	188.99 (34.98)	194.37 (36.94)	200.34 (37.85)	44.012	<0.001
TG (mg/dl)	84.04 (40.44)	103.90 (50.60)	129.42 (71.97)	175.06 (102.42)	384.560	<0.001
HDL-c (mg/dl)	59.94 (16.25)	53.97 (13.94)	49.85 (12.80)	43.84 (11.71)	299.915	<0.001
LDL-c (mg/dl)	109.27 (31.04)	116.10 (31.29)	119.27 (34.24)	120.61 (36.33)	28.590	<0.001
CRP (mg/dl)	2.51 (8.45)	2.28 (7.46)	2.30 (5.67)	2.43 (4.62)	0.314	0.815
HbA1c (%)	5.07 (0.39)	5.08 (0.38)	5.09 (0.37)	5.18 (0.39)	22.631	<0.001
UA (mg/dl)	4.28 (1.17)	4.29 (1.19)	4.37 (1.20)	4.59 (1.25)	17.867	<0.001
Diabetes(yes)	75 (6.1)	95 (7.7)	138 (11.2)	239 (19.3)	131.772	<0.001
TyG	8.23 (0.44)	8.45 (0.46)	8.67 (0.51)	8.99 (0.56)	533.609	<0.001
TyG-BMI	160.08 (14.50)	186.05 (11.65)	208.95 (13.52)	247.64 (24.76)	5970.361	<0.001
Cumulative TyG-BMI	642.30 (47.56)	752.62 (26.66)	845.92 (29.19)	1000.36 (74.33)	12156.636	<0.001

M_{waist}: waist measurement; BMI: body mass index; WBC: white blood cell count; MCV: mean corpuscular volume; PLT: platelet count; BUN: blood urea nitrogen; GLU: Fasting blood glucose; CREA: serum creatinine; CHO: total cholesterol; TG: triglycerides; HDL-c: high-density lipoprotein cholesterol; LDL-c: low-density lipoprotein cholesterol; CRP: C-reactive protein; HbA1c: glycated hemoglobin; UA: uric acid; TyG: triglyceride glucose index; TyG-BMI: baseline triglyceride glucose-body mass index; Cumulative TyG-BMI: cumulative triglyceride glucose-body mass index

Data presented as mean(SD) for continuous variable, or numbers (percentage) for categorical variables.

Association Between Cumulative TyG-BMI Index and Diabetes Incidence

When stratified by the cumulative TyG-BMI index quartiles, the fully adjusted Model 3 demonstrated a significant positive association with diabetes incidence (Table 2). Compared with participants in Q1, those in Q2, Q3, and Q4 had progressively higher risks of developing diabetes, with *OR* of 1.355 (95% *CI*: 0.973–1.886), 2.040 (95% *CI*: 1.453–2.864), and 3.391 (95% *CI*: 2.311–4.975), respectively (P_{trend} <0.001). These findings correspond to 35.5%, 104.0%, and 239.1% increased risks of diabetes in Q2, Q3, and Q4 relative to

Q1.

When cumulative TyG-BMI was analyzed as a continuous variable, each SD increase was associated with a 64.1% higher risk of incident diabetes (*OR* = 1.641, 95% *CI*: 1.439–1.873) in Model 3. To further compare predictive performance, three fully adjusted logistic regression models incorporating TyG, TyG-BMI, and cumulative TyG-BMI were developed. Receiver operating characteristic (ROC) curve analysis revealed that cumulative TyG-BMI demonstrated the highest discriminative ability for predicting diabetes (AUC = 0.719, 95% *CI*: 0.695–0.742), outperforming both TyG-BMI (AUC = 0.705, 95% *CI*: 0.681–0.728) and TyG index alone (AUC = 0.697, 95% *CI*: 0.672–0.722) (Supplementary Figure S1).

To explore the dose-response relationship, an RCS model was fitted using fully adjusted covariates. The RCS analysis indicated a significant linear association between cumulative TyG-BMI and diabetes incidence ($P_{overall} < 0.001$; $P_{nonlinearity} = 0.3083$), suggesting a continuous increase in diabetes risk with rising TyG-BMI values (Figure 2).

Table 2. Association between the cumulative TyG-BMI index and diabetes incidence

Cumulative TyG-BMI	Crude		Model 1		Model 2		Model 3	
	OR（95%*CI*）	*P*	*OR*（95%*CI*）	*P*	*OR*（95%*CI*）	*P*	*OR*（95%*CI*）	*P*
Q2	1.290（0.943~1.765）	0.1111	1.397(1.018~1.917)	0.038	1.374(0.994~1.897)	0.054	1.355(0.973~1.886)	0.072
Q3	1.947(1.453~2.610)	<0.001	2.179(1.616~2.936)	<0.001	2.121(1.535~2.931)	<0.001	2.040(1.453~2.864)	<0.001
Q4	3.714(2.827~4.879)	<0.001	4.371(3.291~5.804)	<0.001	4.068(2.879~5.748)	<0.001	3.391(2.311~4.975)	<0.001
P_{trend}	<0.001		<0.001		<0.001		<0.001	
Per 1 SD increase	1.687(1.545~1.841)	<0.001	1.779(1.625~1.948)	<0.001	1.781(1.588~1.997)	<0.001	1.641(1.439~1.873)	<0.001

Crude：Interquartile grouping of the cumulative TyG-BMI index or Scale cumulative TyG-BMI index.

Model 1：Adjusted for gender and age.

Model 2：Adjusted for the variables in model 1 plus education, marriage, smoking, drinking, digest, Mwaist, sleep, hypertension.

Model 3:Adjusted for the variables in model 2 plus WBC, MCV, PLT, BUN, CHO, HDL-c, LDL-c, HbA1c, UA.

Cumulative TyG-BMI: Cumulative triglyceride glucose-body mass index; *OR*: Odds ratio; *CI*: Confidence interval.

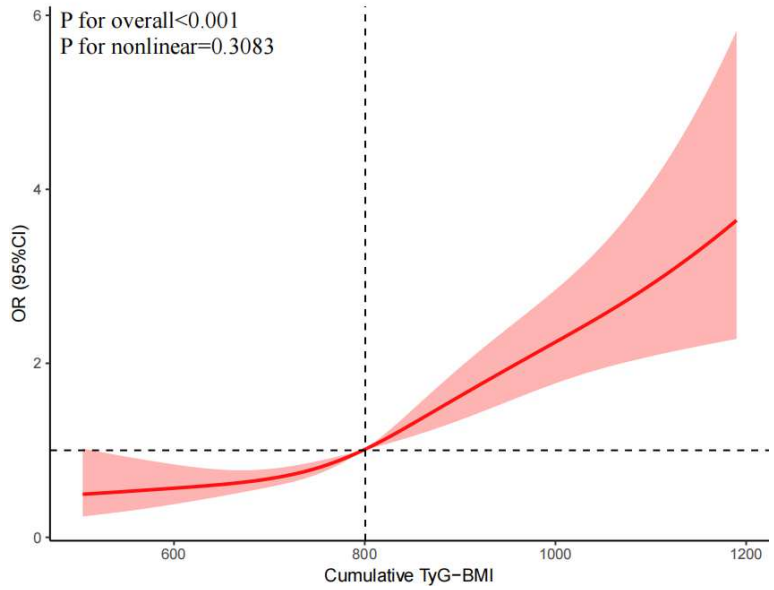


Figure 2. RCS analysis of the association of the cumulative Ty G-BMI index with diabetes incidence

The model was adjusted adjusted for gender , age, education, marriage, smoking, drinking, digest, Mwaist, sleep, hypertension, WBC, MCV, PLT, BUN, CHO, HDL-c, LDL-c, HbA1c, UA.

Cumulative TyG-BMI: Cumulative triglyceride glucose-body mass index; *OR*: Odds ratio; *CI*: Confidence interval.

Subgroup Analysis of the Association Between Cumulative TyG-BMI Index and Diabetes Incidence

Subgroup analyses were conducted to examine the consistency of the association across various stratified factors, including age, sex, smoking status, alcohol consumption, presence of gastrointestinal disorders, M_{waist}, sleep duration, and hypertension status. In all subgroups analyzed, the association between cumulative TyG-BMI and diabetes incidence remained positive and statistically significant (all $OR > 1$, $P < 0.001$).

Among all stratified variables, a statistically significant interaction was observed only for sleep duration ($P_{interaction} = 0.029$), suggesting that the strength of the association between cumulative TyG-BMI and diabetes incidence differed by sleep duration. In contrast, no significant interactions were detected for other variables, including age, sex, smoking, alcohol consumption, gastrointestinal disorders, M_{waist}, or hypertension status (all $P_{interaction} > 0.05$) (Figure 3).

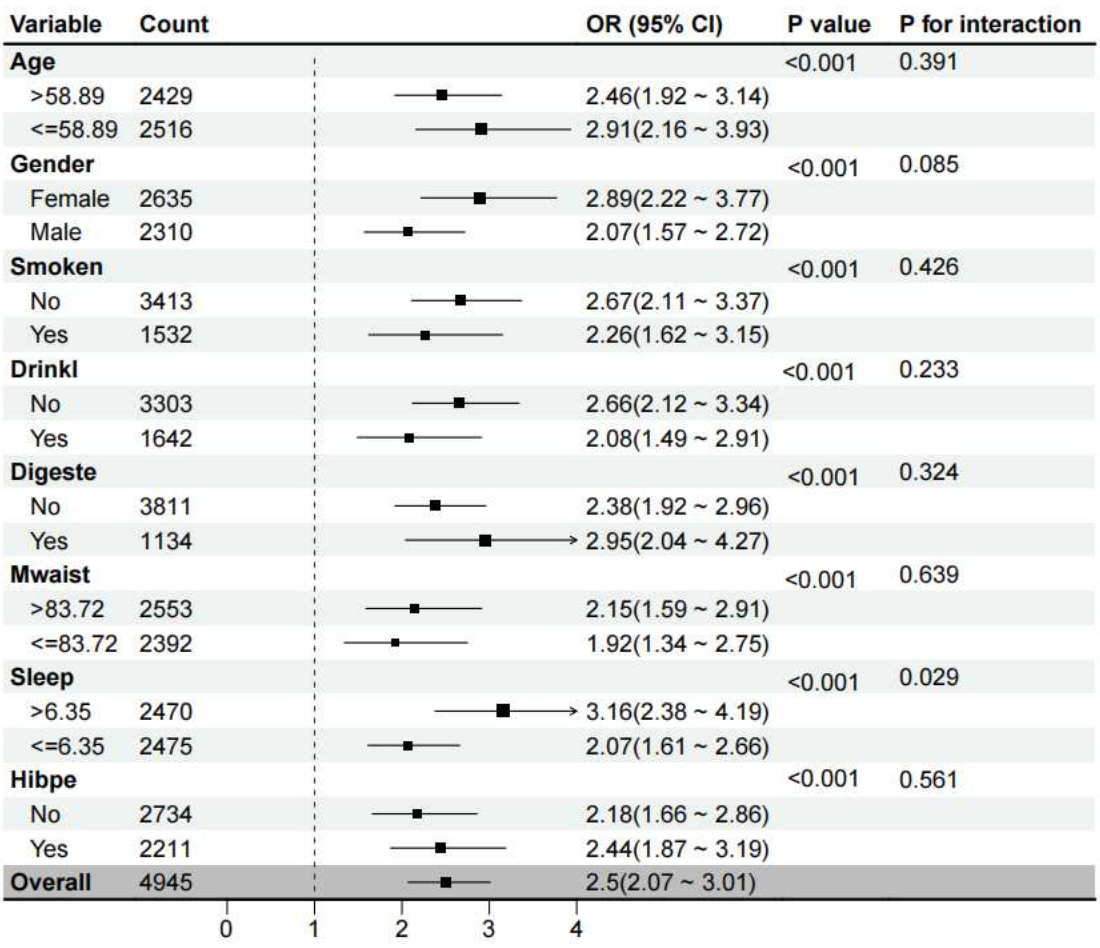


Figure 3. Subgroup analysis of the relationship between the cumulative TyG-BMI index and diabetes incidence

Except the stratification variable itself, all presented covariates including age, gender, smoking, drinking, digest, Mwaist, sleep, and hypertension were adjusted.

OR: Odds ratio; *CI*: Confidence interval.

Sensitivity Analysis

Multiple sensitivity analyses were performed to evaluate the robustness of the primary findings. First, baseline characteristics were compared between included and excluded participants. The analysis showed no clinically meaningful differences between the groups, as all standardized mean differences (SMD) were less than 0.1, indicating minimal selection bias (Supplementary Table S3). Second, to assess whether the association between cumulative TyG-BMI and diabetes incidence was dependent on the method of exposure classification, an unsupervised machine learning approach, namely K-means clustering, was applied to reclassify participants into four clusters (C1 to C4) based on cumulative TyG-BMI. In the fully adjusted logistic regression model, the risk of diabetes increased across clusters, with the following *OR* (95% *CI*): C2, 1.497 (1.090–2.055); C3, 2.522 (1.775–3.358); and C4, 3.577 (2.341–5.465), compared to C1 ($P_{trend} < 0.001$)

(Supplementary Table S4). Third, a subgroup analysis was conducted among participants aged >65 years (N = 1,271) to explore age-specific effects. In this older population, the fully adjusted model showed a similar trend: compared to Q1, the *OR* (95% *CI*) were 0.920 (0.507–1.668) for Q2, 1.348 (0.740–2.457) for Q3, and 2.625 (1.320–5.220) for Q4 (P_{trend} <0.001). When cumulative TyG-BMI was treated as a continuous variable, each 1-SD increase was associated with a 55.4% higher risk of diabetes (*OR* = 1.554, 95% *CI*: 1.211–1.996) (Supplementary Table S5).

Collectively, these sensitivity analyses confirmed the consistency and robustness of the primary findings, supporting a monotonic increase in diabetes risk with greater cumulative exposure to TyG-BMI.

Discussion

According to current projections, the global number of individuals with diabetes is expected to reach 700 million by 2045, accounting for approximately 10.9% of the world's population. As a result, diabetes has emerged as a widespread metabolic disorder with epidemic characteristics, posing a substantial burden on both public health systems and population-level health outcomes worldwide [14]. In China, the prevalence and incidence of diabetes continue to rise steadily, significantly compromising quality of life and survival among affected individuals. Therefore, early identification of high-risk populations and timely implementation of preventive interventions remain essential [13]. Based on longitudinal data from the CHARLS database collected between 2011 and 2015, the present study demonstrates that the cumulative TyG-BMI index is significantly and linearly associated with an increased risk of incident diabetes among middle-aged and older adults.

Although the precise biological mechanisms linking cumulative TyG-BMI to the development of diabetes are not yet fully elucidated, existing evidence suggests a strong association with IR, which represents a state whereby the body's regulation of glucose metabolism through insulin is impaired [15] and is considered a central mechanism in diabetes pathogenesis. Elevated glucose levels may contribute to generating reactive oxygen species, leading to pancreatic β-cell toxicity and dysfunction [16]. Concurrently, excess triglyceride deposition in pancreatic tissues can directly impair β-cell activity and promote the development of IR [17]. Despite the recognized importance of IR, its clinical assessment remains challenging, as the hyperinsulinemic-euglycemic clamp, the gold standard for IR measurement, is both costly and technically demanding, limiting its use in routine settings. In contrast, the TyG index, calculated as the product of FBG and triglyceride levels, has been widely adopted in recent years as a simple and reliable surrogate marker for

IR [18]. In a study by Chen et al. [19], a higher TyG index was associated with an increased risk of new-onset diabetes among middle-aged and elderly individuals; however, BMI was not included in their analysis. A separate cohort study by Min et al. [20] further demonstrated that elevated TyG index levels were a significant risk factor for diabetes onset in the Chinese middle-aged and elderly population, and that this risk was amplified in individuals with higher BMI.

BMI, a commonly used index that reflects the relationship between weight and height, is closely associated with obesity; according to Chinese criteria, a BMI ≥28 is defined as obese [21]. As a standard indicator of obesity in both clinical and research settings, BMI has been repeatedly linked to IR, with numerous epidemiological studies identifying obesity as a major risk factor for both the onset and progression of IR [22]. Building on this understanding, recent research has examined TyG-BMI, a composite index derived from the TyG index and BMI, which has shown a strong association with diabetes incidence across diverse populations [5, 6, 9, 23]. For example, a retrospective cohort study by Wang et al. [7] demonstrated that TyG-BMI effectively predicted the onset of diabetes and performed particularly well in younger, middle-aged, and non-obese individuals. However, evidence regarding its predictive value in middle-aged and elderly populations remains limited. Qiao et al. [24] further reported a nonlinear relationship between TyG-BMI and the risk of diabetes, noting a monotonic increase in diabetes incidence at higher levels of exposure. Despite these findings, the role of cumulative TyG-BMI exposure in predicting diabetes risk over time remains insufficiently characterized. In the present study, by integrating four-year longitudinal trajectories of TyG-BMI and adjusting for a wide range of confounding factors, we found that cumulative TyG-BMI was robustly associated with the risk of incident diabetes among middle-aged and older Chinese adults. Moreover, when compared to single-time-point measurements of TyG or TyG-BMI, the cumulative index demonstrated superior predictive accuracy, as reflected by higher area under the curve (AUC) values in ROC analysis.

In this study, higher levels of cumulative TyG-BMI were associated with progressively younger age, a greater proportion of female participants, and an increased incidence of diabetes, suggesting that middle-aged and older women may represent a high-risk group for diabetes development. Subgroup analyses further supported this observation by demonstrating a significantly stronger positive association between cumulative TyG-BMI and diabetes incidence in women compared to men, consistent with prior findings[25]. This sex-specific disparity may be attributed to differing pathophysiological mechanisms. In men, diabetes is often diagnosed at lower BMI thresholds, whereas women tend to exhibit greater susceptibility to obesity, likely due to sex-specific adipose tissue distribution and declining estrogen levels during the menopausal transition, both

of which are known to increase diabetes risk. Additionally, impaired glucose tolerance has been reported to occur more frequently in women [26].

In the highest quartile (Q4) of cumulative TyG-BMI, the number of new diabetes cases reached 239, corresponding to an incidence rate of nearly 20%, which was slightly higher than reported in previous studies [18]. In contrast, among individuals in the Q2 group, only Model 2 in the logistic regression analysis showed a statistically significant association, likely reflecting the influence of adjusted covariates. More notably, in the Q3 and Q4 groups, the cumulative TyG-BMI index remained significantly associated with diabetes risk across all models, and the trend tests consistently revealed a significant dose-response relationship, with increasing odds ratios observed across TyG-BMI quartiles. These results suggest that higher cumulative TyG-BMI is an independent risk factor for diabetes among middle-aged and older adults, with risk rising proportionally to the index level. Furthermore, RCS analysis curve fitting confirmed a significant linear association between cumulative TyG-BMI and the risk of new-onset diabetes, further supporting a dose-dependent relationship. These findings imply that improving metabolic health and lowering cumulative TyG-BMI in middle-aged and elderly individuals may be beneficial for diabetes prevention and management.

Subgroup analyses also demonstrated that the observed association between cumulative TyG-BMI and diabetes risk was not significantly modified by age, sex, smoking status, alcohol consumption, gastrointestinal conditions, hypertension, or M_{waist}. However, a significant interaction was observed for sleep duration, with a stronger association between cumulative TyG-BMI and diabetes risk seen in individuals reporting longer sleep duration. This finding suggests that lifestyle behaviors, including sleep patterns, may influence diabetes risk in this population. Nevertheless, sleep quality and sleep onset timing were not evaluated in this study. Prior evidence has shown that sleep disturbances and diabetes frequently co-occur [27], with a 16-year cohort study reporting that, among obese individuals, sleep durations exceeding seven hours were associated with higher diabetes risk, possibly due to underlying poor sleep quality and fragmentation leading to prolonged sleep [28].

Using nationally representative longitudinal data from the CHARLS database, this prospective cohort study of Chinese adults aged 45 years and older provides strong evidence on the relationship between cumulative TyG-BMI and the risk of developing diabetes. Building on previous studies, our findings highlight that long-term exposure to higher TyG-BMI levels is linked to a higher chance of developing diabetes in middle-aged and older adults, which suggests that a persistently high TyG-BMI reflects ongoing problems in metabolic health, which may contribute to the development of diabetes. The method used to calculate the cumulative TyG-BMI index has been applied in other studies to assess long-term exposure to risk

factors[12,29-31]. In our analysis, the cumulative TyG-BMI index was evaluated both as a categorical variable and a continuous variable, allowing us to examine how different levels of exposure relate to diabetes risk. This approach also reflects differences that may appear in real clinical settings. To confirm the reliability of our findings, we conducted sensitivity analyses, all of which supported the main results. However, this study has some limitations. First, we only used data from Wave 1 and Wave 3, and the follow-up period was relatively short. In addition, because of differences in age and ethnicity, further research is needed to confirm whether these findings apply to other populations. Second, due to limitations in the CHARLS database, some factors that may affect diabetes risk, such as family history of diabetes or use of statins, were unavailable. Third, the lack of 2-hour oral glucose tolerance test data may have led to an underestimation of diabetes cases. Finally, future studies should explore the relationship between cumulative TyG-BMI and diabetes in younger populations, in people of different backgrounds, and over longer follow-up periods.

In conclusion, cumulative TyG-BMI was found to be associated with new-onset diabetes in middle-aged and older adults, indicating that the regular monitoring of TyG-BMI over time could help identify individuals at higher risk for diabetes, allowing earlier prevention and management.

Author contribution

Renhai Tian was responsible for designing the study framework. Renhai Tian, Lingfen Deng, and Jinyu Xiang extracted and organized the data. Renhai Tian and Chunyun Liu conducted the statistical analyses and drafted the manuscript. Zhijian Dong, Danqing Xu, and Lixian Chang contributed to critical revisions of the manuscript. Li Liu provided guidance throughout the writing process and finalized the manuscript. All authors reviewed and approved the final submitted version.

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Data and Materials Availability

The dataset used in this study is publicly available through the China Health and Retirement Longitudinal Study (CHARLS) at http://charls.pku.edu.cn.

Conflict of Interest Statement

The authors declare that they have no conflicts of interest.

Ethical Approval

All procedures followed the ethical standards outlined in the Declaration of Helsinki. The CHARLS study protocol was reviewed and approved by the Ethics Committee of Peking University (Approval No: IRB00001052-11015). All participants provided written informed consent.

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