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Association of triglyceride glucose index combined with obesity indicators with cognitive impairment

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Abstract

Background The association of a combination of the TyG index and obesity markers, specifically waist circumference (WC), with cognitive function is unknown. This research investigated the relationship between TyG-WC measurements and cognitive impairment in a low-income population in China; moreover, this study evaluated the role of diabetes mellitus and body mass index (BMI) in modulating this relationship.

Methods 1125 eligible individuals aged ≥ 60 years participated in this study. The TyG index and obesity indicators (BMI, WC, and waist-to-height ratio) were calculated for individual participants and categorized into quartiles. Multivariate logistic regression analysis was used to evaluate the correlation between TyG-WC values and cognitive impairment; the possibility of a nonlinear relationship was explored using constrained cubic spline analysis. The participants were divided into different groups according to their diabetes status and BMI category for subgroup analyses. Linear regression was used to investigate the correlation between TyG-WC values and MMSE scores.

Results The prevalence of cognitive impairment in the study participants was 47.3%, with a significant negative association between TyG-WC values and cognitive impairment, (odds ratio [OR] = 0.999; 95% confidence interval [CI], 0.997–1.00, $P = 0.009$). A U-shaped correlation was observed between the TyG-WC values and cognitive impairment ($P = 0.008$). Subgroup analyses showed that the inverse association between TyG-WC values and cognitive impairment was stronger in non-diabetic individuals (OR = 0.998; 95% CI, 0.997–0.999; $P = 0.002$) and in those with a lower BMI (< 24 kg/m^2; OR = 0.996; 95% CI, 0.994–0.998; $P = 0.001$). A positive correlation was found between TyG-WC values and MMSE scores, particularly in men and non-diabetic individuals (β = 0.003; 95% CI, 0.0002–0.005; $P = 0.031$).

Conclusion This study demonstrates a nonlinear U-shaped relationship between TyG-WC values and cognitive function. The stronger inverse association between TyG-WC values and cognitive decline in the non-diabetic and

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low-BMI subgroups suggests that these populations may benefit the most from targeted interventions. These findings are important for clinical practice and formulating disease-prevention policies, emphasizing the need for metabolic health management to prevent cognitive decline, particularly in low-income populations.

Keywords Cognitive impairment, TyG-WC, Metabolic health, BMI, Diabetes mellitus

Background

Cognitive impairment and dementia are becoming increasingly significant global health challenges, particularly in aging populations—it is estimated that by 2050, 2.1 billion people worldwide will be over the age of 60 years [1]. These conditions impose a substantial burden on both individuals and healthcare systems, with an estimated 56.9 million people already affected by Alzheimer's disease and other types of dementia [2]. By 2050, this number is expected to double, making the early identification and prevention of risk factors associated with cognitive decline a public health priority [3]. In China, where the prevalence of mild cognitive impairment and dementia are approximately 15.5% and 6.0%, respectively, this issue presents a particularly large socioeconomic burden [4].

Recent research has shown links between metabolic dysfunction and cognitive decline. The triglyceride-glucose (TyG) index is widely used to evaluate insulin resistance and plays a role in conditions such as cardiovascular disease and diabetes mellitus [5–9]. Insulin resistance reportedly contributes to cognitive impairment through mechanisms involving vascular damage and direct neurodegenerative effects [7–9]. Furthermore, obesity is prevalent worldwide and has been linked to cognitive decline in several studies [10–12]. The TyG index, combined with obesity measures such as the body mass index (BMI), waist circumference (WC), and waist-to-height ratio (WHtR), may provide better evidence of cognitive impairment in health screening compared to any of these single indicators [6, 13–17].

However, despite growing interest, the relationship between the TyG index and cognitive function remains underexplored, with studies reporting conflicting findings. Some findings have suggested that higher TyG values relate to worse cognitive performance, whereas others have found protective effects, particularly when combined with certain obesity metrics [7–9, 15–17]. Moreover, the extent to which different obesity indicators modify this relationship remains unclear, particularly in low-income and rural populations.

In this study, a combination of the TyG index with obesity measures, particularly the TyG-WC index, was hypothesized to provide a more accurate prediction of cognitive impairment risk than either factor alone. Previous studies have explored the independent effects of the TyG index and obesity indicators on cognitive function, with some showing a linear relationship between TyG and cognition [7–9, 16, 17]. This study proposed a new perspective by investigating the still poorly documented U-shaped correlation between TyG-WC values and cognitive function.

Thus, this study aimed to investigate the correlation between the combination of the TyG index with various obesity indices (BMI, WC, and WHtR) and the cognitive function of low-income rural residents in Tianjin, China. By addressing existing gaps in the literature, this study provides increased clarity regarding how metabolic dysfunction and obesity interact to influence cognitive decline. The study also provides valuable insights for early intervention strategies and public health policies.

Methods

Study Design and participants

This cross-sectional analysis was part of a larger prospective cohort study of cognitive function. A baseline survey was conducted in 2012, in which participants aged ≥60 years were assessed. Follow-up cognitive evaluations were conducted from 2018 to 2020, enabling an analysis of cognitive decline and the progression of related factors over time. This study serves as an initial phase in the exploration of the relationship between metabolic health and cognitive impairment, with future analyses planned to assess the factors influencing cognitive function decline and its progression. For inclusion, participants were required to be ≥60 years of age, have lived in the area for more than five years, and provide informed consent. Exclusion criteria included myocardial infarction, stroke, congenital disease, history of psychiatric illness or incomplete data on cognitive function or obesity index. The final 1,125 participants were eligible and were enrolled this study.

This study adhered to the principles of the Declaration of Helsinki, with ethical approval granted by the Tianjin Medical University General Hospital Ethics Committee, and informed consent was obtained from all participants.

Cognitive assessment

Cognitive function was evaluated using the Mini-Mental State Examination (MMSE), a widely accepted tool for assessing cognition. Cognitive impairment was categorized by MMSE scores: <18 for illiterate participants, <21 for those with ≤6 years of education, and <25 for those with >6 years of formal education. Participants were then classified as either cognitively normal or cognitively impaired.

Measurement of TyG index and obesity indicators

The primary parameter of interest was the TyG index, which is an effective tool for assessing insulin resistance. The index was calculated using the following formula: TyG = ln [triglycerides (mg/dL) × fasting glucose (mg/dL)/2]. The obesity indicators BMI, WC, and WHtR were also determined. BMI was determined as weight (kg) / height squared (m^2), WC was measured at the midpoint between the inferior border of the 10th rib and the superior border of the iliac crest, and WHtR was calculated by dividing WC by height. These indices were classified into quartiles for statistical analysis.

Data collection and covariates

Sociodemographic data, lifestyle habits (including smoking and alcohol consumption), and clinical features (including hypertension and diabetes status) were collected via offline conversations and physical examinations. Hypertension was defined as systolic or diastolic blood pressure values of ≥140 or ≥90 mmHg, respectively, or the use of antihypertensive drugs. Diabetes was defined as a fasting blood glucose level of ≥7.0 mmol/L, a diabetes diagnosis, or use of anti-diabetic medications.

Statistical analysis

Descriptive statistics were used to summarize participant characteristics, with means and standard deviations (SD) for continuous variables and frequencies and percentages used to describe categorical data. Both continuous and categorical variables were analyzed to better explore the linear association between continuous variables and outcomes and the relationship between categorical variables and outcomes. Independent t-tests and chi-squared tests were used to assess differences between association and categorical variables between cognitively normal and impaired groups, respectively.

Considering that other confounding factors could affect the results, multivariate logistic regression analysis was applied to explore the relationships of cognitive impairment with the TyG index and TyG combined with obesity indicators; potential confounding factors were adjusted to avoid the potential correlation of independent variables affecting the results of multivariate analysis. We did not adjust for diabetes in conjunction with the TyG index combined with obesity indicators. The odds ratios (OR) and 95% confidence intervals (95%CI) for each quartile of TyG and obesity index were calculated, with the lowest quartile (Q1) serving as the reference group.

Restricted cubic spline analyses were conducted to examine potential nonlinear relationships. The effect of sex, age group, presence of diabetes, or BMI group (BMI < 24 kg/m^2, 24–28 kg/m^2, ≥ 28 kg/m^2) on the relationship between the TyG index and cognitive impairment was assessed using subgroup analyses. Additionally, linear regression analysis was used to assess the association between the TyG indices and MMSE scores after adjusting for the same covariates.

SPSS (version 27.0; IBM, Armonk, NY, USA) was used for statistical analyses, and statistical significance was defined as a two-sided $P < 0.05$. R version 4.4.0 was used to create RCS diagrams (https://www.R-project.org/).

Results

Participant characteristics

In total, 1125 eligible individuals participated in this study, including 521 men (46.3%) and 604 women (53.7%). The mean age of participants was 67.44 ± 6.28 years, with 68.5% aged 60–69-years and 31.5% aged ≥ 70 years. Cognitive impairment was observed in 47.3% ($n = 532$) of the participants, and diabetes prevalence was 17.7% ($n = 199$). Table 1 shows the characteristics of the participants, including their BMI, smoking status, alcohol consumption, and other clinical features.

Association of risk factors with cognitive impairment in the univariate analysis

A univariate analysis showed that sex, age, smoking status, alcohol consumption, and diabetes mellitus were significantly associated with cognitive impairment (all, $P < 0.05$; Table 2). Specifically, cognitive impairment was more prevalent in older individuals, women, nonsmokers, and those with diabetes.

Association between the TyG-WC index and cognitive impairment in the multivariate analysis

Multivariate logistic regression indicated a significant inverse relationship between TyG-WC index levels and cognitive impairment risk, after adjusting for confounders. Each unit increase in TyG-WC was associated with a 0.1% reduction in cognitive impairment risk (OR = 0.999; 95% CI, 0.997–1.00; $P = 0.009$) (Table 3). This inverse association between the TyG-WC index and cognitive impairment persisted after adjusting for confounders.

A restricted cubic spline analysis further revealed a nonlinear association between TyG-WC values and cognitive impairment; both high and low TyG-WC values were associated with greater cognitive impairment ($P = 0.008$; Fig. 1). This U-shaped relationship suggests that maintaining the TyG-WC values within an optimal range may reduce cognitive impairment risk.

Subgroup analyses in the association of the TyG index with cognitive impairment

Subgroup analyses by sex, age group, diabetes status, and BMI category demonstrated that the relationship between the TyG-WC index and cognitive impairment was particularly pronounced in those without diabetes and in those with a BMI < 24 kg/m^2. In the subgroup

Table 1 Characteristics of participants

Characteristics	Men	Women	Total
Case, *n* (%)	521 (46.3)	604 (53.7)	1125 (100.0)
Age, years, means ± SD	67.79 ± 6.32	67.13 ± 6.22	67.44 ± 6.28
Age groups, *n* (%)			
60–69 years	341 (65.5)	430 (71.2)	771 (68.5)
≥ 70 years	180 (34.5)	174 (28.8)	354 (31.5)
BMI, Kg/m^2, means ± SD	24.28 ± 3.38	24.97 ± 3.64	24.65 ± 3.54
BMI groups, *n* (%)			
Under weight	17 (3.3)	14 (2.3)	31 (2.8)
Normal	241 (46.5)	233 (38.7)	474 (42.3)
Overweight	185 (35.7)	239 (39.7)	424 (37.9)
Obesity	75 (14.5)	116 (19.3)	191 (17.1)
Smoking, *n* (%)			
Never smoking	156 (29.9)	558 (92.4)	714 (63.5)
Current smoking	264 (50.7)	40 (6.6)	304 (27.0)
Ever smoking	101 (19.4)	6 (1.0)	107 (9.5)
Alcohol consumption, *n* (%)			
Never drinking	246 (47.2)	591 (97.8)	837 (74.4)
Current drinking	245 (47.0)	13 (2.2)	258 (22.9)
Ever drinking	30 (5.8)	0 (0.0)	30 (2.7)
Education years, means ± SD	5.31 ± 2.79	2.49 ± 2.95	3.80 ± 3.20
Hypertension, *n* (%)	215 (41.3)	301 (49.8)	516 (45.9)
Diabetes, *n* (%)	68 (13.1)	131 (21.7)	199 (17.7)
TyG, means ± SD	8.61 ± 0.66	8.86 ± 0.58	8.74 ± 0.63
TyG groups, *n* (%)			
Q1	174 (33.4)	107 (17.7)	281 (25.0)
Q2	138 (26.5)	144 (23.8)	282 (25.1)
Q3	111 (21.3)	170 (28.1)	281 (25.0)
Q4	98 (18.8)	183 (30.3)	281 (25.0)
TyG-BMI, means ± SD	209.75 ± 38.52	221.68 ± 38.13	216.16 ± 38.75
TyG-BMI groups, *n* (%)			
Q1	168 (32.4)	112 (18.6)	280 (25.0)
Q2	127 (24.5)	153 (25.4)	280 (25.0)
Q3	132 (23.6)	158 (26.2)	280 (25.0)
Q4	101 (19.5)	179 (29.7)	280 (25.0)
TyG-WHtR, means ± SD	4.47 ± 0.73	4.92 ± 0.73	4.71 ± 0.76
TyG-WHtR groups, *n* (%)			
Q1	192 (37.2)	87 (14.5)	279 (25.0)
Q2	136 (26.4)	144 (23.9)	280 (25.0)
Q3	109 (21.1)	171 (28.4)	280 (25.0)
Q4	79 (15.3)	200 (17.9)	279 (25.0)
TyG-WC, means ± SD	741.05 ± 124.67	760.48 ± 116.22	751.51 ± 120.53
TyG-WC groups, *n* (%)			
Q1	155 (30.0)	124 (20.6)	279 (25.0)
Q2	125 (24.2)	155 (25.7)	280 (25.0)
Q3	120 (23.3)	160 (26.6)	280 (25.0)
Q4	116 (22.5)	163 (27.1)	279 (25.0)
Cognitive impairment, *n* (%)	177 (34.0)	355 (58.8)	532 (47.3)
FBG, mmol/L, means ± SD	5.53 ± 1.46	5.93 ± 1.72	5.74 ± 1.61
TG, mmol/L, means ± SD	1.54 ± 1.26	1.74 ± 0.93	1.65 ± 1.10
TC, mmol/L, means ± SD	4.32 ± 1.29	4.67 ± 1.34	4.51 ± 1.33

Table 2 Results of a univariate analysis of clinical characteristics and cognitive impairment

Characteristics	Cognitive Normal	Cognitive Impairment	*P*
Case, *n* (%)	593 (52.7)	532 (47.3)	
Men, *n* (%)	344 (66.0)	177 (34.0)	< 0.001
Age, years, means ± SD	65.89 ± 5.05	69.17 ± 7.02	< 0.001
Age groups, *n* (%):			< 0.001
60–69 years	472 (61.2)	299 (38.8)	
≥ 70 years	121 (34.2)	233 (65.8)	
BMI, Kg/m^2, means ± SD	24.83 ± 3.35	24.45 ± 3.73	0.073
BMI groups, *n* (%):			0.439
Under weight	15 (48.4)	16 (51.6)	
Normal	238 (50.2)	236 (49.8)	
Overweight	235 (55.4)	189 (44.6)	
Obesity	102 (53.4)	89 (46.6)	
Waist, cm, means ± SD	86.87 ± 9.87	84.38 ± 10.76	< 0.001
Smoke status, *n* (%)			< 0.001
Never smoking	319 (44.7)	395 (55.3)	
Current smoking	199 (65.5)	105 (34.5)	
Ever smoking	75 (70.1)	32 (29.9)	
Alcohol consumption, *n* (%)			< 0.001
Never drinking	395 (47.2)	442 (52.8)	
Current drinking	179 (69.4)	79 (30.6)	
Ever drinking	19 (63.3)	11 (36.7)	
Hypertension, *n* (%)	278 (53.9)	238 (46.1)	0.471
Diabetes, *n* (%)	89 (44.7)	110 (55.3)	0.013
FBG, mmol/L, means ± SD	5.66 ± 1.53	5.84 ± 1.70	0.058
TG, mmol/L, means ± SD	1.62 ± 1.09	1.67 ± 1.11	0.466
TC, mmol/L, means ± SD	4.45 ± 1.39	4.57 ± 1.25	0.133
TyG, means ± SD	8.72 ± 0.63	8.77 ± 0.62	0.131
TyG groups, *n* (%)			0.069
Q1	147 (52.3)	134 (47.7)	
Q2	165 (58.5)	117 (41.5)	
Q3	148 (52.7)	133 (47.3)	
Q4	133 (47.3)	148 (52.7)	
TyG-BMI, means ± SD	217.05 ± 37.14	215.18 ± 40.48	0.419
TyG-BMI groups, *n* (%)			0.278
Q1	136 (48.6)	144 (51.4)	
Q2	146 (52.1)	134 (47.9)	
Q3	159 (56.8)	121 (43.2)	
Q4	149 (53.2)	131 (46.8)	
TyG-WHtR, means ± SD	4.71 ± 0.75	4.72 ± 0.78	0.811
TyG-WHtR groups, *n* (%)			0.769
Q1	147 (52.7)	132 (47.3)	
Q2	148 (52.9)	132 (47.1)	
Q3	153 (54.6)	127 (45.4)	
Q4	140 (50.2)	139 (49.8)	
TyG-WC, means ± SD	759.65 ± 117.74	742.48 ± 123.04	0.017
TyG-WC groups, *n* (%)			0.099
Q1	130 (46.6)	149 (53.4)	
Q2	148 (52.9)	132 (47.1)	
Q3	159 (56.8)	121 (43.2)	
Q4	151 (54.1)	128 (45.9)	

Table 3 Results of multivariate analysis between TyG-WC and cognition

	References	OR (95%CI)	*P*
TyG-WC		0.999 (0.997, 1.00)	0.009
Women	Men	2.31 (1.63, 3.29)	< 0.001
Age groups	60–69 years		
≥ 70 years		3.64 (2.73, 4.84)	< 0.001
Smoke status	Never smoking		
Current smoking		0.69 (0.47, 1.02)	0.065
Ever smoking		0.51 (0.29, 0.89)	0.017
Alcohol consumption	Never drinking		
Current drinking		0.77 (0.52, 1.15)	0.205
Ever drinking		1.45 (0.62, 3.42)	0.393

without diabetes, cognitive impairment risk decreased by 0.2% per unit increase in the TyG-WC value (OR = 0.998; 95% CI, 0.997–0.999; $P = 0.002$). For participants with BMI < 24 kg/m², the risk decreased by 0.4% per unit increase in the TyG-WC value (OR = 0.996; 95% CI, 0.994–0.998; $P = 0.001$). However, this significant association was not found for men, patients with diabetes, or participants with a BMI of ≥ 24 kg/m^2 (Fig. 2).

Association between the TyG-WC index and MMSE scores

The univariate analysis showed that sex, age, smoking status, alcohol consumption, total cholesterol, fasting blood glucose, BMI, TyG-WC, diabetes, and hypertension were significantly associated with MMSE scores (all,

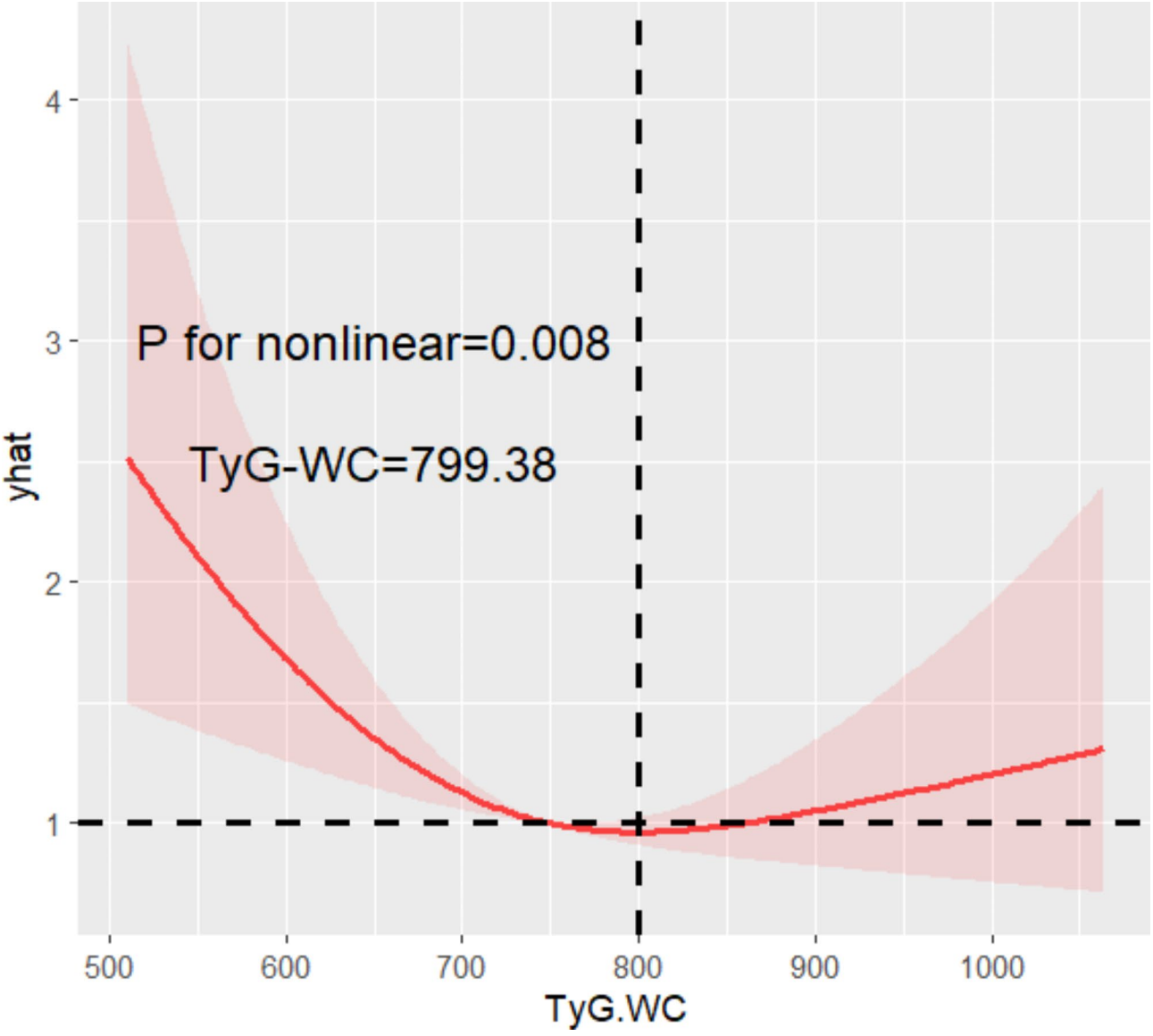

Fig. 1 Restricted cubic spline analysis to evaluate the potential non-linear relationship between TyG-WC and cognitive impairment. This figure shows the non-linear relationship between TyG-WC and cognitive impairment

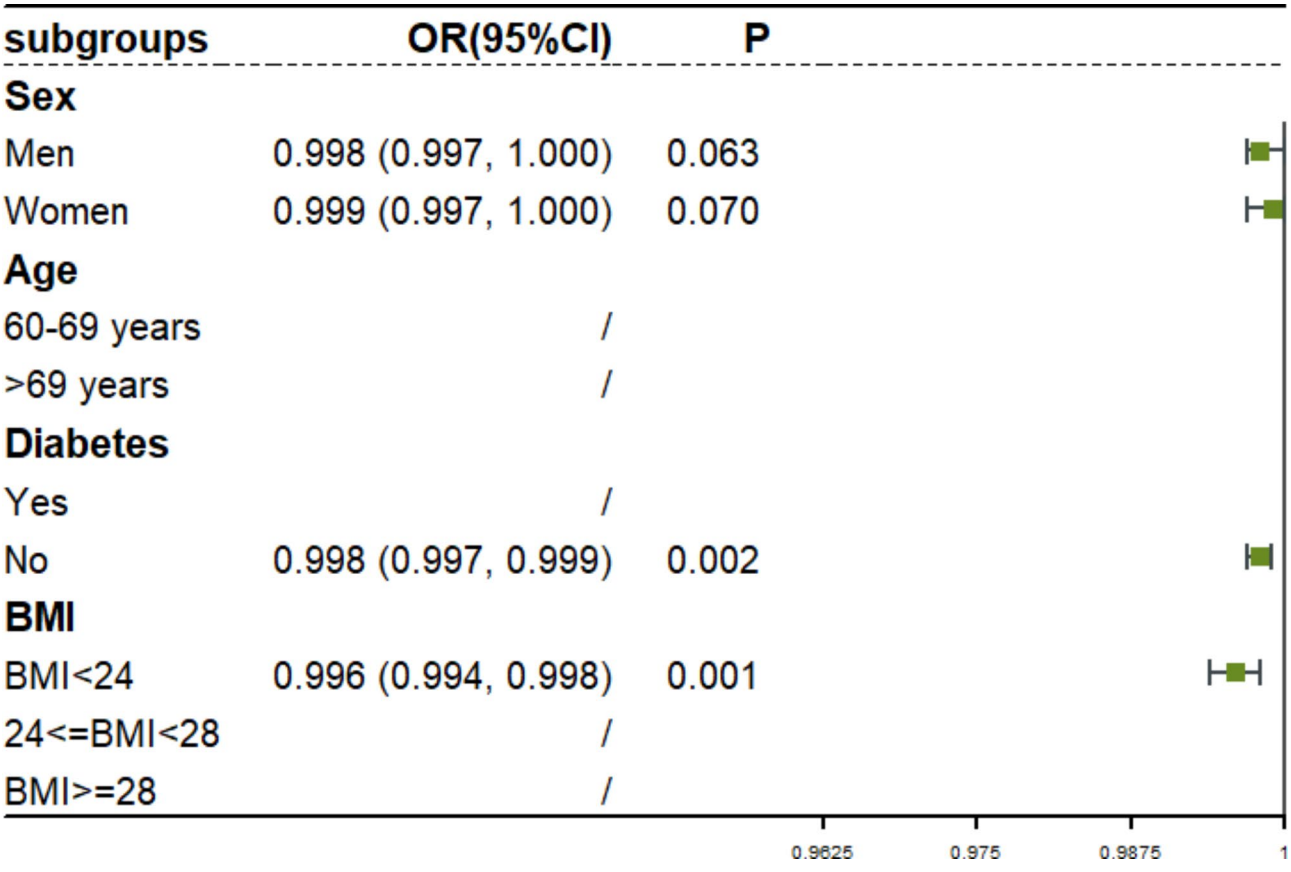

Fig. 2 Association between the TyG-WC and cognitive impairment in sex, age, diabetes mellitus, and BMI subgroups in logistic models. This figure shows that after adjusting for covariates, in the subgroup without diabetes, the risk of cognitive impairment decreased by 0.2% for each higher value of TyG-WC. In participants with a BMI < 24, the risk decreased by 0.4% per unit increase in TyG-WC. No significant association was found between TyG-WC and cognitive impairment in men, participants with diabetes, or those with a BMI ≥ 24

Table 4 Results of a univariate analysis of clinical characteristics and MMSE scores

Characteristics	References	β (95%CI)	*P*
Women	Men	-3.44 (-4.02, -2.86)	< 0.001
Age		-0.29 (-0.34, -0.25)	< 0.001
FBG		-0.23 (-0.42, -0.04)	0.018
TG		-0.07 (-0.35, 0.21)	0.618
TC		-0.31 (-0.54, -0.08)	0.009
Smoke status	Never smoking	1.91 (1.46, 2.35)	< 0.001
Alcohol consumption	Never drinking	2.15 (1.56, 2.74)	< 0.001
TyG		-0.42 (-0.90, 0.07)	0.094
BMI		0.10 (0.01, 0.18)	0.028
TyG-WC		0.003 (0.001, 0.006)	0.016
Age groups	60–69 years	-3.48 (-4.10, -2.85)	< 0.001
BMI groups	Q1	0.35 (-0.04, 0.74)	0.079
Hypertension	No Hypertension	0.65 (0.04, 1.27)	0.037
Diabetes	No Diabetes	-0.94 (-1.74, -0.14)	0.022

Table 5 Results of a multivariate analysis of clinical characteristics and MMSE scores

Characteristics	References	β (95%CI)	*P*
TyG-WC		0.003 (0.0002, 0.005)	0.031
TC		-0.07 (-0.28, 0.14)	0.521
Smoke status	Never smoking	0.63 (0.08, 1.18)	0.025
Alcohol consumption	Never drinking	-0.01 (-0.70, 0.67)	0.973
Women	Men	-3.19 (-3.92, -2.46)	< 0.001
Age groups	60–69 years	-3.61 (-4.20, -3.02)	< 0.001
Hypertension	No Hypertension	0.68 (0.12, 1.24)	0.018

$P<0.05$; Table 4). The multivariate linear regression analysis showed a significant positive association between the TyG-WC index and MMSE score. For each unit increase in TyG-WC values, MMSE scores increased by 0.003 (β=0.003; 95% CI, 0.0002–0.005; $P=0.031$; Table 5). This positive correlation was also found in the male subgroup (β=0.005; 95% CI, 0.002–0.007; $P=0.002$) and in participants without diabetes (β=0.004; 95% CI, 0.001–0.007; $P=0.003$). No significant relationship between the TyG-WC index and MMSE scores was found in other subgroups, including those with higher BMIs or diabetes (Fig. 3).

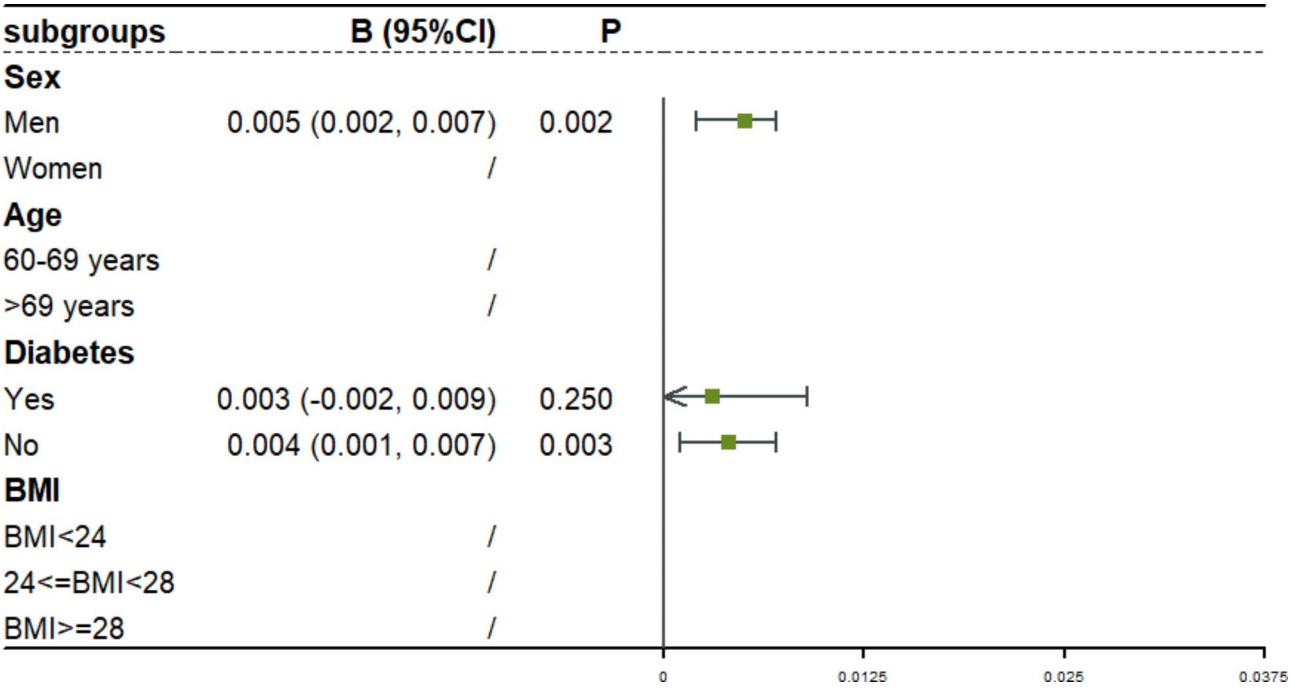

Fig. 3 Association between the TyG-WC and MMSE Scores in sex, age, diabetes mellitus, and BMI subgroups in linear models. This figure shows that after adjusting for covariates, in the male subgroup, for each unit increase in TyG-WC, MMSE scores increased by 0.005. In the non-diabetic subgroup, for each unit increase in TyG-WC, MMSE scores increased by 0.004. No significant association was found in other subgroups

Dose–response relationship between the TyG-WC index and cognitive impairment

The restricted cubic spline analysis showed a U-shaped dose–response correlation between TyG-WC values and cognitive impairment, with both very low and high TyG-WC values linked to greater impairment risk ($P=0.008$). However, a nonlinear association was not apparent between the TyG-WC values and MMSE scores ($P>0.05$; Fig. 4). These findings suggest that maintaining an appropriate TyG-WC range protects against cognitive decline, whereas extremely low and high TyG-WC levels may be detrimental.

Discussion

This study examined the association between the combination of the TyG index and obesity indicators with cognitive function in older, low-income, and rural individuals in Tianjin, China. A notable inverse relationship was identified between TyG-WC values and cognitive impairment. Additionally, a U-shaped association was observed between TyG-WC values and cognitive impairment, with both high and low TyG-WC values associated with an increased risk. Subgroup analyses revealed that the protective effect of the TyG-WC index was particularly pronounced in individuals without diabetes and in those with a BMI of <24 kg/m^2. Additionally, a positive correlation was found between TyG-WC values and MMSE scores, particularly in men and individuals without diabetes, indicating that higher TyG-WC values are associated with better cognition. In men, the MMSE score increased by 0.005 for each unit increase in TyG-WC values. However, no association was found between TyG-WC values and MMSE scores in women.

While prior research has explored the TyG index in relation to cognitive function, the specific link between the TyG-WC index and cognitive impairment remains underreported, with few studies directly addressing this association. Most previous studies have focused on broader metabolic indices, leaving the relationship between TyG combined with WC and cognition less well understood. Some findings have suggested a connection between TyG-related metrics and cognitive decline, but the results have been mixed; the role of the TyG-WC index in cognitive function has yet to be clearly defined. Some studies have found that higher TyG-BMI and TyG-WHtR values may serve as useful markers of cognitive decline [16, 17], whereas others have shown that TyG-BMI appears to play a protective role in cognition [15]. These studies indicate that TyG indices, when combined with obesity measures, may be useful markers of cognitive decline. However, the specific role of the TyG-WC index remains unclear. In contrast, this study provides new insights by identifying a significant inverse relationship between TyG-WC values and cognitive impairment that persists even after adjusting for confounding factors. This inverse correlation suggests that higher TyG-WC values can reduce the risk of cognitive impairment, a finding not widely reported in the literature.

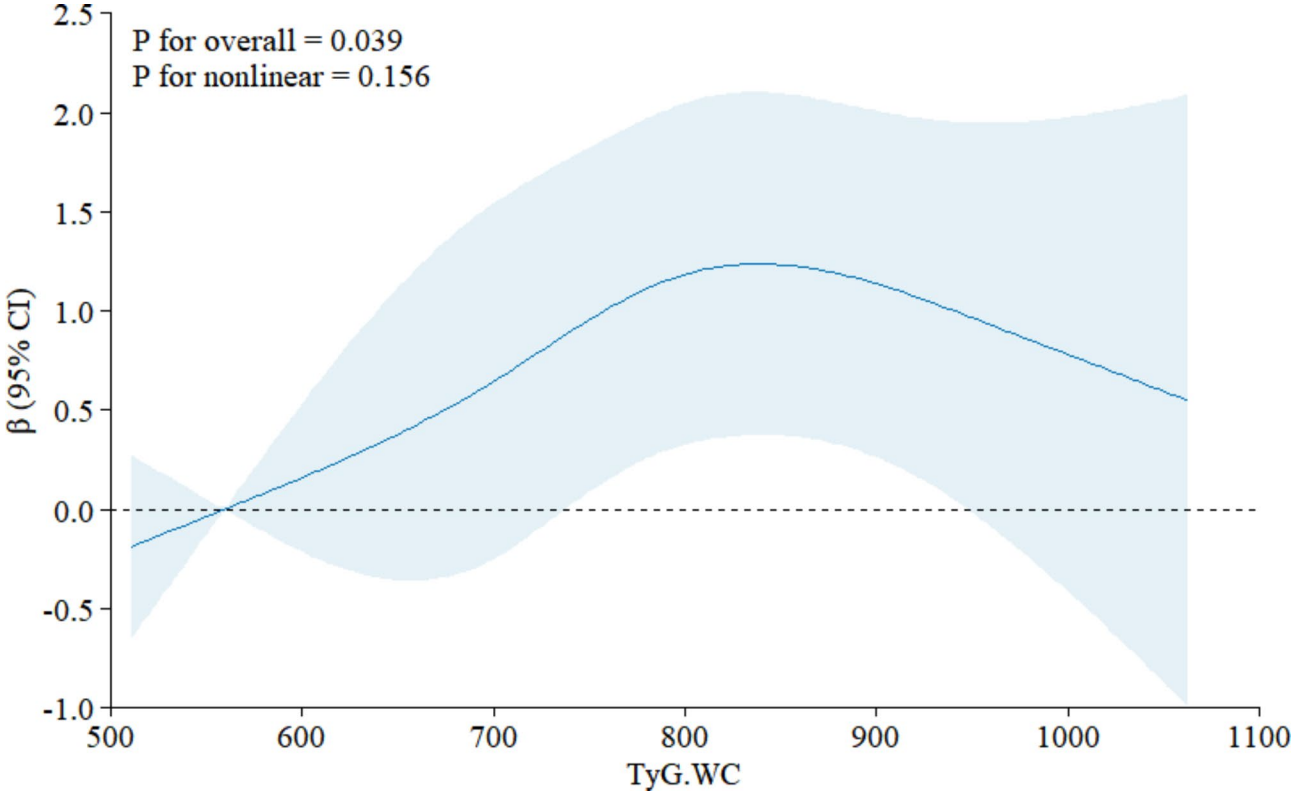

Fig. 4 Restricted cubic spline analysis to evaluate the potential non-linear relationship between TyG-WC and MMSE Scores
This figure shows that there was no nonlinear association between TyG-WC and MMSE Scores

Furthermore, the discovery of a U-shaped correlation between TyG-WC values and cognitive impairment is unique.

These findings showed that excessively low or high TyG-WC values may contribute to cognitive impairment, highlighting the importance of maintaining metabolic and obesity indices within an optimal range. However, this study showed only an association between TyG-WC values and cognitive impairment; related measures did not show this relationship. This is possibly due to the TyG-WC index being more reflective of the degree of central obesity and insulin resistance than other indicators. The mechanism underlying the beneficial effects of TyG-WC values within a fixed range on cognitive function may be related to the metabolic and vascular access affected by insulin resistance and central obesity. Higher TyG-WC levels, within a fixed range, may reflect a balance in energy metabolism that may help protect against cognitive decline by improving insulin sensitivity and glucose utilization in the brain. Conversely, excessively high or low TyG-WC values may disrupt this balance, leading to hyperinsulinemia or an insufficient energy supply to the brain, both of which are detrimental to cognitive function. These mechanisms could explain the U-shaped relationship observed in this finding.

The U-shaped relationship observed in this study has not been widely reported in previous studies. Although correlations between metabolic indicators and cognitive impairment have been explored, few studies have found nonlinear correlations between these indicators and cognitive function. Most existing research has focused on linear relationships, often finding either positive or negative associations. However, the concept of a U-shaped curve reflecting a negative impact of both the high and low extremes of TyG-WC values has been largely unexplored.

A few studies have examined nonlinear associations in related contexts. Tian et al. reported an inverted J-shaped correlation between the TyG index and various cognitive domains, showing that moderate levels of TyG offer cognitive protection, whereas extremely low or high levels are detrimental [8]. In contrast, Hou et al. observed a linear association between the TyG-WHtR values and cognitive impairment, where higher levels consistently led to cognitive decline without evidence of a nonlinear trend [17]. However, none of these studies specifically focused on the TyG-WC index, leaving a gap in the understanding of its unique relationship with cognitive health. The present study expanded on this body of work by demonstrating a U-shaped correlation between TyG-WC values and cognitive impairment.

The U-shaped pattern also supports novel insights into how metabolic- and obesity-related indices may interact with cognitive health. The mechanisms underlying this nonlinear relationship may involve a complex interplay among insulin resistance, lipid metabolism, and brain function. Low TyG-WC values may indicate suboptimal energy metabolism, thereby reducing cognitive maintenance in the brain due to insufficient glucose availability. Conversely, high TyG-WC values may reflect excessive insulin resistance and central obesity, which are known to impair cognitive function through inflammatory and vascular pathways. The U-shaped association may represent a balance between adequate metabolic function and the avoidance of hyperinsulinemia and insufficient energy supply to the brain, both of which can disrupt normal cognitive processes.

The correlation between the TyG-WC index and cognitive function in individuals without diabetes and with lower BMI values is particularly noteworthy and has not been extensively reported in previous studies. Although previous research has explored the relationship between metabolic markers, such as the TyG index, and cognitive function, few studies have specifically investigated how this association varies according to diabetes status and BMI. The interplay of metabolic health and obesity with cognitive function is complex, and this study provides valuable insights, particularly in populations with distinct metabolic profiles.

Several studies have examined the association between metabolic indices and cognitive outcomes. Ruis et al. noted that patients with diabetes tend to experience greater cognitive impairment due to more severe metabolic dysregulation; however, their study did not specifically explore the TyG-WC index [18]. Other studies have shown that increased inositol concentrations and decreased *N*-acetylaspartate/creatine, glutamate, and glutamine in patients with diabetes can be used as metabolic biomarkers of cognitive impairment in this patient group [19]. Glucose can affect the capacity and state of the brain through several mechanisms, such as influencing metabolites and metabolic factors, oxidative stress, and affecting the cerebral blood vessels and cerebral blood flow [20–23]. Insulin influences brain function in many ways, including promoting synapse formation, regulating neurotransmitters, and increasing glucose transport [24–27]. Additionally, higher TyG values have been found to be related to cognitive impairment in patients with type 2 diabetes; however, this association was attenuated in individuals without diabetes, implying different mechanisms in the two groups [16]. These findings highlight the complexity of metabolic influences on cognition and the potential for different effects depending on diabetes status.

The present study identified a stronger inverse association between TyG-WC values and cognitive impairment in those without diabetes and in those with a lower BMI. In non-diabetic participants, there was an association between increased TyG-WC values and a reduced risk of cognitive impairment. This suggests that metabolic dysregulation in non-diabetic individuals may follow pathways that are potentially linked to subclinical insulin resistance. Similarly, the more pronounced association between higher TyG-WC values and reduced cognitive impairment in those with a lower BMI (<24) suggests that the detrimental effects of central obesity on cognitive function may be more evident in those with lower overall adiposity. This result contrasts with previous findings such as those of Hou et al., who reported stronger associations between TyG indices and cognitive decline in overweight and obese populations [17]. The potential mechanisms underlying these differential associations may involve varying degrees of metabolic compensation in individuals with and without diabetes. In non-diabetic individuals, the TyG-WC index may better capture the early stages of insulin resistance, when metabolic disturbances are less severe but are significant enough to affect cognitive function. In contrast, diabetic individuals may experience more advanced metabolic dysfunction in which the TyG-WC index is less predictive of cognitive outcomes due to chronic hyperglycemia and related complications. Additionally, individuals with a lower BMI may exhibit different metabolic patterns, where central obesity plays a more significant role in cognitive decline than in those with higher overall body fat, where the effects of central obesity may be diluted by other factors.

Few studies have specifically explored the correlation between the TyG-WC index and cognitive performance as measured by MMSE scores. Research in this area typically examines the association between cognitive decline and general metabolic markers or obesity indices, leaving the connection between the TyG-WC index and cognitive performance relatively unexplored. Moreover, the present findings were somewhat unexpected, as insulin resistance and central obesity are typically linked to cognitive dysfunction rather than to improved cognitive outcomes. Several studies have investigated the association between metabolic indices and cognitive function. A correlation between higher TyG-BMI values and better cognition has been found in some populations, suggesting a protective effect of metabolic health under certain conditions [15]. Higher TyG levels have been linked to better cognitive scores in non-diabetic individuals, but this association is reversed in those with type 2 diabetes [16]. In contrast, a previous finding did not find a significant correlation between the TyG index and cognitive function but did find a negative association between TyG-WHtR values and MMSE scores, particularly in overweight individuals

[7, 17]. These mixed findings highlight the complexity of metabolic factors in cognitive health and suggest that the relationship between metabolic indices and cognition may vary across populations and subgroups.

This study identified a positive association between TyG-WC values and MMSE scores, especially in men and non-diabetic individuals. This suggests that within certain metabolic ranges, higher TyG-WC values may be linked to better cognitive performance. This finding contradicts the generally accepted view that higher TyG values or central obesity metrics are associated with cognitive decline. It also raises questions regarding whether moderate levels of insulin resistance or central obesity offer compensatory protective effects on brain function in specific subgroups. One possible mechanism for this positive association may involve a balance between glucose availability and insulin signaling in the brain. TyG-WC values within a fixed range might reflect an optimal metabolic state in which glucose supply to the brain is maintained at levels that support cognitive function without progressing to hyperinsulinemia or severe insulin resistance. Additionally, non-diabetic individuals may experience different metabolic dynamics, where mild elevations in TyG-WC values do not yet lead to the neurodegenerative effects observed in more advanced insulin resistance. Alternatively, this relationship might be context dependent, reflecting the interplay of other unmeasured factors, such as physical activity, diet, or genetic predisposition, which could influence both metabolic health and cognitive outcomes.

Strengths and limitations

This study has several strengths and limitations. A major strength is its focus on a low-income rural Chinese population, a demographic often underrepresented in research on metabolic health and cognitive impairment. By examining this group, the study provides valuable insights into metabolic and obesity-related risk factors for cognitive decline, particularly in settings with different lifestyle and health challenges compared to those of urban populations. Additionally, the comprehensive evaluation of the TyG index combined with obesity indicators (WC, BMI, WHtR) enhances understanding of how central obesity and insulin resistance affect cognitive function. However, this study has several limitations. As a cross-sectional study, it cannot establish causality between TyG-WC values and cognitive impairment, and longitudinal studies are needed for a clearer understanding of the temporal relationship. Furthermore, this study relied solely on the MMSE to assess cognitive function, which may not capture all cognitive aspects, such as executive function or memory; accordingly, future research should use a broader set of cognitive assessments. Moreover, the study's sample, which focuses on a low-income rural population in Tianjin, limits the generalizability of the findings to other populations, such as urban dwellers or individuals from different socioeconomic backgrounds. The study also did not account for potential confounders such as diet, physical activity, genetic factors, or psychological stress, which may influence both TyG-WC and cognitive function. Future studies should address these factors to better isolate the association of TyG-WC with cognitive outcomes. Additionally, since the population had limited use of hypoglycemic or lipid-lowering drugs, the impact of medication history was not assessed, which may have influenced the results. Future research should include medication history and consider a broader range of comorbidities.

Conclusion

This study highlights the significant association between TyG-WC values and cognitive impairment, particularly in a low-income rural Chinese population. The U-shaped association between TyG-WC values and cognitive impairment suggests that maintaining metabolic indicators within optimal ranges may be help slow cognitive decline. The stronger association observed in non-diabetic individuals and those with a lower BMI indicates that certain subgroups may benefit more from early metabolic health management. This finding provides important preliminary evidence for the identification and management of cognitive impairment risk. The TyG-WC combination offers a simple and accessible tool for clinicians to assess metabolic health and potentially identify cognitive decline risk, particularly in resource-limited settings. Incorporating the TyG-WC index into routine assessments could help healthcare providers identify high-risk patients and offer earlier interventions, such as lifestyle modifications. Improved lifestyle, including dietary changes and consistent exercise, may help optimize metabolic markers and reduce cognitive risk. The U-shaped relationship between TyG-WC values and cognitive impairment suggests that maintaining metabolic indicators within an optimal range is critical, emphasizing the need for personalized strategies to balance metabolic health and reduce cognitive decline in aging populations.

Abbreviations

TyG	triglyceride-glucose
BMI	body mass index
WC	waist circumference
WHtR	waist-to-height ratio
MMSE	Mini-Mental State Examination
SD	standard deviations
OR	odds ratios
CI	confidence intervals

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Author contributions
YLi, XN, CY were involved in conception and design, and data interpretation for this article. JH, YLu, LZ, XL, HW, XZ, LW, JT were involved in data collection, case diagnosis and confirmation for this article. JH, YLu, XL were involved in manuscript drafting. JW was involved in data analysis for this article. YLi, XN, CY were involved critical review in for this article.

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Data availability
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from the Ethics Committee of Tianjin Medical University General Hospital. Informed consent was obtained from all participants before enrollment in the study.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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