

Gender differences in triglyceride glucose index predictive power for type 2 diabetes mellitus: a Chinese cohort study

Rubing Guo^{1,2,3} · Jingjing Tong⁴ · Ruirui Wang¹ · Songtai Ma¹ · Lianhua Wei³ · Wei Zhao² 

Received: 21 April 2024 / Accepted: 10 June 2024 / Published online: 6 July 2024

© The Author(s), under exclusive licence to Research Society for Study of Diabetes in India 2024

Abstract

Objective This study aims to explore the association between the triglyceride glucose (TyG) index and type 2 diabetes mellitus (T2DM) in Chinese men and women while assessing its predictive capability by gender.

Methods Data from the DRYAD database were used in this study, which also performed a secondary analysis of 48,230 participants from the China Rui-Ci group. Data on lifestyle habits, detailed health indicators, and demographics were gathered. The TyG index was calculated, and statistical techniques such as multivariate Cox regression and generalized additive models were used to analyze the correlation between the TyG index and the incidence of T2DM. Gender-specific predictive capacity was evaluated through subgroup analyses and receiver operating characteristic curves (ROC).

Results A cohort of 48,230 individuals demonstrated a significant positive link between the TyG index and T2DM risk in both genders. In the adjusted model, T2DM risk rose by 1.68 times (95% CI, 1.23–2.28) in males and 3.59 times (95% CI, 2.29–5.65) in females. Female participants showed a higher TyG index predictive value for T2DM (AUC=0.812) compared to males (AUC=0.721). Notably, females with hypertension displayed significantly elevated T2DM risk in various age groups compared to males (p for interaction < 0.05).

Conclusion The study reveals a positive correlation between the TyG index and T2DM risk in both genders. Moreover, the predictive capacity of this relationship is notably stronger in females.

Keywords Triglyceride glucose index · Type 2 diabetes mellitus · Sex differences · Insulin resistance · Predictive capability

Introduction

The incidence of diabetes is predicted to rise to 536.6 million adults in the world between the ages of 20 and 79 by 2021, and this number is expected to increase to 783.2 million by 2045 [1]. Of particular concern is the fact that nearly half of

all adults worldwide—that is, 239.7 million—do not know they have diabetes, with China leading the world in the number of cases of undiagnosed diabetes [2]. As a result, early identification of type 2 diabetes mellitus (T2DM) through easily applied and practical screening indicators is critical.

In addition, chronic inflammation exacerbates the public health challenges posed by T2DM, with patients experiencing an increased inflammatory load [3]. Notably, triglyceride-based markers, such as the TG/HDL-C ratio and TyG index, have been validated as valuable indicators of a variety of diseases characterized by inflammation, including T2DM [4, 5], atherosclerosis [6], hypertension [7], and cardiovascular disease [8, 9]. The prognostic nutritional index (PNI), which correlates with inflammatory status, further emphasizes the significance of metabolic and nutritional assessment in understanding the development of T2DM complications [10]. Previous study also showed that T2DM patients with complications had elevated TG/HDL-C ratios associated with poor glycemic control, thus enhancing its potential as a biomarker for monitoring diabetic complications [11].

✉ Lianhua Wei
weilianhua0199@sina.com

✉ Wei Zhao
zhaowei@zryhyy.com.cn

¹ School of Public Health, Gansu University of Traditional Chinese Medicine, Lanzhou 730000, China

² Department of Clinical Laboratory, China-Japan Friendship Hospital, 2 Yinghuayuan East Street, Chaoyang District, Beijing 100029, China

³ Department of Clinical Laboratory, Gansu Provincial Hospital, 204 Donggang West Road, Lanzhou 730000, China

⁴ Department of Infectious Diseases, China-Japan Friendship Hospital, Beijing 100029, China

Insulin resistance (IR) is a crucial metabolic abnormality in the development of T2DM, typically measured through the hyperinsulinemic-euglycemic clamp (HEC), which is costly and cumbersome, limiting its feasibility for widespread use [12]. Most IR indexes are derived from plasma glucose and insulin measurements, but few are routinely used due to practical reasons [13]. In recent years, the triglyceride glucose (TyG) index, derived from triglyceride (TG) and fasting blood glucose (FPG), has gained attention as an alternative method for evaluating insulin resistance. Compared to HEC, the TyG index offers greater convenience in data collection and is cost-effective, presenting a promising avenue for practical application. The TyG index has also been shown to be a more effective predictor of diabetes [14]. However, gender-based differences exist in the occurrence and progression of diabetes due to physiological, cultural, and environmental factors [15]. Previous studies have indicated that females exhibit lower insulin sensitivity compared to males of the same age, potentially rendering them more susceptible to insulin resistance and consequently increasing their risk of developing diabetes [16]. Moreover, females tend to accumulate fat around the waist and abdomen after childbirth and menopause, which is closely associated with an increased risk of metabolic syndrome and diabetes [17]. Given these disparities and the need for risk-stratifying tools in large-scale diabetes prevention strategies, exploring the TyG index's predictive efficacy in women is crucial for refining gender-specific risk categorization and targeted interventions.

There is a growing body of research on the TyG index and its correlation with insulin resistance and T2DM, but there is no definitive report on the correlation between the TyG index and T2DM in different genders. The purpose of this study is to investigate the association and potential non-linear relationship between the TyG index and T2DM in Chinese male and female populations. It will also evaluate the predictive role of the TyG index in T2DM in different genders. Understanding the role of gender in the association between the TyG index and diabetes could help identify and intervene with T2DM in different genders.

Methods and Materials

Data source

The dataset used in this study was sourced from the DRYAD database (<https://doi.org/10.5061/dryad.ft8750v>), originally published by Chen et al. [18]. The dataset for this study was extracted from the original research data of a study titled “Association of body mass index and age with incident diabetes in Chinese adults: a population-based cohort study.” According to the authors' instructions, these data can be

freely accessed for other analyses, given proper acknowledgment of the data source and reference to the literature. This work is licensed under a CC0 1.0 Universal (CC0 1.0) Public Domain Dedication license. Ethical approval and individual patient consent were unnecessary as all health information was anonymized, rendering formal consent unnecessary for the retrospective data collection.

Study design

This study is a secondary analysis of a cohort study conducted on the China Rui-Ci group, with detailed design explanations provided in previous literature [18]. The database used in this study comprised 685,277 study participants aged ≥ 20 years who had undergone at least two visits between 2010 and 2016. Participants lacking baseline weight, height, gender, extreme body mass index (BMI) values ($< 15 \text{ kg/m}^2$ or $> 55 \text{ kg/m}^2$), or unavailable FPG values ($n = 103,946$, $n = 1$, $n = 152$, $n = 31,370$, respectively) were excluded. There were 211,833 participants in the original study after excluding people with a baseline diagnosis of diabetes (2997 self-reported and 4115 diagnosed based on $\text{FPG} \geq 7.0 \text{ mmol/L}$), follow-up intervals of less than 2 years ($n = 324,233$), and unclear diabetes status at follow-up ($n = 6630$). Among the 211,833 participants, 163,603 were further excluded from this study due to a lack of baseline data on systolic blood pressure (SBP), diastolic blood pressure (DBP), total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL), blood urea nitrogen (BUN), and creatinine clearance rate (Ccr), resulting in 48,230 participants included in the data analysis. The participants screening process is illustrated in Fig. S1.

Data collection

Age, BMI, SBP, DBP, TC, TG, HDL, LDL, aspartate transaminase (AST), alanine transaminase (ALT), FPG, BUN, and Ccr were collected as continuous variables; gender, smoking status, drinking status, and family history of diabetes were collected as categorical variables from all participants. Comprehensive questionnaire surveys were conducted during each visit to the health examination center to gather detailed information on family history of diabetes and demographic characteristics such as age and gender. After a minimum fasting period of 10 h, TC, TG, HDL, and LDL were tested using an automated analyzer (Beckman 5800), and FPG was tested using the glucose oxidase method with the same automated analyzer. Trained personnel measured height, weight, and blood pressure using standardized protocols. The formulas used to calculate BMI and TyG index were $\text{weight (kg)} / \text{height (m)}^2$ and $\ln (\text{FPG (mg/dL)} \times \text{TG (mg/dL)} / 2)$.

Definition of type 2 diabetes mellitus

T2DM was diagnosed based on one or more of the previously established and validated criteria, which included self-reported T2DM during follow-up and an FPG level of 7.0 mmol/L or higher [19].

Statistical analysis

Normal distribution of continuous variables was evaluated with quantile–quantile plots. Mean $\pm$ standard deviation or median (Q1–Q3) were used to represent normally distributed or non-normally distributed continuous variables, and proportions were used for categorical variables. One-way analysis of variance (for normally distributed variables), Kruskal–Wallis H test (for non-normally distributed), and χ^2 test (for categorical variables) were used to assess baseline characteristic differences in TyG index quartiles. A multivariate Cox regression model was used to examine the impact of TyG index on the incidence of T2DM. Covariates were considered for adjustment if their exclusion from the full model resulted in a change in the regression coefficients for TyG index by more than 10% or if the regression coefficients of the covariates were associated with a p -value < 0.1 for the incidence of T2DM. Confounding factors identified in this study included age, BMI, SBP, DBP, smoking status, drinking status, hypertension, family history of diabetes, TC, HDL, LDL, AST, ALT, BUN, and Ccr. Additionally, a generalized additive model was used to evaluate the non-linear relationship between TyG index and T2DM. Receiver operating characteristic curves (ROC) were used to evaluate the diagnostic capacity of TyG index for the occurrence of T2DM in male and female participants. Subgroup analyses were performed using stratified Cox regression models, and the likelihood ratio test was used to assess interactions between subgroups. Statistical analyses were performed using R version 4.3.2 (<http://www.R-project.org>). The two-sided significance level was set at 0.05.

Results

Baseline characteristics of individuals

The results of this study involved a total of 48,230 participants, with an average age of 43.90 years, consisting of 55.95% males and 44.05% females. Over the average follow-up period of 3.09 years, 1223 individuals (2.54%) were diagnosed with T2DM. The participants were divided into four groups based on the quartiles of TyG index (Table 1). It was observed that males and females with higher TyG indexes displayed higher age, BMI, SBP, DBP, FPG, TC, TG, LDL, LAT, AST, and BUN, and lower levels of HDL. Furthermore, they were more likely

to smoke, consume alcohol, and have a family history of diabetes and hypertension. Apart from the non-significant difference in Ccr in males ($p = 0.132$), all other parameters showed statistically significant differences ($p < 0.001$). Table S1 shows baseline characteristics by gender in the total population and in the T2DM population. In the total population, there was no significant statistical difference in age between males and females. However, the proportion of females with a family history of diabetes and the levels of HDL were higher than those of males, while the other variables in males were significantly higher than in females ($p < 0.001$). Among males and females with T2DM, there were no significant statistical differences in SBP, family history of diabetes, or the proportion of individuals with hypertension. Age, TC, HDL, and LDL were higher in females compared to males.

Multifactorial regression analysis of TyG index and T2DM in males and females

In the unadjusted model 1, there was a positive correlation between TyG index quartiles and the risk of T2DM in both males and females (Table 2). After adjusting for age, BMI, SBP, DBP, smoking status, drinking status, hypertension, family history of diabetes, TC, HDL, LDL, ALT, AST, BUN, and Ccr in model 3, the risk of T2DM for both males and females decreased slightly. However, the positive correlation between TyG index and the risk of T2DM in males [hazard ratio (HR) = 1.68; 95% confidence interval (95% CI), 1.23–2.28] and females (HR = 3.59; 95% CI, 2.29–5.65) remained significant ($p < 0.001$). In the fully adjusted model 3, whether the TyG index was considered a continuous variable or a four-category variable, the data indicated that as the TyG index increased, the incidence of T2DM in both males and females also increased (p for trend < 0.05).

Linear relationship between TyG index and T2DM in males and females

To assess the correlation between TyG index and the risk of T2DM in males and females, we utilized a restricted cubic splines analysis (Fig. 1). After adjusting for potential confounders, there remains a consistent positive correlation between TyG index and T2DM in both males and females, without any apparent inflection point. This suggests that as the TyG index increases, the risk of T2DM in males and females does not exhibit threshold effects or saturation effects.

Predictive value of TyG index for T2DM in males and females

ROC analysis indicated that the predictive value of TyG index was stronger for T2DM in females (AUC = 0.812)

Table 1 Baseline characteristics of males and females by TyG index quartiles

Variable	TyG index quartiles				<i>p</i> -value
	Q1	Q2	Q3	Q4	
Male					
Participants (<i>n</i>)	4061	6107	7636	9183	
T2DM	22 (0.54%)	84 (1.38%)	175 (2.29%)	548 (5.97%)	0.000
TyG index	0.35±0.21	0.82±0.12	1.22±0.13	1.88±0.37	0.000
Age (yr)	39.99±12.61	42.42±13.37	44.42±13.14	46.13±12.15	0.000
BMI (kg/m ²)	22.36±2.79	23.30±2.89	24.41±2.96	25.72±2.94	0.000
SBP (mmHg)	118.96±14.69	120.66±15.08	122.97±15.66	125.98±16.13	0.000
DBP (mmHg)	73.35±9.96	75.01±10.14	76.91±10.65	79.59±10.77	0.000
FPG (mmol/L)	4.72±0.57	4.90±0.56	5.05±0.57	5.28±0.61	0.000
TC (mmol/L)	4.28±0.69	4.54±0.76	4.82±0.83	5.16±0.90	0.000
TG (mmol/L)	0.62±0.14	0.94±0.15	1.37±0.22	2.70±1.38	0.000
HDL (mmol/L)	1.37±0.25	1.34±0.26	1.31±0.27	1.23±0.26	0.000
LDL (mmol/L)	2.47±0.54	2.67±0.60	2.87±0.65	2.96±0.71	0.000
ALT (U/L)	18.00 (14.00–25.00)	20.00 (15.00–28.00)	23.00 (17.00–33.00)	29.00 (20.50–42.00)	0.000
AST (U/L)	22.00 (19.00–26.00)	22.20 (19.00–26.90)	23.50 (20.00–28.00)	25.50 (21.40–31.15)	0.000
BUN (mmol/L)	5.01±1.23	4.95±1.18	4.90±1.15	4.93±1.14	0.000
Ccr (μmol/L)	81.42±12.01	81.66±11.56	81.91±12.13	81.88±12.62	0.132
Smoker	342 (8.42%)	578 (9.46%)	839 (10.99%)	1291 (14.06%)	0.000
Drinker	381 (9.38%)	553 (9.06%)	770 (10.08%)	1074 (11.70%)	0.000
Family history of diabetes	49 (1.21%)	86 (1.41%)	133 (1.74%)	203 (2.21%)	0.000
Hypertension	451 (11.11%)	860 (14.08%)	1390 (18.20%)	2323 (25.30%)	0.000
Female					
Participants (<i>n</i>)	7997	5950	4420	2876	
T2DM	26 (0.33%)	46 (0.77%)	106 (2.40%)	216 (7.51%)	0.000
TyG index	0.29±0.24	0.80±0.11	1.21±0.12	1.80±0.33	0.000
Age (yr)	39.05±9.96	42.68±11.78	48.07±13.60	53.68±13.10	0.000
BMI (kg/m ²)	21.07±2.50	22.04±2.86	23.25±3.24	24.64±3.20	0.000
SBP (mmHg)	110.10±13.64	113.87±15.68	119.53±17.57	127.44±19.18	0.000
DBP (mmHg)	68.59±9.34	70.86±10.01	73.43±10.63	77.24±11.66	0.000
FPG (mmol/L)	4.72±0.50	4.92±0.49	5.09±0.52	5.33±0.59	0.000
TC (mmol/L)	4.43±0.76	4.74±0.81	5.01±0.91	5.39±0.99	0.000
TG (mmol/L)	0.58±0.13	0.92±0.14	1.33±0.21	2.43±1.10	0.000
HDL (mmol/L)	1.51±0.30	1.48±0.29	1.43±0.28	1.34±0.28	0.000
LDL (mmol/L)	2.51±0.56	2.75±0.61	2.94±0.69	3.10±0.77	0.000
ALT (U/L)	12.70 (10.00–16.10)	13.70 (10.90–18.00)	15.00 (12.00–21.00)	18.75 (14.00–27.00)	0.000
AST (U/L)	19.20 (17.00–22.50)	20.00 (17.00–23.50)	21.00 (18.00–25.00)	23.30 (19.30–28.00)	0.000
BUN (mmol/L)	4.35±1.07	4.31±1.10	4.47±1.24	4.57±1.16	0.000
Ccr (μmol/L)	58.81±9.16	59.29±9.58	60.21±16.08	60.74±11.96	0.000
Smoking	4 (0.05%)	3 (0.05%)	5 (0.11%)	4 (0.14%)	0.022
Drinking	36 (0.45%)	42 (0.71%)	25 (0.57%)	19 (0.66%)	0.000
Family history of diabetes	176 (2.20%)	163 (2.74%)	149 (3.37%)	93 (3.23%)	0.000
Hypertension	347 (4.34%)	513 (8.62%)	698 (15.79%)	835 (29.03%)	0.000

T2DM, type 2 diabetes mellitus; *TyG*, triglyceride glucose index; *BMI*, body mass index; *SBP*, systolic blood pressure; *DBP*, diastolic blood pressure; *FPG*, fasting plasma glucose; *TC*, total cholesterol; *TG*, triglycerides; *HDL*, high-density lipoprotein; *LDL*, low-density lipoprotein; *ALT*, alanine aminotransferase; *AST*, aspartate aminotransferase; *BUN*, blood urea nitrogen; *Ccr*, creatinine clearance rate

Table 2 Relationship between TyG and incidence of T2DM by gender

	Non-adjusted		Model 1		Model 2		Model 3	
	HR (95% CI)	<i>p</i> -value	HR (95% CI)	<i>p</i> -value	HR (95% CI)	<i>p</i> -value	HR (95% CI)	<i>p</i> -value
Male								
TyG	3.17 (2.87, 3.50)	0.000	2.93 (2.65, 3.25)	<0.0001	2.31 (2.07, 2.58)	<0.000	1.68 (1.23, 2.28)	0.001
TyG quartile								
TyG Q1	1 (ref.)	—	1 (ref.)	—	1 (ref.)	—	1 (ref.)	—
TyG Q2	2.76 (1.73, 4.42)	0.000	2.32 (1.45, 3.72)	0.000	1.99 (1.25, 3.19)	0.004	1.48 (0.92, 2.37)	0.103
TyG Q3	4.88 (3.13, 7.61)	0.000	3.74 (2.40, 5.83)	0.000	2.76 (1.77, 4.32)	0.000	1.53 (0.97, 2.40)	0.067
TyG Q4	12.32 (8.05, 18.87)	0.000	9.11 (5.94, 13.96)	0.000	5.48 (3.55, 8.44)	0.000	2.03 (1.28, 3.21)	0.003
<i>p</i> for trend	0.000		0.000		0.000		0.000	
Female								
TyG	5.28 (4.66, 5.97)	0.000	3.51 (3.04, 4.04)	0.000	2.91 (2.50, 3.39)	<0.0001	3.59 (2.29, 5.65)	0.000
TyG quartile								
TyG Q1	1 (ref.)	—	1 (ref.)	—	1 (ref.)	—	1 (ref.)	—
TyG Q2	2.71 (1.68, 4.39)	0.000	2.01 (1.24, 3.26)	0.005	1.73 (1.06, 2.81)	0.028	1.35 (0.83, 2.21)	0.225
TyG Q3	9.00 (5.86, 13.82)	0.000	4.86 (3.13, 7.53)	0.000	3.64 (2.33, 5.68)	0.000	2.31 (1.46, 3.66)	0.000
TyG Q4	28.93 (19.25, 43.47)	0.000	11.74 (7.68, 17.95)	0.000	7.75 (5.01, 11.98)	0.000	3.11 (1.90, 5.10)	0.000
<i>p</i> for trend	0.000		0.000		0.000		0.000	

Model 1: adjusted for age; model 2: adjusted for age, BMI, SBP, DBP, smoking status, drinking status, and hypertension; model 3: adjusted for age, BMI, SBP, DBP, smoking status, drinking status, hypertension, family history of diabetes mellitus, TC, HDL, LDL, AST, ALP, BUN, and Ccr. Abbreviations: as in Table 1

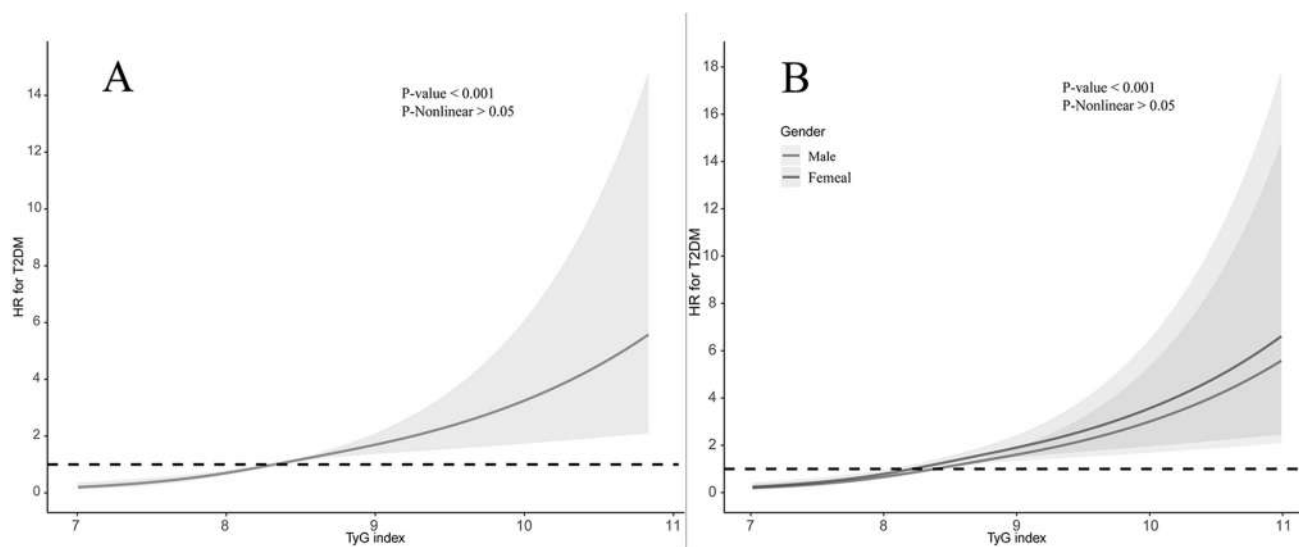


Fig. 1 **A** Relationship between Tyg index and T2DM in all patients. **B** Relationship between Tyg index and T2DM grouped by gender. T2DM, type 2 diabetes mellitus; TyG index, triglyceride glucose index

as compared to males (AUC = 0.721) ($p < 0.001$), refer to Fig. 2. The optimal cut-off value for females was 8.457, with a sensitivity of 0.708 and specificity of 0.794. For males, the optimal cut-off value was 8.784, with a sensitivity of 0.648 and specificity of 0.682 (Table 3).

Subgroup analyses

We conducted a subgroup analysis to investigate the gender differences in the association between TyG index and T2DM. Stratification by gender was performed among

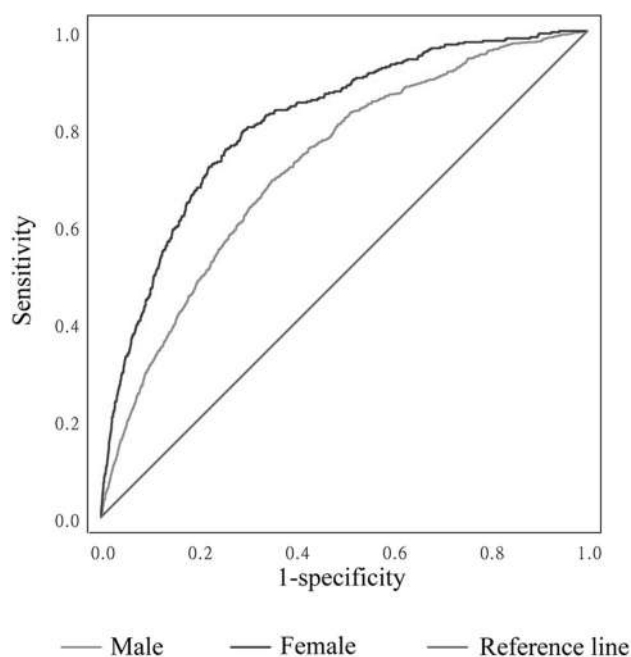


Fig. 2 TyG for predicting ROC curves in males and females with T2DM

Table 3 ROC analysis of TyG index for predicting T2DM in male and female

	AUC (95% CI)	Cutoff	Sensitivity	Specificity	<i>p</i> -value
Male	0.721 (0.704, 0.738)	8.784	0.648	0.692	0.000
Female	0.812 (0.791, 0.833)	8.457	0.708	0.794	

p-value was calculated by comparison with the AUC of males and females. AUC, area under the curve

different age groups, BMI groups, and participants with or without hypertension (Fig. 3). The risk of T2DM in females [HR (95% CI)=2.73 (2.70, 3.62)] was higher than that of males [HR (95% CI)=1.98 (1.52, 2.52)] (*p* for interaction <0.05). This gender difference was statistically significant across different age groups and those with hypertension (*p* for interaction <0.05), while no statistical differences were observed across different BMI levels and those without hypertension (*p* for interaction >0.05).

Discussion

In this extensive queue investigation, we have discovered a positive correlation between the TyG index and the risk of T2DM, particularly among females, highlighting its significant predictive value. It is noteworthy that for every incremental unit in the TyG index, the risk of T2DM increases

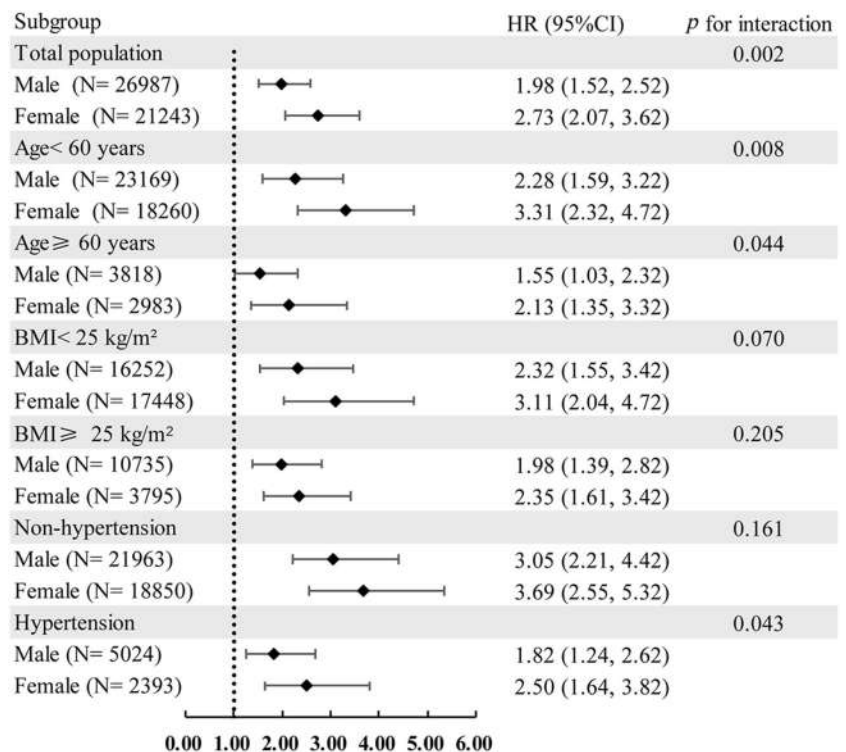
by 3.59 times for females and 1.68 times for males. Furthermore, our study findings suggest that across all subgroups, females generally face a higher risk of developing T2DM compared to males. These findings underscore the importance of the TyG index in assessing the risk of T2DM, particularly in females.

In previous studies, the TyG index has been shown to serve as a surrogate measure for insulin resistance and has demonstrated good predictive performance in the context of T2DM [20–23]. In a cohort study involving 5575 participants, after adjusting for other confounding factors, the TyG index was found to be associated with the incidence of T2DM. Furthermore, in comparison to TyG-BMI, TyG-WC, and TyG-WHtR, the TyG index was considered a more effective predictor of T2DM [14]. Our findings revealed a significant positive correlation between the TyG index and the risk of developing T2DM in both male and female. These results confirm the conclusion reached in previous research that the TyG index is an effective indicator of insulin resistance and the risk of T2DM. The progression of T2DM mainly involves diminished β -cell function and insulin resistance [24]. Elevated blood glucose levels increase oxidative stress, causing toxic damage to β -cells, leading to insulin resistance and the onset of T2DM [25]. Additionally, the excessive accumulation of TG within the β -cells interferes with the metabolic process of glucose, further impairing β -cell function [26]. When both fatty acids and glucose are elevated, the resulting metabolic products also damage the β -cells [27, 28]. Therefore, higher levels of TG and FPG affect the secretion of insulin and the extent of insulin resistance. Furthermore, our study found that across the entire range of the TyG index, its association with the incidence of T2DM is positively correlated without a clear inflection point, further validating the importance of the TyG index in predicting T2DM.

Past research has indicated significant disparities in the development of diabetes based on gender [29]. A cohort study focused on the Japanese population observed a more pronounced association between body roundness index (RBI) and T2DM in female [30]. Similarly, a cohort study in the Netherlands found that TG, visceral adiposity index (VAI), and lipid accumulation product (LAP) exhibited a stronger correlation with T2DM in females compared to males [31]. In our study, we discovered a notable gender difference in the association between TyG index and the risk of T2DM. Even after accounting for various confounding factors, we found that the risk of T2DM in females remained higher than in males. This finding underscores the significant role of gender in the link between TyG index and T2DM, further emphasizing the gender-specific impact on the onset of T2DM.

Subgroup analysis results demonstrate that regardless of age, BMI groups, or the presence of hypertension, females

Fig. 3 Subgroup analysis stratified by gender in different population groups. BMI, body mass index



still have a higher risk of developing T2DM compared to males, highlighting the importance of gender in assessing the risk of T2DM. Our research outcomes further corroborate previous findings, offering more specific and conclusive evidence, and underscore the propensity of females to develop T2DM. This discovery suggests the need for heightened attention to gender-specific factors in the prevention and management of T2DM. Various potential mechanisms may underlie the results arising from gender disparities. From a physiological perspective, estrogen exerts an impact on glucose metabolism and insulin sensitivity [32–34]. Consequently, the levels of sugar metabolism and insulin resistance in women may differ from those in men under different physiological circumstances, potentially partially explaining the increased risk of T2DM attributed to gender differences. Furthermore, females exhibit distinct physiological characteristics from males in terms of visceral fat distribution, hormone levels, and lipid metabolism. These disparities might be closely associated with the gender disparity in the relationship between TyG index and T2DM [17]. Therefore, the heightened risk of developing T2DM due to gender differences might result from the interaction of multiple physiological mechanisms.

Our research findings indicate significant gender disparities in the predictive performance of the TyG index for T2DM. In comparison to males, we discovered that the predictive value of the TyG index for T2DM is higher in females, with a greater AUC for females. This indicates a pronounced gender-specificity of the TyG index in

evaluating the risk of T2DM, demonstrating higher predictive accuracy in females. Therefore, it can be considered an important tool with a higher predictive value in assessing the risk of T2DM in females. Consistent with our research findings, previous studies have also identified gender differences in the predictive value of the TyG index. For instance, research by Yuling Xing et al. observed that the predictive effect of the TyG index on female T2DM risk is significantly superior to other biomarkers [14]. Additionally, Ming Zhang et al. found in their study that the predictive ability of the TyG index for female T2DM risk is higher than that for male [35]. These research findings further emphasize the predictive value of the TyG index in gender-specific assessments of T2DM risk, providing strong support for its application in clinical practice.

The results of our study suggest potential implications for the clinical management of T2DM. Given the high predictive efficacy demonstrated by the TyG index in women, it can be incorporated into the diabetes screening process in primary care settings, especially for women with a family history of diabetes, obesity, or who have experienced gestational diabetes [36]. By identifying high-risk individuals early, clinicians are able to initiate timely lifestyle interventions, regular monitoring, and medications as necessary to delay or prevent the onset of T2DM [37]. In addition, considering its simplicity and cost-effectiveness, the TyG index also has a high potential for application in large-scale population-based screening programs, which can help optimize the allocation of healthcare resources

and implement targeted interventions for high-risk groups [37]. In the future, in combination with other clinical parameters and biomarkers, a customized risk scoring system may further enhance prediction accuracy and support individualized medical strategies.

This study also has limitations. Firstly, lifestyle factors, such as diet, exercise, and other lifestyle factors that play an important role in the development of diabetes, were not taken into consideration. Therefore, a comprehensive assessment of their potential impact on the study results was not achieved. Secondly, this study primarily focused on the Chinese population, lacking research samples from other races or countries. The generalization of the results to other races or countries may be limited due to potential genetic, environmental, and lifestyle differences between different races or countries, which could affect the assessment of diabetes risk. Thirdly, the diagnosis of T2DM in this study was solely based on FPG levels, without utilizing the 2-h oral glucose tolerance test (OGTT) or glycosylated hemoglobin (HbA1c). This approach may underestimate the incidence of T2DM.

Conclusion

In summary, our study unveiled a positive association between the TyG index and T2DM risk, with superior predictive performance observed in women compared to men. These findings highlight the potential simplicity and effectiveness of the TyG index as a tool for assessing T2DM risk, especially in the female population.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s13410-024-01369-7>.

Acknowledgements We appreciate the contributors to the original data. These are Ying Chen, Xiao Ping Zhang, Jie Yuan, Bo Cai, Xiao Li Wang, Xiao Li Wu, Yue Hua Zhang, Xiao Yi Zhang, Tong Yin, Xiao Hui Zhu, Yun Juan Gu, Shi Wei Cui, Zhi Qiang Lu, and Xiao Ying Li.

Author contribution Rubing Guo conceived the study. Rubing Guo and Jingjing Tong conducted methodological research, software analysis, and data verification. Wei Zhao performed a formal analysis. Lianhua Wei and Wei Zhao provided writing guidance. All authors contributed to resource and data organization. Rubing Guo drafted the original manuscript. All authors have read and approved the published version of the manuscript.

Funding This work was supported by the National High Level Hospital Clinical Research Funding (grant number 2023-NHLHCRF-PY-04); the Wu Jieping Medical Foundation (grant number 320.6750.2023–06–60); and the Research Projects of Gansu Provincial Hospital (grant number 23GSSYD-25).

Data availability Publicly available datasets were analyzed in this study. This data can be found here: 10.5061/dryad.ft8750v.

Declarations

Ethics approval and consent to participate All patient data was anonymized to safeguard confidentiality, as the study involved retrospective data retrieval. Due to anonymization and the retrospective nature, individual patient consent was not required, as no interventions or collection of personally identifiable information occurred.

Consent for publication Not applicable.

Competing interests The authors declare no competing interests.

References

1. Sun H, Saeedi P, Karuranga S, Pinkepank M, Ogurtsova K, Duncan BB, et al. IDF Diabetes Atlas: global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. *Diabetes Res Clin Pract.* 2022;183:109119.
2. Ogurtsova K, Guariguata L, Barengo NC, Ruiz PL, Sacre JW, Karuranga S, et al. IDF Diabetes Atlas: global estimates of undiagnosed diabetes in adults for 2021. *Diabetes Res Clin Pract.* 2022;183:109118.
3. Cruz NG, Sousa LP, Sousa MO, Pietrani NT, Fernandes AP, Gomes KB. The linkage between inflammation and type 2 diabetes mellitus. *Diabetes Res Clin Pract.* 2013;99:85–92.
4. Guo R, Wei L, Cao Y, Zhao W. Normal triglyceride concentration and the risk of diabetes mellitus type 2 in the general population of China. *Front Endocrinol (Lausanne).* 2024;15:1330650.
5. Yin JL, Yang J, Song XJ, Qin X, Chang YJ, Chen X, et al. Triglyceride-glucose index and health outcomes: an umbrella review of systematic reviews with meta-analyses of observational studies. *Cardiovasc Diabetol.* 2024;23:177.
6. Park K, Ahn CW, Lee SB, Kang S, Nam JS, Lee BK, et al. Elevated TyG index predicts progression of coronary artery calcification. *Diabetes Care.* 2019;42:1569–73.
7. Wu Z, Zhou D, Liu Y, Li Z, Wang J, Han Z, et al. Association of TyG index and TG/HDL-C ratio with arterial stiffness progression in a non-normotensive population. *Cardiovasc Diabetol.* 2021;20:134.
8. Alizargar J, Bai CH, Hsieh NC, Wu SV. Use of the triglyceride-glucose index (TyG) in cardiovascular disease patients. *Cardiovasc Diabetol.* 2020;19:8.
9. Aktas G. Letter regarding “Associations of non-HDL-C and triglyceride/HDL-C ratio with coronary plaque burden and plaque characteristics in young adults.” *Biomol Biomed.* 2023;23:187.
10. Aktas G. Association between the Prognostic Nutritional Index and Chronic Microvascular Complications in Patients with Type 2 Diabetes Mellitus. *J Clin Med.* 2023;12(18):5952. <https://doi.org/10.3390/jcm12185952>.
11. Bilgin S, Aktas G, Atak T, Kurtkulagi O, Kahveci G, Duman T, et al. Triglyceride to high density lipoprotein cholesterol ratio is elevated in patients with complicated type 2 diabetes mellitus. *Acta Facultatis Medicae Naissensis.* 2022;39(1):66–73.
12. Mohd Nor NS, Lee S, Bacha F, Tfayli H, Arslanian S. Triglyceride glucose index as a surrogate measure of insulin sensitivity in obese adolescents with normoglycemia, prediabetes, and type 2 diabetes mellitus: comparison with the hyperinsulinemic-euglycemic clamp. *Pediatr Diabetes.* 2016;17:458–65.
13. Stern SE, Williams K, Ferrannini E, DeFronzo RA, Bogardus C, Stern MP. Identification of individuals with insulin resistance using routine clinical measurements. *Diabetes.* 2005;54:333–9.

14. Xing Y, Liu J, Gao Y, Zhu Y, Zhang Y, Ma H. Stronger associations of TyG index with diabetes than TyG-obesity-related parameters: more pronounced in young, middle-aged, and women. *Diabetes Metab Syndr Obes.* 2023;16:3795–805.
15. Greenhill C. Obesity: sex differences in insulin resistance. *Nat Rev Endocrinol.* 2018;14:65.
16. Xie Q, Kuang M, Lu S, Huang X, Wang C, Zhang S, et al. Association between MetS-IR and prediabetes risk and sex differences: a cohort study based on the Chinese population. *Front Endocrinol (Lausanne).* 2023;14:1175988.
17. Hadaegh F, Abdi A, Kohansal K, Hadaegh P, Azizi F, Tohidi M. Gender differences in the impact of 3-year status changes of metabolic syndrome and its components on incident type 2 diabetes mellitus: a decade of follow-up in the Tehran Lipid and Glucose Study. *Front Endocrinol (Lausanne).* 2023;14:1164771.
18. Chen Y, Zhang XP, Yuan J, Cai B, Wang XL, Wu XL, et al. Association of body mass index and age with incident diabetes in Chinese adults: a population-based cohort study. *BMJ Open.* 2018;8:e021768.
19. American Diabetes Association. 4. Comprehensive Medical Evaluation and Assessment of Comorbidities: Standards of Medical Care in Diabetes-2021. *Diabetes Care.* 2021;44(Suppl 1):S40–S52. <https://doi.org/10.2337/dc21-S004>.
20. Wen J, Wang A, Liu G, Wang M, Zuo Y, Li W, et al. Elevated triglyceride-glucose (TyG) index predicts incidence of prediabetes: a prospective cohort study in China. *Lipids Health Dis.* 2020;19:226.
21. Dikaiakou E, Vlachopapadopoulou EA, Paschou SA, Athanasouli F, Panagiotopoulos I, Kafetzi M, et al. Triglycerides-glucose (TyG) index is a sensitive marker of insulin resistance in Greek children and adolescents. *Endocrine.* 2020;70:58–64.
22. Pan L, Gao Y, Han J, Li L, Wang M, Peng H, et al. Comparison of longitudinal changes in four surrogate insulin resistance indexes for incident T2DM in middle-aged and elderly Chinese. *Front Public Health.* 2022;10:1046223.
23. Lee DY, Lee ES, Kim JH, Park SE, Park CY, Oh KW, et al. Predictive value of triglyceride glucose index for the risk of incident diabetes: a 4-year retrospective longitudinal study. *PLoS One.* 2016;11:e0163465.
24. Wu WC, Wei JN, Chen SC, Fan KC, Lin CH, Yang CY, et al. Progression of insulin resistance: a link between risk factors and the incidence of diabetes. *Diabetes Res Clin Pract.* 2020;161:108050.
25. Zhang P, Li T, Wu X, Nice EC, Huang C, Zhang Y. Oxidative stress and diabetes: antioxidative strategies. *Front Med.* 2020;14:583–600.
26. Den Hartogh DJ, Vlavcheski F, Giacca A, MacPherson REK, Tsiani E. Carnosic acid attenuates the free fatty acid-induced insulin resistance in muscle cells and adipocytes. *Cells.* 2022;11(1):167. <https://doi.org/10.3390/cells11010167>
27. Vilas-Boas EA, Almeida DC, Roma LP, Ortis F, Carpinelli AR. Lipotoxicity and β -Cell failure in type 2 diabetes: Oxidative stress linked to NADPH oxidase and ER stress. *Cells.* 2021;10(12):3328. <https://doi.org/10.3390/cells10123328>.
28. Plötz T, von Hanstein AS, Krümmel B, Laporte A, Mehmeti I, Lenzen S. Structure-toxicity relationships of saturated and unsaturated free fatty acids for elucidating the lipotoxic effects in human EndoC- β H1 beta-cells. *Biochim Biophys Acta Mol Basis Dis.* 2019;1865:165525.
29. Harreiter J, Kautzky-Willer A. Sex and gender differences in prevention of type 2 diabetes. *Front Endocrinol (Lausanne).* 2018;9:220.
30. Zhao W, Tong J, Li J, Cao Y. Relationship between body roundness index and risk of type 2 diabetes in Japanese men and women: a reanalysis of a cohort study. *Int J Endocrinol.* 2021;2021:4535983.
31. Brahimaj A, Rivadeneira F, Muka T, Sijbrands EJG, Franco OH, Dehghan A, et al. Novel metabolic indices and incident type 2 diabetes among women and men: the Rotterdam Study. *Diabetologia.* 2019;62:1581–90.
32. Kautzky-Willer A, Leutner M, Harreiter J. Sex differences in type 2 diabetes. *Diabetologia.* 2023;66:986–1002.
33. Tramunt B, Smati S, Grandgeorge N, Lenfant F, Arnal JF, Montagner A, et al. Sex differences in metabolic regulation and diabetes susceptibility. *Diabetologia.* 2020;63:453–61.
34. Kautzky-Willer A, Harreiter J, Pacini G. Sex and gender differences in risk, pathophysiology and complications of type 2 diabetes mellitus. *Endocr Rev.* 2016;37:278–316.
35. Zhang M, Wang B, Liu Y, Sun X, Luo X, Wang C, et al. Cumulative increased risk of incident type 2 diabetes mellitus with increasing triglyceride glucose index in normal-weight people: the Rural Chinese Cohort Study. *Cardiovasc Diabetol.* 2017;16:30.
36. Brown J, Grzeskowiak L, Williamson K, Downie MR, Crowther CA. Insulin for the treatment of women with gestational diabetes. *Cochrane Database Syst Rev.* 2017;11:Cd012037.
37. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med.* 2002;346:393–403.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Springer Nature or its licensor (e.g. a society or other partner) holds exclusive rights to this article under a publishing agreement with the author(s) or other rightsholder(s); author self-archiving of the accepted manuscript version of this article is solely governed by the terms of such publishing agreement and applicable law.