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Triglyceride glucose-waist circumference as a useful predictor for diabetes mellitus: a secondary retrospective analysis utilizing a Japanese cohort study

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Abstract

Background and objective While the connection between the Triglyceride glucose-waist circumference (TyG-WC) index and the risk of diabetes remains understudied, this particular research delves into the potential predictive value of the TyG-WC index within a significant Japanese population.

Methods This retrospective cohort study encompassed a comprehensive analysis of 15,413 Japanese adults, all of whom were diabetes-free at the outset of the study period from 2004 to 2015. Comprehensive medical records were obtained for all participants who underwent physical examinations. The study employed Cox proportional-hazards regression, smooth curve fitting, various sensitivity, and subgroup analyses to explore the association between TyG-WC and the development of diabetes. Furthermore, a Receiver Operating Characteristic (ROC) curve was created to detect the predictive capability of TyG-WC for diabetes risk.

Results After a maximum of 13.0 years of follow-up, 358 people finally developed diabetes. Upon adjusting for covariates, the result showed TyG-WC was positively and independently associated with incident Diabetes Mellitus (DM) (Hazard Ratio (HR): 1.004, 95%C: 1.001–1.006). Furthermore, ROC curve analysis demonstrated that TyG-WC outperformed both the triglycerides-glucose index and triglyceride glucose-body mass index in predicting the onset of diabetes.

Conclusion High levels of TyG-WC are autonomously linked to a heightened risk of diabetes in the Japanese demographic, indicating its potential as a dependable predictive indicator for diabetes mellitus in individuals at elevated risk.

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Keywords Triglyceride glucose-body mass index, TyG-WC, Incident diabetes mellitus, Insulin resistance

Introduction

Diabetes mellitus (DM) is a metabolic disorder characterized by persistent high blood sugar levels. During this process, insufficient insulin secretion or impaired cellular response to insulin results in ineffective entry of glucose into cells. Epidemiological statistics from 2019 indicate that approximately 463 million individuals worldwide were living with diabetes, representing an incidence rate of 9.3% [1]. Diabetes imposes a significant economic burden on both individuals and society as a whole [2]. The damage caused by diabetes is irreversible; however, the disease is preventable [3]. Therefore, it is crucial to comprehend the risk factors for diabetes to effectively prevent the disease.

Correlations have been established between diabetes and factors such as body weight, waist circumference (WC), fasting plasma glucose (FPG), and triglycerides [4, 5]. Dyslipidemia and obesity are significant contributors to the increased risk of incident diabetes and can be mitigated through lifestyle adjustments. These factors also serve as major risk factors for cardiovascular diseases associated with diabetes [6, 7]. Insulin resistance (IR) is recognized as a primary underlying factor in diabetes, with the triglyceride-glucose (TyG) index emerging as a novel and reliable measure for assessing IR [8]. The TyG index has shown potential in detecting metabolic conditions associated with IR, including type 2 diabetes mellitus (T2DM) [9–11]. A meta-analysis of 14 trials, including 270,229 participants, indicated that individuals with elevated TyG index levels were 2.54 times more likely to develop diabetes than those with lower TyG scores [12]. TyG-WC generated by Triglycerides (TG), Fasting Plasma Glucose (FPG), and WC have recently been shown to predict IR [13] more superior than glucose waistlines generated TyG alone. In a small sample survey, TyG-WC reliably predicted DM compared to the triglyceride glucose-Body Mass Index (TyG-BMI) and triglyceride glycosomal mass index [14]. Unfortunately, the study did not conduct subgroup analyses or demonstrate relationship between TyG-WC and DM. Moreover, the link between TyG-WC and DM in the Japanese population has not been fully studied. For this reason, our study was conducted to investigate the correlation between TyG-WC and DM in a substantial Japanese adult cohort and to clarify the quantitative link between TyG-WC and DM for practical clinical use.

Materials and methods

Data source

The data for this study was sourced from a research conducted by Takuro Okamura [15]. Researchers are permitted to utilize the data for secondary analysis in compliance with the Dryad terms of service, ensuring no harm is caused to the original authors.

Study participants

The study received approval from the First Affiliated Hospital Ethics Committee of Shenzhen University. The research adhered to the Declaration of Helsinki guidelines during the original investigation. Each aspect of the study, including the declarations.

Initially, the study included 20,944 Japanese individuals who had undergone physical examinations. Subsequently, 5,531 participants were excluded from the study, resulting in a final sample size of 15,413 participants (8387 men and 7026 women) for data analysis (refer to Fig. 1 for a detailed flowchart) [15]. Participants were excluded if they met any of the following criteria: 1) Diagnosed with Type 2 diabetes. 2) Known liver diseases or alcoholic fatty liver disease, defined as daily alcohol consumption > 40 g for men or > 20 g for women and a drinking history > 5 years. 3) Fasting plasma glucose (FPG) ≥ 6.1 mmol/L, as this indicates a prediabetic or diabetic state. 4) Missing data for covariates. 5) Taking medications that could influence metabolic parameters, including diabetes management drugs (e.g., insulin, oral hypoglycemic agents), lipid-lowering drugs (e.g., statins, fibrates), antihypertensive drugs (e.g., beta-blockers, ACE inhibitors), and other medications known to affect glucose or lipid metabolism. 6) Identified as having TyG-WC outliers, which were excluded to reduce the influence of extreme values on the analysis [16].

TyG-WC

The relationship between triglyceride glucose and waist size was handled as a continuous variable. The TyG-WC index is calculated by combining fasting plasma glucose (FPG) and triglycerides (TG) levels along with waist circumference (WC). The specific calculation formula is: [ln(TG(mg/dL)×FPG(mg/dL)/2)]×WC(cm). Where TG and FPG are measured in milligrams per deciliter (mg/dL), and WC is measured in centimeters (cm).) [14].

Diagnosis of incident diabetes

DM, a dichotomous variable with the values 1 for DM and 0 for non-DM, was our intriguing outcome variable. Participants with DM were those whose FPG was 7 mmol/l [17], whose HbA1c was not less than 6.5%, or who self-reported throughout the follow-up period.

The selection of variables for this study was informed. As covariates [15]: (1) The continuous variables considered in the study encompass age, BMI, alcohol

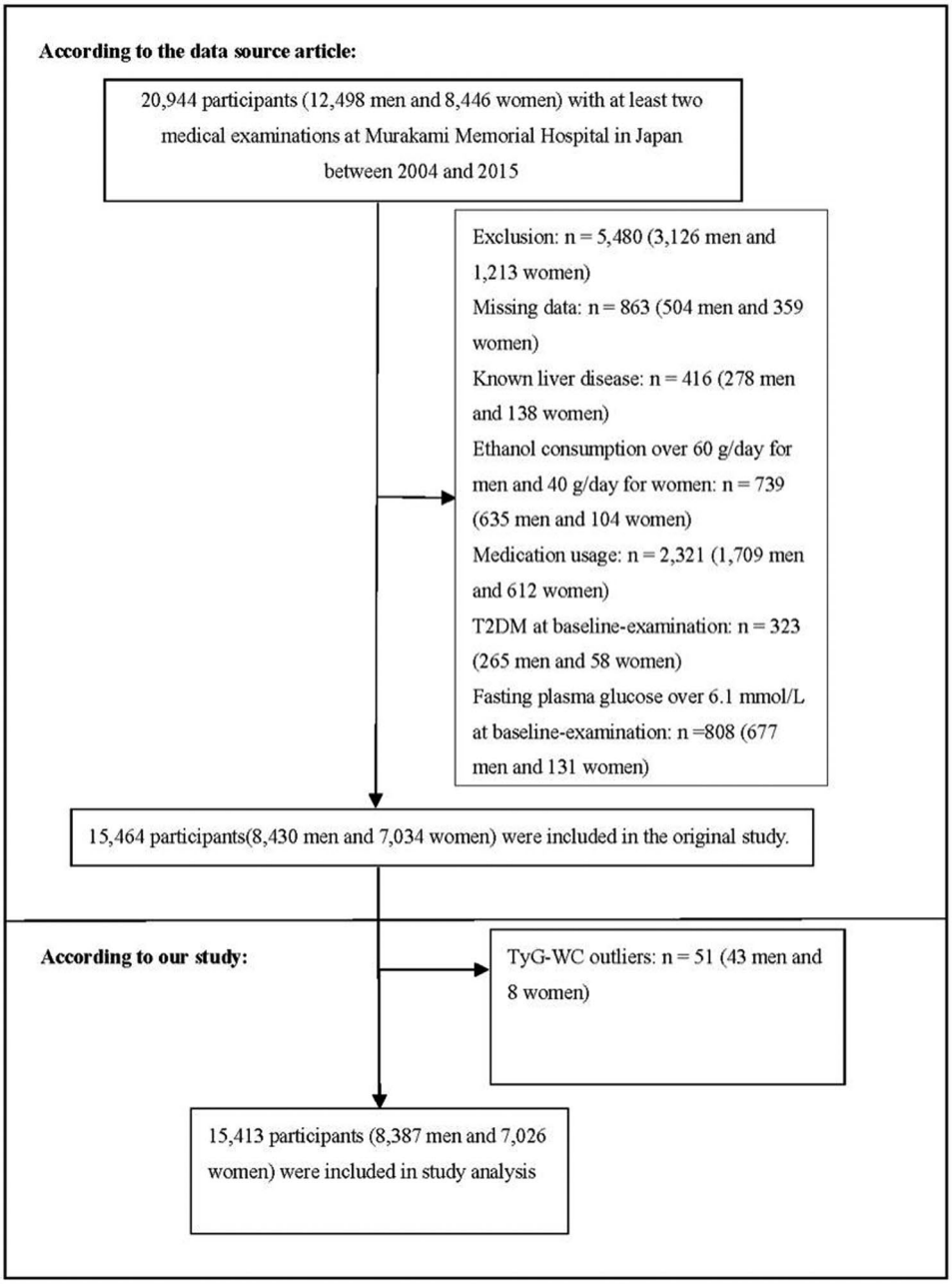

Fig. 1 Participant Flowchart. The flowchart provides a clear visual representation of the study's recruitment and exclusion criteria, ensuring transparency and allowing for the evaluation of potential selection biases

consumption, baseline levels of diastolic and systolic blood pressure, gamma-glutamyl transferase, AST, ALT, TC, HDL-C, and glycosylated hemoglobin. (2) Categorical variables: fatty liver, regular exerciser, smoking status, and gender. For the initial trial, data on each participant's lifestyle traits were acquired. The research team followed a standardized procedure to gather data from controlled laboratory tests [18]. The initial study determined the average weekly ethanol intake after evaluating the subjects' alcohol consumption over the course of the previous month. Following fasting for the previous night, venous blood was taken for the testing of hematological indicators. Based on the findings of an abdominal ultrasound, a skilled technician determined that the patient had fatty liver.

Statistical analysis

TyG-WC quartiles using R language and EmpowerStats software, and appropriate statistical methods were employed to present the data. Differences between

different TyG-WC groups were analyzed using chi-square tests, ANOVA, and Kruskal-Wallis H tests [19–20], and Kaplan-Meier methods were used to assess the diabetes-free survival probability [21, 22]. Cox regression models were used to analyze the association between TyG-WC and DM risks, taking into account nonlinear relationships. We employed a stratified approach to assess the relationship between TyG-WC and diabetes risk, accounting for various confounding factors. Here, we outline the established schemes for Model I, II, and III presented in Table 1: Model I: This minimally adjusted model includes age and gender as covariates to control for the basic demographic variations that could influence the relationship between TyG-WC and diabetes risk. Model II: Building on Model I, this model further adjusts for lifestyle factors such as smoking status, alcohol consumption, and physical activity, which are known to impact both metabolic health and diabetes risk. Model III: This fully adjusted model incorporates all the variables from Model II, as well as additional clinical parameters including BMI, systolic and diastolic blood pressure, and lipid profiles (HDL-C, and LDL-C), to provide a comprehensive assessment of the independent association between TyG-WC and incident diabetes. Furthermore, in other sensitivity analyses, we disregarded persons who had fatty livers. TyG-WC was also shown to be positively linked with DM risk [23, 24]. The models were evaluated using generalized additive models (GAM) [25]. Finally, the predictive value for DM risk were assessed through ROC curve analysis [20, 26]. All results adhered to the STROBE statement, with p-value < 0.05 considered statistically significant.

Table 1 The Association between TyG-WC and Incident Diabetes in various models

Variable	Crude model (HR.,95% CI, *P*)	Model I (HR,95% CI, *P*)	Model II (HR,95% CI, *P*)	Model III (HR,95% CI, *P*)
TyG-WC	1.009 (1.008, 1.010) < 0.00001	1.005 (1.004, 1.007) < 0.00001	1.004 (1.001, 1.006) 0.00072	1.003 (1.001, 1.005) 0.00102
TyG-WC (quartile)				
Q1	ref	ref	ref	ref
Q2	2.638 (1.474, 4.721) 0.00109	1.751 (0.962, 3.184) 0.06662	1.466 (0.797, 2.694) 0.21823	1.462 (0.749, 2.855) 0.27851
Q3	4.702 (2.737, 8.078) < 0.00001	1.930 (1.058, 3.521) 0.03204	1.465 (0.791, 2.713) 0.22483	1.624 (0.788, 3.342) 0.19843
Q4	14.477 (8.722, 24.031) < 0.00001	2.905 (1.513, 5.578) 0.00135	1.763 (0.879, 3.536) 0.11052	1.986 (0.895, 4.405) 0.09214
P for trend	< 0.00001	0.00074	0.15512	0.09250

Note. Crude model: This unadjusted model evaluates the direct association between TyG-WC and diabetes risk without adjusting for any covariates. It represents the raw relationship, providing a baseline estimate of the risk before accounting for potential confounding factors. Model I: This minimally adjusted model includes age and gender as covariates to control for the basic demographic variations that could influence the relationship between TyG-WC and diabetes risk. Model II: Building on Model I, this model further adjusts for lifestyle factors such as smoking status, alcohol consumption, and physical activity, which are known to impact both metabolic health and diabetes risk. Model III: This fully adjusted model incorporates all the variables from Model II, as well as additional clinical parameters including BMI, systolic and diastolic blood pressure, and lipid profiles (HDL-C, and LDL-C), to provide a comprehensive assessment of the independent association between TyG-WC and incident diabetes

Results

Participants characteristics

Table 2 displays: Final analysis included 15,413 participants, of which 54.42% were male (Fig. 1). The participants had an average age of 43.72 ± 8.90 years. The follow-up duration ranged up to 13.0 years, with a median follow-up period of 5.4 years, 358 people finally developed diabetes.

The BMI, WC, TG, FPG, and TyG-WC were 22.08 ± 3.06 kg/m^2, and 76.37 ± 8.93 cm, 80.35 ± 57.23 mg/dL, 92.94 ± 7.43 mg/dL and 616.10 ± 105.88. We assigned participants into subgroups using TyG-WC quartiles (≤ 533.92, 533.92-608.15, 608.15-689.03, > 689.03). I In the highest TyG-WC group, participants tended to have higher values for age, SBP, DBP, BMI, WC, ALT, AST, GGT, TG, TC, HbA1c, FPG, and TyG. Additionally, they exhibited higher proportions of men, smokers, and heavy drinkers, along with lower HDL-C levels and lower rates of regular physical exercise. The distribution of TyG-WC levels was displayed in Fig. 2. With an average of 616.10 and a range of 339.45 to 940.03, it displayed a normal distribution. The participants were divided into two groups based on their diabetes mellitus (DM) status. Figure 3 illustrates the TyG-WC values for each group, showing that the DM group had higher levels of TyG-WC compared to the non-DM group. In age stratification with 10-year intervals, male participants exhibited a higher prevalence of DM than female participants across all age groups (Fig. 4). Moreover, we discovered that both among male and female individuals, the prevalence of DM rose with advancing age.

The incidence rate of diabetes

During the follow-up period, a total of 358 individuals developed incident diabetes, as detailed in Table 3. The overall incidence rate among all participants was 2.32% (95% CI: 2.08-2.56%). Specifically, the incidence rates for the four TyG-WC groups were 0.42% (95% CI: 0.21-0.62%), 1.01% (95% CI: 0.70-1.33%), 1.92% (95% CI: 1.49-2.35%), and 5.94% (95% CI: 5.20-6.69%), respectively. Furthermore, the cumulative incidence rates for

Table 2 The baseline characteristics of participants

TyG-WC	Q1(≤ 533.92)	Q2(533.92 to ≤ 608.15)	Q3(608.15 to ≤ 689.03)	Q4 > 689.03	*P*-value
Participants	3853	3853	3853	3854	
Gender					< 0.001
Women	3251(84.38%)	2108 (54.71%)	1133 (29.41%)	534 (13.86%)	
Men	602(15.62%)	1745 (45.29%)	2720 (70.59%)	3320(86.14%)	
Age(years)	40.61 ± 8.29	43.38 ± 8.86	45.23 ± 8.89	45.64 ± 8.66	< 0.001
Baseline Alcohol consumption					< 0.001
non	3252 (84.40%)	2790 (72.41%)	2471 (64.13%)	2224 (57.71%)	
light	437 (11.34%)	683 (17.73%)	814 (21.13%)	849 (22.03%)	
moderate	141 (3.66%)	292 (7.58%)	403 (10.46%)	517 (13.41%)	
heavy	23 (0.60%)	88 (2.28%)	165 (4.28%)	264 (6.85%)	
Smoking status					< 0.001
Never-smoker	3123 (81.05%)	2485 (64.50%)	1919 (49.81%)	1480 (38.40%)	
Ex-smoker	335 (8.69%)	629 (16.32%)	885 (22.97%)	1098(28.49%)	
Current-smoker	395 (10.25%)	739 (19.18%)	1049 (27.23%)	1276(33.11%)	
Regular exerciser					< 0.001
No	3200 (83.05%)	3104 (80.56%)	3123 (81.05%)	3281 (85.13%)	
Yes	653 (16.95%)	749 (19.44%)	730 (18.95%)	573 (14.87%)	
SBP (mmHg)	105.54 ± 12.32	111.39 ± 13.00	117.33 ± 13.64	123.43 ± 14.37	< 0.001
DBP (mmHg)	65.31 ± 8.50	69.25 ± 9.32	73.50 ± 9.59	78.08 ± 9.87	< 0.001
BMI (kg/m^2)	19.22 ± 1.68	20.99 ± 1.76	22.73 ± 1.93	25.38 ± 2.65	< 0.001
WC (cm)	66.13 ± 4.33	73.12 ± 3.83	79.18 ± 3.84	87.05 ± 5.76	< 0.001
Fatty liver					< 0.001
No	3841 (99.69%)	3701 (96.06%)	3237 (84.01%)	1939 (50.31%)	
Yes	12 (0.31%)	152 (3.94%)	616 (15.99%)	1915 (49.69%)	
ALT (IU/L)	13 (11, 17)	15 (12, 19)	18 (14, 23)	24 (18, 34)	< 0.001
AST (IU/L)	16 (13, 19)	16 (13, 20)	17 (14, 21)	20 (16,24)	< 0.001
HDL-C (mg/dL)	66.95 ± 14.63	60.74 ± 14.43	53.41 ± 12.85	45.26 ± 10.87	< 0.001
TG (mg/d)	37 (28, 49)	55 (43, 70)	75 (59, 97)	124 (93, 168)	< 0.001
TC (mg/d)	185.47 ± 30.74	193.70 ± 32.17	201.60 ± 31.87	211.64 ± 32.93	< 0.001
HbA1c (%)	5.11 ± 0.30	5.15 ± 0.31	5.18 ± 0.32	5.24 ± 0.34	< 0.001
FPG (mg/dL)	88.14 ± 6.68	91.73 ± 6.79	94.58 ± 6.54	97.32 ± 6.42	< 0.001
TyG-WC	487.77 ± 33.21	571.45 ± 21.76	646.77 ± 23.27	758.36 ± 55.50	< 0.001

Values are n(%) or mean ± SD

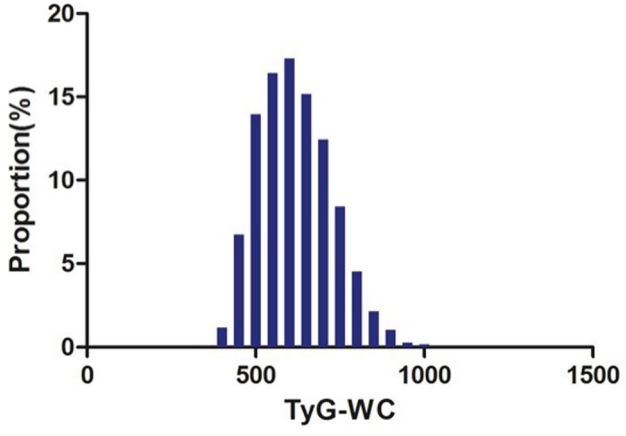

Fig. 2 Distribution of TyG-WC (ranging from 339.45 to 940.03) displayed a normal distribution. The TyG-WC values are plotted on the x-axis, while the frequency of participants within each TyG-WC range is shown on the y-axis

the entire population and the four TyG-WC groups were 383.87 per 100,000 person-years, 67.31 per 100,000 person-years, 172.44 per 100,000 person-years, 317.76 per 100,000 person-years, and 970.99 per 100,000 person-years, respectively. Participants with high TyG-WC levels had a significantly higher incidence of diabetes compared to those in the lowest TyG-WC group ($P < 0.0001$ for trend), as illustrated in Fig. 5.

Univariate analysis

Table 4 displays: The findings indicated positive relationships between age, heavy alcohol consumption, smoking habits, SBP, DBP, BMI, WC, TG, TC, HbA1c, FPG, and TyG-WC with diabetes risk. Conversely, HDL-C was negatively correlated with the risk of diabetes in the univariate analysis. Male participants exhibited a higher likelihood of developing diabetes compared to females. Figure 6 displays the Kaplan-Meier curves illustrating the probability of diabetes-free survival.

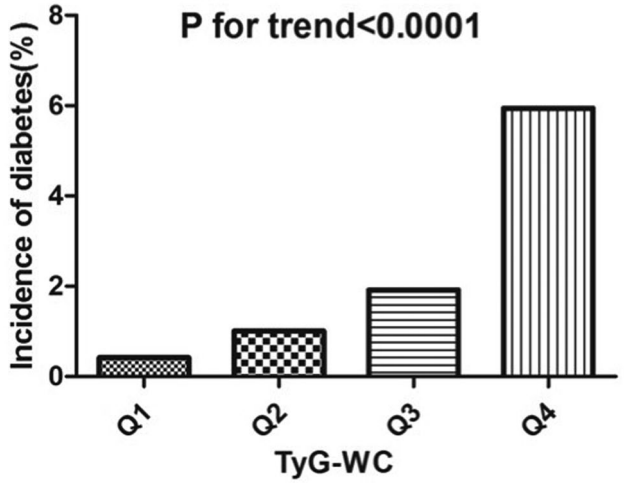

Fig. 3 Visualization of TyG-WC in participants from the DM and non-DM groups. The boxplot displays the median, interquartile range, and any potential outliers for both groups, allowing for a visual comparison of the central tendency and variability of TyG-WC in relation to the development of DM

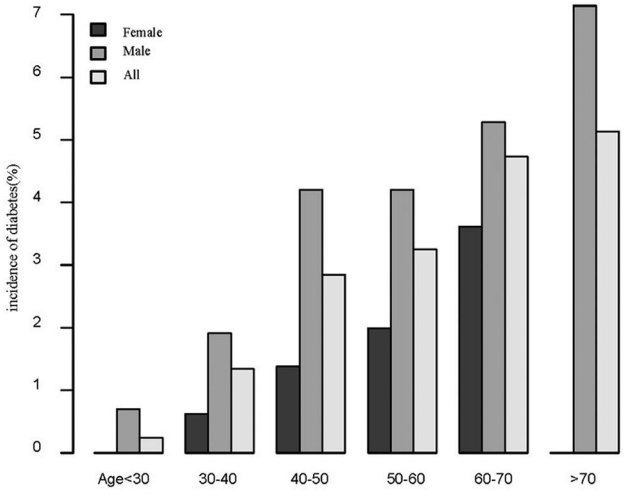

Fig. 4 Prevalence of DM across age stratification intervals of 10 years. The x-axis represents the age groups, while the y-axis displays the prevalence of DM. The figure highlights any trends or patterns in DM prevalence as age increases, with male and female participants shown separately to account for potential gender differences

Table 3 Incidence rate of incident diabetes

TyG-WC	Participants(*n*)	DM events(*n*)	Cumulative incidence (95% CI)(%)	Per 100,000 person-year
Total	15,413	358	2.32(2.08–2.56)	383.87
Q1	3,853	16	0.42(0.21–0.62)	67.31
Q2	3,853	39	1.01(0.70–1.33)	172.44
Q3	3,853	74	1.92(1.49–2.35)	317.76
Q4	3,854	229	5.94(5.20–6.69)	970.99

The association between TyG-WC and the onset of diabetes

An increase of 1 unit in TyG-WC was linked in the unadjusted model to a 0.9% increase in the probability of developing diabetes (HR:1.009, 95% CI:1.008 to 1.010, $P<0.001$). The outcomes were statistically noteworthy. Each additional unit of TyG-WC could result in an enhanced risk of DM by 0.5% in the minimum adjusted model (HR: 1.005, 95% CI: 1.004 to 1.007, $P<0.001$). The fully adjusted model did not appear to change as a result of the findings. Each additional unit of TyG-WC was associated with a 0.3% increase in the risk of developing diabetes (HR: 1.003, 95% CI: 1.001–1.005, $P=0.00102$). The revised confidence interval underscores the model's robustness in estimating the association between TyG-WC and diabetes risk, and the results are consistent with the previous analysis (Refer to Table 1 for more details).

Sensitive analysis

According to the findings after controlling for confounding variables (HR:1.001, 95% CI: 0.998 to 1.004) (Table 5). Participants who consumed alcohol were likewise not included in the sensitivity analysis. The outcomes of the sensitivity analysis further validated the dependability and uniformity of our results.

The analyses of the non-linear relationship

In Fig. 7, we observed a non-linear relationship between TyG-WC and diabetes risk, analyzed using a GAM. The smooth curve fitting indicates that the risk of diabetes remains relatively stable at lower TyG-WC levels but increases sharply as TyG-WC exceeds a certain threshold. This trend was further examined using Cox proportional hazards regression, adjusting for confounders such as gender, age, alcohol consumption, smoking habits, physical activity, and biochemical markers including GGT, ALT, HDL-C, AST, and TC. The results revealed a significant increase in diabetes risk with higher levels of TyG-WC ($P<0.001$), consistent with the non-linear trend depicted in Fig. 7. These findings suggest that while lower TyG-WC levels have limited impact on diabetes risk, higher levels are associated with a disproportionate increase in risk, highlighting the importance of monitoring individuals with elevated TyG-WC.

The subgroup analysis

Regarding the stratification of liver enzymes in Table 6, the high and low groups for Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), and Gamma-Glutamyl Transferase (GGT) were defined based on their respective median values within the study population: ALT: Participants were categorized into low ALT group (below the median value of 30 U/L) and high ALT group (at or above the median value). AST: The low AST group consisted of individuals with values below the median

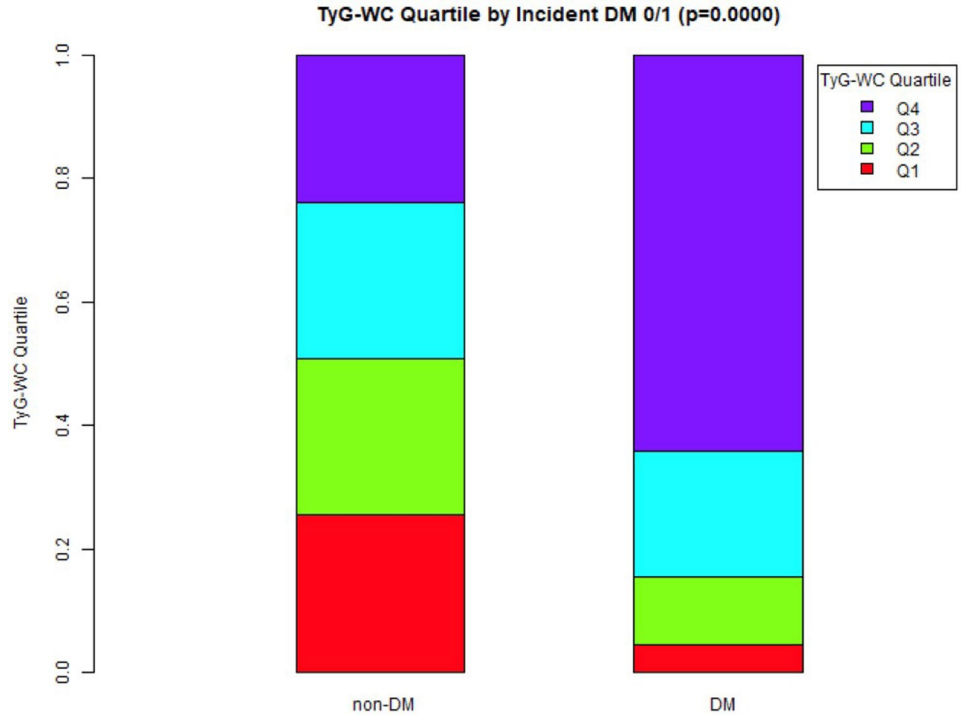

Fig. 5 Cumulative DM prevalence based on TyG-WC quartiles. Participants with high TyG-WC showed significantly higher cumulative DM prevalence compared to the lowest TyG-WC group ($p < 0.001$ for trend). The x-axis represents the TyG-WC quartiles, and the y-axis shows the cumulative prevalence of DM

of 25 U/L, while the high AST group had values at or above the median. GGT: For GGT, the boundary was set at the median value of 40 U/L, with participants below this value classified as the low GGT group and those at or above as the high GGT group. These stratifications allowed us to explore the modifying effects of liver function on the relationship between TyG-WC and diabetes risk, providing insights into potential mechanistic pathways. A stronger association was observed in individuals with high levels of ALT and AST (Hazard Ratio (HR): 1.004, 95% Confidence Interval (CI): 1.002–1.007; HR: 1.005, 95% CI: 1.003–1.007, respectively). Conversely, the association between TyG-WC and diabetes risk was not significant in those with low ALT and AST levels (HR: 0.999, 95% CI: 0.995–1.004; HR: 0.998, 95% CI: 0.994–1.003, respectively). These findings suggest that the relationship between TyG-WC and incident diabetes remained robust across most subgroups(see Table 6).

ROC curve analysis

Furthermore, a ROC curve was constructed to evaluate the predictive performance for diabetes risk assessment (Fig. 8). The Area Under the Curve (AUC) was largest for TyG-WC in predicting diabetes (AUC: 0.772, 95% CI: 0.7479–0.7964, $P < 0.0001$), followed by TyG-Body Mass Index (BMI) (AUC: 0.7662, 95% CI: 0.7416–0.7909, $P < 0.0001$) and TyG index (AUC: 0.7441, 95% CI: 0.7185–0.7698, $P < 0.0001$). The superior AUC value of TyG-WC indicates its higher predictive capability for incident diabetes compared to the other variables (see Table 7).

Discussion

The HR for TyG-WC observed in our study was small (HR: 1.001 per unit increase, 95% CI: 0.998–1.004), and its confidence interval includes 1, suggesting the need for cautious interpretation. However, while the incremental risk per unit increase may appear modest, the clinical relevance of TyG-WC lies in its cumulative impact across its wide range of values (339.45 to 940.03) and its ability to stratify diabetes risk effectively across quartiles. This is further supported by the ROC analysis, where an AUC of 0.772 highlights TyG-WC's comparable predictive capability compared to other indices such as the TyG index and TyG-BMI [27, 28]. Furthermore, previous studies have shown that HOMA-IR, a widely used marker of insulin resistance, exhibits an AUC ranging about 0.60 in predicting diabetes risk depending on the population studied [29]. Similarly, OGTT, considered a gold standard for diagnosing impaired glucose tolerance, typically demonstrates high predictive accuracy but requires invasive and time-consuming procedures [30]. Compared to these established methods, TyG-WC offers a practical advantage due to its simplicity, non-invasiveness, and

Table 4 The results of the univariate analysis

	Statistics	HR (95% CI)	*P* value
Gender			
Women	7026 (45.58%)	ref	
Men	8387 (54.42%)	2.51 (1.97, 3.21)	< 0.0001
Age(years)	43.72 ± 8.90	1.06 (1.05, 1.07)	< 0.0001
Baseline Alcohol consumption			
non	10,737 (69.66%)	ref	
light	2783 (18.06%)	1.01 (0.77, 1.33)	0.9402
moderate	1353 (8.78%)	1.19 (0.84, 1.70)	0.3261
heavy	540 (3.50%)	2.39 (1.63, 3.49)	< 0.0001
Smoking status			
Never-smoker	9007 (58.44%)	ref	
Ex-smoker	2947 (19.12%)	1.71 (1.30, 2.27)	0.0002
Current-smoker	3459 (22.44%)	2.60 (2.06, 3.28)	< 0.0001
Regular exerciser			
No	12,708 (82.45%)	ref	
Yes	2705 (17.55%)	0.77 (0.57, 1.04)	0.0921
SBP (mmHg)	114.42 ± 14.93	1.03 (1.02, 1.04)	< 0.0001
DBP (mmHg)	71.53 ± 10.48	1.05 (1.04, 1.06)	< 0.0001
BMI (kg/m^2)	22.08 ± 3.06	1.27 (1.23, 1.30)	< 0.0001
WC (cm)	76.37 ± 8.93	1.10 (1.09, 1.11)	< 0.0001
Fatty liver			
No	12,718 (82.51%)	ref	
Yes	2695 (17.49%)	6.64 (5.38, 8.19)	< 0.0001
ALT (IU/L)	19.90 ± 14.22	1.01 (1.01, 1.01)	< 0.0001
AST (IU/L)	18.37 ± 8.61	1.01 (1.01, 1.01)	< 0.0001
HDL-C (mg/dL)	56.59 ± 15.56	0.95 (0.94, 0.96)	< 0.0001
TG (mg/dL)	80.35 ± 57.23	1.01 (1.01, 1.01)	< 0.0001
TC (mg/dL)	198.10 ± 33.37	1.01 (1.01, 1.01)	< 0.0001
HbA1c (%)	5.17 ± 0.32	55.63 (40.21, 76.97)	< 0.0001
FPG (mg/dL)	92.94 ± 7.43	1.19 (1.17, 1.22)	< 0.0001
TyG-WC	616.10 ± 105.88	1.01 (1.01, 1.01)	< 0.0001

Values are n(%) or mean ± SD

Table 5 The relationship between TyG-WC and incident diabetes in various sensitivity anal

Exposure	Modell (HR,95%CI, *P*)	Model II (HR,95%CI, *P*)
TyG-WC	1.001 (0.998, 1.004) 0.58245	1.005 (1.001, 1.009) 0.02874
TyG-WC (quartile)		
Q1	Ref	Ref
Q2	1.548 (0.794, 3.019) 0.20000	1.613 (0.566, 4.594) 0.37046
Q3	1.441 (0.690, 3.011) 0.33048	1.796 (0.594, 5.429) 0.29959
Q4	1.696 (0.697, 4.125) 0.24420	2.848 (0.754, 10.755) 0.12271
P for trend	0.41645	0.12450

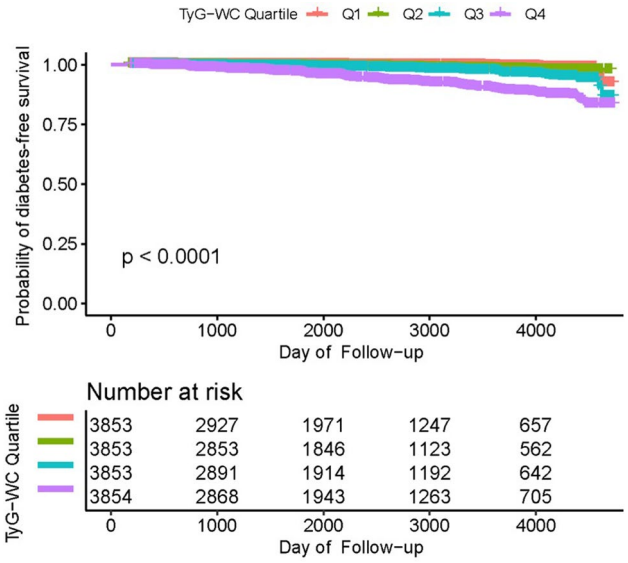

Fig. 6 Kaplan-Meier event-free survival curve. the Kaplan-Meier survival curve for the probability of remaining free from diabetes mellitus (DM) over time. The curve shows the proportion of participants who have not developed DM at various time points during the follow-up period

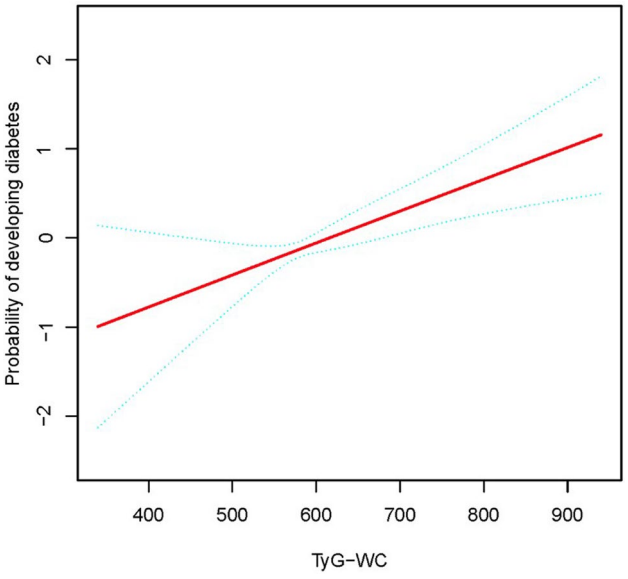

Fig. 7 Non-linear relationship between TyG-WC and incident diabetes, indicating a non-linear association after adjusting for various factors

reliance on routine clinical measurements. While the AUC of TyG-WC is comparable to HOMA-IR, its accessibility makes it more suitable for large-scale population screening and resource-limited settings. Nevertheless, direct comparative studies between TyG-WC, HOMA-IR, and OGTT are warranted to validate these findings and explore their complementary roles in diabetes risk stratification.

As a composite measure incorporating fasting plasma glucose, triglyceride levels, and waist circumference,

Table 6 Impact of TyG-WC on diabetes in Prespecified and exploratory subgroups

Characteristic	No of patients	Effect size(95%CI)	*P* value	*P* for interaction
Age(years)				0.8054
<60	14,701	1.004 (1.002, 1.006)	0.0001	
≥ 60	712	1.005 (0.998, 1.013)	0.1725	
Gender				0.2293
Women	7026	1.006 (1.002, 1.009)	0.0036	
Men	8387	1.003 (1.001, 1.005)	0.0082	
Ethanol consumption (g/week)				0.2348
0	4717	1.005 (1.002, 1.007)	0.0003	
> 0	10,696	1.003 (1.001, 1.006)	0.0012	
Smoking status				0.4882
Never-smoker	9007	1.004 (1.001, 1.008)	0.0116	
Ex-smoker	2947	1.005 (1.000, 1.009)	0.0527	
Current-smoker	3459	1.002 (0.999, 1.005)	0.2007	
Regular exerciser				0.5797
No	12,708	1.004 (1.001, 1.006)	0.0011	
Yes	2705	1.005 (1.000, 1.009)	0.0351	
SBP (mmHg)				0.6649
<140	14,648	1.004 (1.002, 1.006)	0.0006	
≥ 140	765	1.002 (0.997, 1.008)	0.4237	
DBP (mmHg)				0.6398
<90	14,666	1.004 (1.002, 1.006)	0.0007	
≥ 90	747	1.002 (0.995, 1.009)	0.5427	
BMI (kg/m^2)				0.5635
<25	12,939	1.003 (1.001, 1.005)	0.0029	
≥ 25	2474	1.004 (1.002, 1.006)	0.0009	
Fatty liver				0.1077
No	12,718	0.002 (1.000, 1.005)	0.0642	
Yes	2695	1.004 (1.002, 1.007)	0.0001	
ALT				0.0431
Low	7580	0.999 (0.995, 1.004)	0.7592	
High	7833	1.004 (1.002, 1.007)	0.0001	
AST				0.0063
Low	6783	0.998 (0.994, 1.003)	0.4820	
High	8630	1.005 (1.003, 1.007)	< 0.0001	
GGT				0.5222
Low	7245	1.002 (0.997, 1.007)	0.4094	
High	8168	1.004 (1.001, 1.006)	0.0012	

TyG-WC reflects critical metabolic disruptions, including IR and β-cell dysfunction, which are key in the pathogenesis of type 2 diabetes [13, 14]. The robustness of these findings across multiple analytical methods underscores its potential as a non-invasive supplementary tool for early diabetes risk assessment and its broader applicability in population-level health management. The biological mechanisms underlying the TyG-WC index's association with DM risk may involve several pathways. Firstly, insulin resistance is characterized by the body's reduced ability to respond to insulin, leading to impaired glucose homeostasis [31]. The product of triglycerides and glucose may serve as a surrogate measure of IR, as elevated levels can impair insulin signaling and action [32]. Secondly, chronic low-grade inflammation, common in individuals with IR, has been linked to the development of type 2 diabetes [33]. Inflammatory cytokines can interfere with insulin signaling pathways, exacerbating IR and glucose intolerance [34]. The TyG-WC index may capture this inflammatory component, as adipose tissue, expanded in insulin-resistant states, is a significant source of pro-inflammatory cytokines [35]. Lastly, dysregulated lipid metabolism, particularly elevated fasting triglycerides, has been associated with increased hepatic glucose production and decreased glucose uptake by peripheral tissues, contributing to hyperglycemia and diabetes risk [36]. Our findings underscore the importance of monitoring individuals with higher TyG-WC levels, as they may represent a critical threshold for targeted interventions.

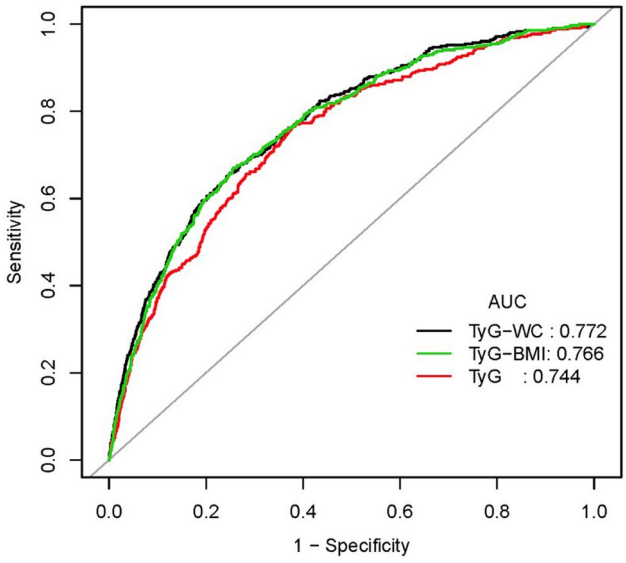

Fig. 8 ROC curve analysis results evaluating the predictive ability of TyG, TyG-BMI, and TyG-WC for diabetes risk assessment. The x-axis represents the false positive rate, while the y-axis shows the true positive rate. The area under the curve (AUC) for each index is displayed, with a larger AUC indicating better predictive performance for DM risk assessment

Our study also suggests that ALT and AST may act as effect modifiers in the relationship between TyG-WC and incident DM. Higher levels of these liver enzymes have been associated with hepatic IR and the development of DM [37, 38].In the context of the Japanese population, our incidence rate of DM (3.84 per 1000 people per year) is lower than the national average (8.8 cases per 1000 individuals per year), likely due to the exclusion criteria of our study [39]. This underscores the need to identify additional risk factors in the management of DM, as risk factors such as frequent drinking, viral hepatitis, and elevated fasting plasma glucose levels were excluded from our study population [39].

Our findings are consistent with a prospective cohort study that found the greatest TyG-WC values were associated with a 3.69-fold higher risk of diabetes (HR: 3.69, 95%CI 1.65–8.28) [14]. This further supports the predictive value of TyG-WC in diabetes risk assessment. We adjusted for additional biochemical factors such as BMI, alcohol intake, smoking status, regular exercise, fatty liver, ALT, AST, GGT, and HbA1c, which have been linked to diabetes risk [40, 41].

While our study provides valuable insights, it has limitations. Firstly, our findings are specific to the Japanese population, and further research is needed to determine if these results are generalizable to other ethnic groups. Secondly, we were unable to account for certain factors such as insulin concentration and LDL-C levels in our analysis, which may have influenced our results [40, 41]. Thirdly, the absence of information on deaths during the follow-up period and the lack of a 2-hour oral glucose tolerance test may have led to an underestimation of DM prevalence [42]. Moreover, the strict exclusion criteria may reduce the generalizability of our results. Future research should aim to validate these findings in more diverse cohorts, including populations with higher baseline risks. This would provide a more comprehensive understanding of TyG-WC's predictive capabilities and its applicability across different demographic and clinical contexts. Moreover, we acknowledge certain limitations in the scope of the variables considered. Specifically, key biomarkers such as insulin levels, insulin resistance markers, C-reactive protein (CRP), and genetic factors were not included in this study due to limitations in the available dataset. These factors are known to influence metabolic health and diabetes risk, and their inclusion in future studies could enhance the comprehensiveness of the analysis. Further research incorporating these variables is needed to validate our findings and explore potential mechanisms underlying the observed associations.

Conclusion

In conclusion, our study provides evidence that TyG-WC is independently associated with diabetes risk in a large Japanese cohort. While the observed hazard ratio is modest, the consistent associations across different analyses highlight its potential role as a supplementary predictive tool for identifying at-risk individuals. We acknowledge the limitations of our findings and emphasize the need for further studies to confirm these results in diverse populations and under varying clinical contexts.

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Author contributions
Yawei Li, Linlin Shan and Qiong Wen made significant contributions to research design, specific experimental process management, data analysis, and manuscript writing; Changchun Cao made significant contributions to research design and data analysis; Meiling Huang made significant contributions to experimental technical support and results section; Chunxia Zhang contributed to research design; Xiaoping Li, Kun Wang and Tianlun Zhou contributed to experimental operation and data collection; Fubing Zha and Yulong Wang made significant contributions to research design and manuscript review process. All authors reviewed the manuscript.

Table 7 AUROC each parameter assessed in diabetes identification

Test	AUROC	95%CI	Best threshold	Specificity	Sensitivity	Youden Index	*P*
TyG	0.7441	0.7185–0.7698	8.1960	0.6212	0.7654	0.3866	< 0.0001
TyG-BMI	0.7662	0.7416–0.7909	197.2987	0.7433	0.6704	0.4137	< 0.0001
TyG-WC	0.7721	0.7479–0.7964	685.5660	0.7502	0.6592	0.4094	< 0.0001

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Data availability
The data used to support the findings of this study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study received approval from the First Affiliated Hospital Ethics Committee of Shenzhen University. Informed consent was obtained from all the participants. The research adhered to the Declaration of Helsinki guidelines during the original investigation. Each aspect of the study, including the declarations.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Clinical trial number
Not applicable.

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References

1. Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, Colagiuri S, Guariguata L, Motala AA, Ogurtsova K, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: results from the International Diabetes Federation Diabetes Atlas, 9(th) edition. Diabetes Res Clin Pract. 2019;157:107843.
2. Economic Costs of Diabetes in the U.S. in 2017. *Diabetes Care* 2018, 41(5):917–928.
3. Wu Y, Hu H, Cai J, Chen R, Zuo X, Cheng H, Yan D. A prediction nomogram for the 3-year risk of incident diabetes among Chinese adults. Sci Rep. 2020;10(1):21716.
4. Chamroonkiadtikun P, Ananchaisarp T, Wanichanon W. The triglyceride-glucose index, a predictor of type 2 diabetes development: a retrospective cohort study. Prim Care Diabetes. 2020;14(2):161–7.
5. Park B, Lee HS, Lee YJ. Triglyceride glucose (TyG) index as a predictor of incident type 2 diabetes among nonobese adults: a 12-year longitudinal study of the Korean genome and epidemiology study cohort. Transl Res. 2021;228:42–51.
6. Peng J, Zhao F, Yang X, Pan X, Xin J, Wu M, Peng YG. Association between dyslipidemia and risk of type 2 diabetes mellitus in middle-aged and older Chinese adults: a secondary analysis of a nationwide cohort. BMJ Open. 2021;11(5):e42821.
7. La Sala L, Pontiroli AE. Prevention of Diabetes and Cardiovascular Disease in obesity. Int J Mol Sci. 2020;21(21).
8. Sanchez-Garcia A, Rodriguez-Gutierrez R, Mancillas-Adame L, Gonzalez-Nava V, Diaz GA, Solis RC, Alvarez-Villalobos NA, Gonzalez-Gonzalez JG. Diagnostic Accuracy of the Triglyceride and Glucose Index for Insulin Resistance: A Systematic Review. Int J Endocrinol 2020;2020:4678526.
9. Lee SH, Kwon HS, Park YM, Ha HS, Jeong SH, Yang HK, Lee JH, Yim HW, Kang MI, Lee WC, et al. Predicting the development of diabetes using the product of triglycerides and glucose: the Chungju Metabolic Disease Cohort (CMC) study. PLoS ONE. 2014;9(2):e90430.
10. Zhang S, Du T, Li M, Jia J, Lu H, Lin X, Yu X. Triglyceride glucose-body mass index is effective in identifying nonalcoholic fatty liver disease in nonobese subjects. Med (Baltim). 2017;96(22):e7041.
11. Ding X, Wang X, Wu J, Zhang M, Cui M. Triglyceride-glucose index and the incidence of atherosclerotic cardiovascular diseases: a meta-analysis of cohort studies. Cardiovasc Diabetol. 2021;20(1):76.
12. Pranata R, Huang I, Irvan, Lim MA, Vania R. The association between triglyceride-glucose index and the incidence of type 2 diabetes mellitus-a systematic review and dose-response meta-analysis of cohort studies. Endocrine. 2021;74(2):254–62.
13. Lim J, Kim J, Koo SH, Kwon GC. Comparison of triglyceride glucose index, and related parameters to predict insulin resistance in Korean adults: an analysis of the 2007–2010 Korean National Health and Nutrition Examination Survey. PLoS ONE. 2019;14(3):e212963.
14. Dang K, Wang X, Hu J, Zhang Y, Cheng L, Qi X, Liu L, Ming Z, Tao X, Li Y. The association between triglyceride-glucose index and its combination with obesity indicators and cardiovascular disease: NHANES 2003–2018. Cardiovasc Diabetol. 2024;23:8.
15. Okamura T, Hashimoto Y, Hamaguchi M, Obora A, Kojima T, Fukui M. Ectopic fat obesity presents the greatest risk for incident type 2 diabetes: a population-based longitudinal study. Int J Obes (Lond). 2019;43(1):139–48.
16. Zhang N, Hu X, Zhang Q, Bai P, Cai M, Zeng TS, Zhang JY, Tian SH, Min J, Huang HT, et al. Non-high-density lipoprotein cholesterol: high-density lipoprotein cholesterol ratio is an independent risk factor for diabetes mellitus: results from a population-based cohort study. J Diabetes. 2018;10(9):708–14.
17. American Diabetes Association Professional Practice Committee. 2. Diagnosis and classification of diabetes: standards of Care in Diabetes-2024. Diabetes Care. 2024;47(Suppl 1):S20–42.
18. Shibata M, Sato KK, Uehara S, Koh H, Oue K, Kambe H, Morimoto M, Hayashi T. Serum Gamma-Glutamyltransferase, Daily Alcohol Consumption, and the risk of chronic kidney disease: the Kansai Healthcare Study. J Epidemiol. 2020;30(4):163–9.
19. Robson ME, Tung N, Conte P, Im SA, Senkus E, Xu B, Masuda N, Delaloge S, Li W, Armstrong A, et al. OlympiAD final overall survival and tolerability results: Olaparib versus chemotherapy treatment of physician's choice in patients with a germline BRCA mutation and HER2-negative metastatic breast cancer. Ann Oncol. 2019;30(4):558–66.
20. Skrivankova VW, Richmond RC, Woolf BAR, Davies NM, Swanson SA, VanderWeele TJ, Timpson NJ, Higgins JPT, Dimou N, Langenberg C, Loder EW, Golub RM, Egger M, Davey Smith G, Richards JB. Strengthening the reporting of observational studies in epidemiology using mendelian randomisation (STROBE-MR): explanation and elaboration. BMJ. 2021;375:n2233.
21. Zhu F, Chen C, Zhang Y, Chen S, Huang X, Li J, Wang Y, Liu X, Deng G, Gao J. Elevated blood mercury level has a non-linear association with infertility in U.S. women: data from the NHANES 2013–2016. Reprod Toxicol. 2020;91:53–8.
22. Zheng X, Cao C, He Y, Wang X, Wu J, Hu H. Association between nonalcoholic fatty liver disease and incident diabetes mellitus among Japanese: a retrospective cohort study using propensity score matching. Lipids Health Dis. 2021;20(1):59.
23. Mullee A, Romaguera D, Pearson-Stuttard J, Viallon V, Stepien M, Freisling H, Fagherazzi G, Mancini FR, Boutron-Ruault MC, Kuhn T, et al. Association between Soft Drink Consumption and mortality in 10 European countries. Jama Intern Med. 2019;179(11):1479–90.
24. Keidel D, Anto JM, Basagana X, Bono R, Burte E, Carsin AE, Forsberg B, Fuertes E, Galobardes B, Heinrich J et al. The role of Socioeconomic Status in the Association of Lung Function and Air Pollution-A Pooled Analysis of three adult ESCAPE cohorts. Int J Environ Res Public Health. 2019;16(11).
25. Sun D, Li W, Zhang H, Li Y, Zhang Q. Inverted U-shaped relationship between body mass index and multivessel lesions in Chinese patients with myocardial infarction: a cross-sectional study. J Int Med Res. 2020;48(7):1220732372.
26. von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The strengthening the reporting of Observational studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. INT J SURG. 2014;12(12):1495–9.
27. Goto A, Goto M, Noda M, Tsugane S. Incidence of type 2 diabetes in Japan: a systematic review and meta-analysis. Plos One. 2013;8(9):e74699.
28. Chen Z, Hu H, Chen M, Luo X, Yao W, Liang Q, Yang F, Wang X. Association of Triglyceride to high-density lipoprotein cholesterol ratio and incident of diabetes mellitus: a secondary retrospective analysis based on a Chinese cohort study. Lipids Health Dis. 2020;19(1):33.

29. Son DH, Lee HS, Lee YJ, Lee JH, Han JH. Comparison of triglyceride-glucose index and HOMA-IR for predicting prevalence and incidence of metabolic syndrome. Nutr Metab Cardiovasc Dis. 2022;32(3):596–604.
30. Valent A, Price DA. Earlier detection of GDM Via OGTT: is it helpful? J Clin Endocrinol Metab. 2021;23(2):e1048–9.
31. Hua S, Qi Q, Kizer JR, Williams-Nguyen J, Strickler HD, Thyagarajan B, Daviglus M, Talavera GA, Schneiderman N, Cotler SJ, et al. Association of liver enzymes with incident diabetes in US Hispanic/Latino adults. Diabet Med. 2021;38(8):e14522.
32. Keating ST, Plutzky J, El-Osta A. Epigenetic changes in Diabetes and Cardiovascular Risk. Circ Res. 2016;118(11):1706–22.
33. Tao LC, Xu JN, Wang TT, Hua F, Li JJ. Triglyceride-glucose index as a marker in cardiovascular diseases: landscape and limitations. Cardiovasc Diabetol. 2022;21(1):68. https://doi.org/10.1186/s12933-022-01511-x. PMID: 35524263; PMCID: PMC9078015.
34. Er LK, Wu S, Chou HH, Hsu LA, Teng MS, Sun YC, Ko YL. Triglyceride glucose-body Mass Index is a simple and clinically useful surrogate marker for insulin resistance in nondiabetic individuals. PLoS ONE. 2016;11(3):e149731.
35. Vasques AC, Novaes FS, de Oliveira MS, Souza JR, Yamanaka A, Pareja JC, Tambascia MA, Saad MJ, Geloneze B. TyG index performs better than HOMA in a Brazilian population: a hyperglycemic clamp validated study. Diabetes Res Clin Pract. 2011;93(3):e98–100.
36. Cho YK, Lee J, Kim HS, Kim EH, Lee MJ, Yang DH, Kang JW, Jung CH, Park JY, Kim HK et al. Triglyceride Glucose-Waist Circumference Better Predicts Coronary Calcium Progression Compared with other indices of insulin resistance: a longitudinal observational study. J Clin Med. 2020;10(1).
37. Khamseh ME, Malek M, Abbasi R, Taheri H, Lahouti M, Alaei-Shahmiri F. Triglyceride glucose index and related parameters (triglyceride glucose-body Mass Index and triglyceride glucose-Waist circumference) identify nonalcoholic fatty liver and liver fibrosis in individuals with Overweight/Obesity. Metab Syndr Relat Disord. 2021;19(3):167–73.
38. Fontana L, Eagon JC, Trujillo ME, Scherer PE, Klein S. Visceral fat adipokine secretion is associated with systemic inflammation in obese humans. Diabetes. 2007;56(4):1010–3.
39. Brambilla P, La Valle E, Falbo R, Limonta G, Signorini S, Cappellini F, Mocarelli P. Normal fasting plasma glucose and risk of type 2 diabetes. Diabetes Care. 2011;34(6):1372–4.
40. Zheng S, Zhou H, Han T, Li Y, Zhang Y, Liu W, Hu Y. Clinical characteristics and beta cell function in Chinese patients with newly diagnosed type 2 diabetes mellitus with different levels of serum triglyceride. BMC Endocr Disord. 2015;15:21.
41. Sakharkar P, Deb S. Examining liver function in adults with diabetes in the United States. J Pharm Pharm Sci. 2021;24:317–28.
42. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. Nat Rev Endocrinol. 2018;14(2):88–98.

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