The Dose-Response Relationship between The triglyceride-glucose index and Risk of Diabetes Mellitus Using Publicly Available Data: A Longitudinal Study in Chinese Obesity adult population

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Original investigation

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Abstract

Background

Triglyceride-glucose index (TyG index) is associated with type 2 diabetes mellitus (T2DM), but research on this relationship is limited in Obesity population. The purpose of this study was to evaluate the correlation between TyG index and the risk of incident T2DM in Chinese Obesity adult population.

Methods

80,919 participants with $BMI \geq 24$ were selected from a prospective cohort study data which was collected between 2010 and 2016 across 32 sites and 11 cities in China. The risk of incident T2DM according to TyG index was estimated using multivariable Cox proportional hazards models and a two-piece wise linear regression model was developed to find out the threshold effect. The formula for TyG index was expressed as $\ln[\text{fasting triglyceride level (mg/dL)} \times \text{fasting plasma glucose level (mg/dL)} / 2]$.

Results

After follow-up, 3008 (3.7%) patients developed T2DM. After adjusting for potential confounders, as a continuous variable, TyG index was associated with an increased risk of incident T2DM (adjusted hazard ratio (aHR), 3.81; 95% confidence interval (95% CI), 3.56-4.09). Further analysis revealed a positive curvilinear association between TyG index and incident T2DM, with a saturation effect predicted at 9.328. When the TyG index was less than 9.328, the risk of incident T2DM increased significantly [HR 4.778 (4.149, 5.462), $P < 0.001$], while the risk became gentle when beyond 9.328 [HR 2.61 (2.123, 3.209), $P < 0.001$]. Subgroup analyses showed that the association between TyG index and incident T2DM stably existed in different subgroups.

Conclusions

TyG index was a significant predictor of subsequent risk of incident T2DM in Chinese Obesity adult population. An increase in TyG index of one unit increased the risk of developing T2DM by 3.81-fold.

Introduction

diabetes is a growing health problem imposing heavy financial burden on individuals and society [1-4]. Almost one in four of patients with diabetes all over the world lives in China, which makes China become the country with the largest DM population in the world [5]. According to reports, the prevalence of diabetes in adults is 10.4% in China in 2013 [6]. Therefore, early prevention and appropriate intervention to avoid diabetes is very necessary. The detection of early predictive markers for incident DM in adults is considered as a key point from a public health perspective.

Prospective studies have indicated insulin resistance (IR) is the main pathogenesis of diabetes, which is present many years before diagnosis [7-9]. Obviously, IR can improve the prediction of progression to

diabetes. The hyperinsulinemic-euglycemic clamp (HIEC) technique has always been the gold standard for quantitative IR[10], but it is costly and time-consuming to apply in clinical practice. The triglyceride glucose (TyG) index, which was proposed by Simental-Mendía et al. calculated by the formula, $\ln[\text{fasting triglycerides (mg/dL)} \times \text{fasting blood glucose (mg/dL)} / 2]$, is a new marker that could measure insulin resistance in patients with diabetes. Using HIEC or in-vivo steady-state model assessment-IR (HOMA-IR) as a reference standard, some studies have confirmed the accuracy of its diagnosis of IR[11, 14-16]. Additionally, the TyG index could be obtained by calculations instead of a blood test, and it is inexpensively. Previous studies have shown that the TyG index was relevant with high risk of diabetes[17-20]. In Asian populations, TYG index association with incident DM had been conducted in low-weight and normal-weight groups[21, 22]. But the relationship between TyG index and T2DM has not yet been studied in Chinese Obesity adult population.

Here, study data were downloaded freely and a secondary analysis was performed[23]. Our research goal was to evaluate the correlation of TyG index with the risk of developing incident DM in Chinese Obesity adult population.

Methods

Data source

Data was downloaded from the DATADRYAD website (www.datadryad.org). The DATADRYAD database allows others to freely obtain original data. In accordance with the Dryad Terms of Service, we gained the following Dryad data package: Chen, Ying et al. (2018), data from: Association of body mass index and age with incident diabetes in Chinese adults: a population-based cohort study, Dataset, <https://doi.org/10.5061/dryad.ft8750v>. The following variables were included in the database materials: sex, age, BMI, drinking, smoking, family history of diabetes, low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), total cholesterol (TC), TG, FPG, concentration of creatinine (CCR), aspartate aminotransferase (AST), alanine aminotransferase (ALT), systolic blood pressure (SBP), diastolic blood pressure (DBP), FPG of final visit, incident diabetes at follow up and follow-up time. In the original paper[23], the authors declared that they have relinquished copyright and relevant ownership of the database. Thus, this database can be used for secondary analyses without violating the authors' rights.

Study population

Data were obtained from a database provided by the Rich Healthcare Group in China, and the study enrolled 685,277 participants who received a health check and were at least 20 years old with at least two visits between 2010 and 2016 across 32 sites and 11 cities in China (Shanghai, Beijing, Nanjing, Suzhou, Shenzhen, Changzhou, Chengdu, Guangzhou, Hefei, Wuhan, Nantong). The data we got has been initially screened, as follows: (1) no available information about weight, height, gender, fasting plasma glucose value at baseline, (2) extreme BMI values ($< 15 \text{ kg/m}^2$ or $> 55 \text{ kg/m}^2$), (3) excluded participants with visit intervals less than 2 years, (4) participants diagnosed with diabetes at baseline and participants with

undefined diabetes status at follow-up[23]. Finally, 211,833 participants took part in the analysis. The institutional ethics committee did not require any obtainment of study approval or informed consent for the retrospective component of the research. For further research, some data were removed from the analysis cohort:excluded BMI<24 at baseline(128893); missing TyG values at baseline(2021). In total, 80,919 subjects (58,470 males and 22,449 females) were included for analysis in this study(Figure 1).

Measurement of the TyG index and other covariates

Researchers obtained information (values) for our retrospective cohort study. The design of the study has been documented elsewhere[23]. Demographic characteristics, lifestyle, disease history, and medical history were obtained by a detailed questionnaire. Height measurement was accurate to 0.1 cm. Weight measurement was accurate to 0.1 kg, required to wear lightweight and no shoes. BMI was calculated as weight / height squared (kg/m²). Fasting venous blood was drawn to detect serum LDL, TG, TC, HDL-C, FPG, BUN, Ccr, ALT and AST values by an automatic biochemical analyzer (Beckman 5800). The TyG index was calculated as $\text{Ln} [\text{FPG (mg/dL)} \times \text{fasting TG (mg/dL)} / 2]$ [23]. Because this was a retrospective cohort study, observation bias was naturally reduced.

Ascertainment of diabetes

Diabetes was defined according to $\text{FPG} \geq 126 \text{ mg/dL}$ or self-reported diabetes. Ascertainment of diabetes depended on the date of diagnosis or the last visit.

Statistical Analysis

Continuous variables (normal distribution) are presented as mean with standard deviation (SD) and continuous variables (skewed distribution) are expressed as median with interquartile range (IQR).Categorical variables are presented as frequencies and percentages. The remaining missing values were imputed by multivariable chained imputation with fully conditional specification[24]; imputed and reported results were similar.We used the chi-square test, one-way analysis of variance, or Kruskal-Wallis test to examine the statistical differences in the groups stratified by TyG index quartiles.We employed the univariate and multivariate Cox proportional hazard models to assess the relationship between TyG index and the risk of DM.We used three models: model 1, a crude (univariate) model; model 2, adjusted for age and sex; and model 3, adjusted for age, sex, height, weight, LDL, TC, HDL-C, BUN, Ccr, AST, ALT, SBP, DBP, drinking status, smoking status and family history of diabetes. In the models, we used a median value in each quartile of TyG index to perform the linear trend tests. In addition, the nonlinear relationship between TyG and incident DM was estimated using the Cox proportional hazards regression model with cubic spline functions. To find modifications and interactions, we used a stratified linear regression model and likelihood ratio test in the different subgroups according to sex, age (<65 years or ≥ 65 years), smoking status (never, ever, or current), drinking status (never, ever, or current), family.histroy.of.diabetes, HBP, and $\text{BUN}(\leq 7.1 \text{ or } >7.1)$. We used the Statistical Packages R (The R Foundation, Vienna, Austria) to analyze the data. When the calculated P value was less than 0.05, the statistical difference was considered significant.

Results

Baseline characteristics of patients

Baseline characteristics of study participants according to quartiles of triglyceride-glucose index were presented in Table 1. A total of 80,919 subjects (72.3% male and 27.7% female) were involved in this study. The baseline characteristics of the participants grouped by quartile of TyG index. The mean age of the participants was 45.1 ± 13.0 years. After an average follow-up of 3.1 ± 0.9 years, 3008 (3.7%) participants were developed diabetes mellitus. Participants in the highest group of TyG (Q4) had higher values of age, height, weight, TC, TG, FPG, BUN, Ccr, ALT, AST, SBP, and DBP. And consisted of more males, smokers, drinkers, hypertension and family history of diabetes than the other groups (Q1-3). Participants with the highest TyG (Q4) had lower values in HDL than those with lower TyG (Q1-Q3).

Univariate analysis for diabetes mellitus

Table 2 presents the results of the univariate analysis for the association between risk factors and incident DM. Using the univariate Cox proportional hazard model, we discovered that SCR was not associated with DM. In contrast, univariate analysis showed that age, BMI, LDL, TC, TG, FPG, TyG index, ALT, AST, Ccr, SBP, DBP, drinking and family history of diabetes were positively related to future risk of diabetes. Moreover, never smoking and height were negative correlation. Furthermore, compared with males, females showed a lower risk of diabetes. Ever smoke status was not associated with DM compared with Current smoke status.

Unadjusted and Adjusted Cox Proportional Hazard Model

We used Cox proportional hazard models to assess the independent effects of TyG index on the risk of incident DM (univariate and multivariate Cox proportional hazard models). Table 3 presents the effect sizes (hazard ratio (HR) and 95% confidence intervals (95% CI)). In the unadjusted model (model 1), an increase in TyG index of one unit was associated with a 2.83-fold higher risk of incident T2DM (HR 2.83, 95% CI 2.69-2.99). In model 2, an increase in TyG index of one unit increased the risk of developing DM by 2.65-fold (HR 2.65, 95% CI 2.5-2.8) after adjusting for age and sex. In model 3, each additional unit of TyG index was associated with a 3.81-fold higher risk of incident DM (HR 3.81, 95% CI 3.56-4.09). For sensitivity analysis, TyG index was transformed into a categorical variable (quartile of TyG index), and the P value for the trend of TyG index with categorical variables was consistent with the result of TyG index as a continuous variable in the different models.

Threshold Effect Analysis of TyG on Incident DM

To evaluate whether a dose-response relationship between TyG index and incident DM existed, we used a smoothing function analysis. After adjusting for potential confounding factors, a nonlinear relationship between TyG index and DM was observed (Figure 2). The risk of developing DM was positively correlated with the TyG index. The risk of developing DM increases significantly with TyG until it peaks at 9.328 [HR 4.778 (4.179, 5.462), $P < 0.001$]. However, when the concentration of TyG index was higher than

9.328, the hazard ratios for risk of developing DM was 2.61 (2.123,3.209), indicating that the risk of developing DM became gentle with an increase in TyG index ($P < 0.001$) (Table 3).

In the figure 2, the solidline curve indicates the estimated risk of incident DM, and the dotted lines represent point-wise 95% confidence interval adjusted for age, sex, height, weight, LDL, TC, HDL-C, BUN, Ccr, AST, ALT, SBP, DBP, drinking status, smoking status and family history of diabetes.

Subgroup Analyses

To see if the association between TyG index and incident T2DM is stable in different subgroups, we did stratified analyses and interactive analyses (figure 3). The participants were divided into subgroups according to age, sex, HBP, BUN, smoking status, drinking status and family history of diabetes. The results showed that the association between TyG index and incident T2DM stably existed in the different subgroups. The additive interactions between TyG index and incident T2DM were observed in sex, age and BUN (P -value for interaction < 0.05). Stronger correlations were found in females or in participants with age < 65 years, $BUN < 7.1$.

Discussion

In this population-based cohort study, TyG index was found to be associated with an elevated risk of the incident DM in Chinese Obesity adult population, independent of age, sex, height, weight, LDL, TC, HDL-C, BUN, Ccr, AST, ALT, SBP, DBP, drinking status, smoking status and family history of diabetes. We further revealed a nonlinear relationship between TyG index and risk of incident DM. The relationship was characterized as follows: the risk of incident DM increased significantly with an increase in TyG index when the TyG index was less than 9.328 and the risk became gentle when the TyG index was beyond 9.328. The significant association was observed in the subgroups of sex, age and BUN.

T2DM is characterized by IR and decreased β -cell function[25-27]. In individuals with IR, insulin cannot function properly to stimulate glucose uptake. This condition is also associated with obesity and metabolic syndrome, characterized by central, visceral, and ectopic fat accumulation[28]. The storage of TG in nonadipose tissues, such as skeletal muscle, liver, pancreas, and heart, causes dysfunction at the cellular level and disruption of organ function[29]. Excess lipids may accumulate intercellularly and interfere with organ function through the paracrine effects of the released adipokines, whereas intracellular lipid deposition is associated with reduced insulin sensitivity[30]. Adipocyte dysfunction enhanced lipolysis, and free fatty acid (FFA) oxidation impairment results in a continuous oversupply of FFA and consequently lipid accumulation intracellularly[28, 31]. The FFA metabolites, including ceramides, diacylglycerol, and long-chain acylCoA, have deleterious effects on the cell and cause defects in insulin signaling[32]. High TG concentrations reduce glucokinase activity and glucose-stimulated insulin secretion in pancreatic islets, and high glucose levels cause islet cell destruction due to continuous oxidative stress[32]. Thus, glucose toxicity and lipotoxicity may exert an impact on β -cell failure[34]. Simental-Mendía et al. proposed TyG index, which combines fasting triglycerides and fasting

blood glucose[13]. In 748 apparently healthy participants, the sensitivity and specificity of TyG index for identifying IR were 84.0% and 45.0%, respectively[13]. A systematic review and meta-analysis showed that the TyG index was significantly associated with an increased incidence of T2DM[30]. This is consistent with our findings with TyG index. Furthermore some studies have indicated that TyG index is associated with IR and proposed it as a reliable and useful surrogate indicator for identifying IR[11, 14, 21, 35]. A cohort study with 11,113 nondiabetic participants in rural Chinese followed for 6 years firstly showed that, compared to participants in the lowest quartile of TyG, participants in the highest quartile of TyG had a higher risk of diabetes (relative risk 3.54 ; 95% CI 2.08-6.03) after adjusting for age, family history of diabetes, family history of hypertension, education level, marital status, smoking, alcohol consumption, physical activity and SBP[36]. They found that the association was stable in both men and women(HR 3.54, 95% CI 2.08–6.03 for men; HR 6.15, 95% CI 3.48–10.85 for women; P for interaction < 0.001)[36]. Also, in a cohort of 4820 White Europeans had similar results both in men and women[37]. These conclusions are consistent with our findings (TyG as continuous variable: HR 3.61, 95% CI 3.34-3.91 for men; HR 4.91, 95% CI 4.2-5.73 for women; P for interaction = 0.006). A meta regression analysis showed that the correlation between TyG index and T2DM incidence was affected by baseline age (coefficient: -0.05, p = 0.015)[37]. This also agrees with our study. HR 3.85, 95% I 3.57–4.16 for age<65; HR 3.14 , 95% CI 2.64–3.73 for age>65; P for interaction = 0.001). One of the possible explanations is that as age increases, TyG index became less influential for determining the risk of T2DM[30].

However, compared with previous studies, although TyG was positively associated with an increased risk of T2DM after adjusting for confounding factors. But there are still some conclusions different from our study. We assessed the dose-response relation- ship between TyG index and risk of T2DM and found that there was a nonlinear association with a turning point 9.328 of TyG index: the risk of developing DM increased significantly with an increase in TyG index when the TyG index was less than 9.328 and the risk became gentle when the TyG index was beyond 9.328. But, a meta-analysis[30], which included 270,229 subjects from 14 cohort studies, found the dose–response curve became increasingly steeper at TyG index above 8.6. This may be attributed to our study population being obese, which is a major risk factor for diabetes development. Obesity patients are often accompanied with fat metabolism, high TG concentrations reduce glucokinase activity and glucose-stimulated insulin secretion in pancreatic islets, and high glucose levels cause islet cell destruction due to continuous oxidative stress[33, 38, 39]. After the lipid and glucose metabolism abnormalities reach to some extent, the impact of the tyg index may be weakened. Another article suggests that tyg index had a linear relationship with diabetes. But the number of cases was only 12723 and our study was 80919; and the population was Japanese adults. The relationship between tyg index and diabetes varies between races[33, 38, 39]. And the dietary structure may vary between the Japanese and the Chinese, so there is a gap with our research[41]. Our study has several strengths. (1) Compared to previous similar studies, our study had a relatively large sample size. (2) The correlation between TyG index and T2DM was performed in Chinese Obesity adult population for the first time. (3) To decrease the result contingency and

elevate the robustness of the results, TyG was treated both as a continuous and categorical variable. (4) In the subgroup analysis, we used stratified linear regression models and likelihood ratio tests to find modifications and interactions and to obtain stable results in different subgroups. (5) We used the Cox proportional hazards regression model with cubic spline functions to estimate the nonlinear relationship between TyG and DM.

Our study also has some limitations. First, the study sample is selected from China, which may hamper the representativeness of study results. However, One quarter of diabetics live in China, and our data comes from multiple centers in China with a wide geographical and age range, which makes the results widely applicable to the Chinese population and even Chinese around the world. Second, In this study, we did not distinguish between type 1 diabetes and type 2 diabetes. However, since type 2 diabetes accounts for about 95% of all diabetes cases, our findings may be more representative of type 2 diabetes[42]. Third, Raw data were limited. We cannot adjust physical activity, dietary factors, fat distribution and weight changes which may affect the relationship between TyG index and T2DM. However, our results remain stable after multiple adjustments of the correlation variables.

Conclusion

In conclusion, an increase of TyG index was independently associated with a higher incidence of diabetes mellitus in this prospective study during 6-year follow-up of Chinese Obesity adult population, independent of age, sex, height, weight, LDL, TC, HDL-C, BUN, Ccr, AST, ALT, SBP, DBP, drinking status, smoking status and family history of diabetes. A positive curvilinear association between GGT and incident diabetes mellitus was present, with a saturation effect predicted at 9.328 of TyG index.

Abbreviations

T2DM: Type 2 diabetes mellitus

IR: Insulin resistance

TyG index: Triglyceride-glucose index

BMI: Body mass index

HDL-C: High-density lipoprotein cholesterol

TC: Total cholesterol

TG: Triglycerides

SBP: Systolic blood pressure

DBP: Diastolic blood pressure

Declarations

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Authors' contributions

The author designed the research, analysed the data and drafted the manuscript by himself.

Ethics approval and consent to participate

Not applicable

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None

Availability of data and material

Data can be downloaded from the DRYAD database ([http:// www.Datadryad.org](http://www.Datadryad.org)).

Competing interests

The author declares no conflicts of interest in this work.

Consent to publication

Not applicable/all data used for the present study have been anonymized, and the submission does not include information that may identify individual persons.

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Tables

Table 1: Baseline characteristics of study participants according to quartiles of TyG.

TyG	Overall	Q1	Q2	Q3	Q4	P-value
Number	80919	20228	20212	20249	20230	
Age (years)	45.1 ± 13.0	42.3 ± 12.4	44.9 ± 13.3	46.2 ± 13.3	47.0 ± 12.6	< 0.001
Height(cm)	167.9 ± 8.4	166.6 ± 8.6	167.7 ± 8.4	168.4 ± 8.3	169.1 ± 7.9	< 0.001
Weight(kg)	75.2 ± 10.1	72.4 ± 9.3	74.4 ± 9.7	76.1 ± 10.2	77.7 ± 10.3	< 0.001
BMI (kg/m2)	26.6 ± 2.2	26.0 ± 1.9	26.4 ± 2.1	26.8 ± 2.3	27.1 ± 2.4	< 0.001
SBP(mmHg)	125.3 ± 16.3	121.5 ± 15.5	124.4 ± 15.9	126.6 ± 16.4	128.6 ± 16.7	< 0.001
DBP(mmHg)	78.1 ± 11.0	75.2 ± 10.6	77.4 ± 10.8	79.0 ± 10.9	80.8 ± 11.1	< 0.001
FPG(mmol/L)	5.1 ± 0.6	4.8 ± 0.6	5.0 ± 0.6	5.1 ± 0.6	5.3 ± 0.6	< 0.001
TC(mmol/L)	4.9 ± 0.9	4.5 ± 0.8	4.8 ± 0.8	5.0 ± 0.9	5.3 ± 1.0	< 0.001
TG(mmol/L)	1.8 ± 1.3	0.8 ± 0.2	1.2 ± 0.2	1.8 ± 0.3	3.3 ± 1.7	< 0.001
TyG index	8.7 ± 0.6	8.0 ± 0.3	8.5 ± 0.1	8.9 ± 0.1	9.5 ± 0.4	< 0.001
HDL-C(mmol/L)	1.3 ± 0.3	1.4 ± 0.3	1.3 ± 0.3	1.3 ± 0.3	1.2 ± 0.3	< 0.001
LDL(mmol/L)	2.9 ± 0.7	2.7 ± 0.6	2.9 ± 0.6	3.0 ± 0.7	3.0 ± 0.8	< 0.001
ALT(U/L)	31.8 ± 25.9	24.8 ± 24.3	29.3 ± 23.4	33.6 ± 25.3	39.4 ± 28.0	< 0.001
AST(U/L)	26.7 ± 12.6	24.2 ± 12.2	25.7 ± 13.0	27.4 ± 12.0	29.8 ± 12.7	< 0.001
BUN(mmol/L)	4.8 ± 1.2	4.8 ± 1.2	4.8 ± 1.2	4.9 ± 1.2	4.9 ± 1.2	< 0.001
Follow-up ^a year ^a	3.1 ± 0.9	3.2 ± 1.0	3.1 ± 0.9	3.1 ± 0.9	3.1 ± 0.9	< 0.001
Ccr(umol/L)	74.4 ± 15.7	71.5 ± 16.5	73.9 ± 15.8	75.4 ± 14.9	76.9 ± 14.9	< 0.001

Sex (%)						< 0.001
Male	58470 (72.3)	12059 (59.6)	14217 (70.3)	15472 (76.4)	16722 (82.7)	
Female	22449 (27.7)	8169 (40.4)	5995 (29.7)	4777 (23.6)	3508 (17.3)	
developed DM(%)						< 0.001
No	77911 (96.3)	19996 (98.9)	19738 (97.7)	19447 (96)	18730 (92.6)	
Yes	3008 (3.7)	232 (1.1)	474 (2.3)	802 (4)	1500 (7.4)	
HBP(%)						< 0.001
No	74532 (92.1)	19289 (95.4)	18838 (93.2)	18468 (91.2)	17937 (88.7)	
Yes	6387 (7.9)	939 (4.6)	1374 (6.8)	1781 (8.8)	2293 (11.3)	
Smoking status (%)						< 0.001
Current	6371 (26.2)	870 (16.6)	1381 (22.9)	1761 (27.7)	2359 (35.2)	
Ever	1325 (5.4)	249 (4.7)	351 (5.8)	344 (5.4)	381 (5.7)	
Never	16635 (68.4)	4126 (78.7)	4298 (71.3)	4253 (66.9)	3958 (59.1)	
Drinking status(%)						< 0.001
Current	787 (3.2)	111 (2.1)	172 (2.9)	199 (3.1)	305 (4.6)	
Ever	4709 (19.4)	888 (16.9)	1130 (18.7)	1234 (19.4)	1457 (21.8)	
Never	18835 (77.4)	4246 (81)	4728 (78.4)	4925 (77.5)	4936 (73.7)	
Family history of diabetes(%)						0.046
No	79272 (98.0)	19854 (98.2)	19802 (98)	19840 (98)	19776 (97.8)	
Yes	1647 (2.0)	374 (1.8)	410 (2)	409 (2)	454 (2.2)	

BMI: body mass index; HDL-C: high-density lipoprotein cholesterol; FPG: fasting plasma glucose; TC: total cholesterol; TG: triglyceride; SBP: systolic blood pressure; DBP: diastolic blood pressure; TyG: triglyceride-glucose index; CCR: concentration of creatinine; AST: aspartate aminotransferase; ALT: alanine aminotransferase; BUN: blood urea nitrogen, T2DM: type 2 diabetes mellitus; CI: confidence interval; HR: hazard ratio.

Table 2: Univariate analysis for type 2 diabetes mellitus.

	HR(95%CI)	P-value
Age (years)	1.05 (1.05,1.05)	< 0.001
Height(cm)	0.99 (0.99,0.99)	< 0.001
Weight(kg)	1.02 (1.02,1.03)	< 0.001
BMI (kg/m ²)	1.17 (1.16,1.19)	< 0.001
SBP(mmHg)	1.03 (1.02,1.03)	< 0.001
DBP(mmHg)	1.03 (1.02,1.03)	< 0.001
FPG(mmol/L)	7.69 (7.29,8.1)	< 0.001
TC(mmol/L)	1.19 (1.14,1.23)	< 0.001
TG(mmol/L)	1.17 (1.16,1.19)	< 0.001
TyG index	2.83 (2.69,2.99)	< 0.001
HDL-C(mmol/L)	1.29 (1.1,1.5)	0.002
LDL(mmol/L)	1.07 (1.01,1.14)	0.027
ALT(U/L)	1.0045 (1.0038,1.0051)	< 0.001
AST(U/L)	1.0051 (1.0038,1.0064)	< 0.001
BUN(mmol/L)	1.12 (1.08,1.15)	< 0.001
Ccr(umol/L)	0.9988 (0.9964,1.0012)	0.335
Sex (%)		
Male	Ref	
Female	0.87 (0.8,0.95)	0.001
HBP(%)		
No	Ref	
Yes	2.1 (1.9,2.33)	< 0.001
Smoking status (%)		
Current	Ref	
Ever	0.88 (0.68,1.16)	0.364
Never	0.58 (0.51,0.67)	< 0.001
Drinking status(%)		

Current	Ref	
Ever	0.51 (0.37,0.72)	< 0.001
Never	0.58 (0.43,0.8)	< 0.001
Family history of diabetes(%)		
No	Ref	
Yes	1.59 (1.32,1.92)	< 0.001

BMI: body mass index; HDL-C: high-density lipoprotein cholesterol; FPG: fasting plasma glucose; TC: total cholesterol; TG: triglyceride; SBP: systolic blood pressure; DBP: diastolic blood pressure; TyG: triglyceride-glucose index; CCR: concentration of creatinine; AST: aspartate aminotransferase; ALT: alanine aminotransferase; BUN: blood urea nitrogen, T2DM: type 2 diabetes mellitus; CI: confidence interval; HR: hazard ratio.

Table 3: Relationship between TyG and incident diabetes mellitus in different models.

Variable	model 1		model 2		model 3	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
TyG	2.83 (2.69,2.99)	<0.001	2.65 (2.5,2.8)	<0.001	3.81 (3.56,4.09)	<0.001
TyG levels						
Q1	Ref		Ref		Ref	
Q2	2.2 (1.88,2.58)	<0.001	1.92 (1.64,2.25)	<0.001	2.03 (1.73,2.38)	<0.001
Q3	3.83 (3.31,4.44)	<0.001	3.16 (2.72,3.66)	<0.001	3.51 (3.02,4.09)	<0.001
Q4	7.27 (6.33,8.35)	<0.001	5.81 (5.05,6.68)	<0.001	7.31 (6.29,8.5)	<0.001
P for trend		<0.001		<0.001		<0.001

Model 1 was not adjusted. Model 2 was adjusted for age and sex. Model 3 was adjusted for age, sex, height, weight, LDL, TC,HDL-C,BUN, CCR, AST, ALT, SBP, DBP, drinking status, smoking status and family history of diabetes.TyG: triglyceride-glucose index.

Table 4: Threshold effect analysis of TyG on incident diabetes mellitus

Outcome:	HR (95% CI)	P value
One-line linear regression model	3.81 (3.56,4.09)	< 0.001
Two-piecewise linear regression model		
TyG<9.328	4.778 (4.179,5.462)	< 0.001
TyG>=9.328	2.61 (2.123,3.209)	< 0.001
Log-likelihood ratio test		< 0.001

Notes: adjusted for age, sex, height, weight, LDL, TC,HDL-C,BUN, Ccr, AST, ALT, SBP, DBP, drinking status, smoking status and family history of diabetes.

Figures

according to the data source article:

Figure 1

Flowchart of study participants.

Figure 2

Fitting a curve for incident T2DM according to the TyG index adjust for age, sex, height, weight, LDL, TC, HDL-C, BUN, Ccr, AST, ALT, SBP, DBP, drinking status, smoking status and family history of diabetes.

Figure 3

Effect size of TyG index on incident T2DM in each subgroup. Notes: adjust for age, sex, height, weight, LDL, TC, HDL-C, BUN, Ccr, AST, ALT, SBP, DBP, drinking status, smoking status and family history of diabetes.