Association of Triglyceride Glucose-Body Mass Index and Incident Diabetes Mellitus: A Secondary Retrospective Analysis Based On a Chinese Cohort Study

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Keywords: TyG-BMI, Incident diabetes, Nonlinearity

Posted Date: August 5th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-773598/v1

Abstract

Background

The triglyceride glucose-body mass index (TyG-BMI) has been proposed as a marker of insulin resistance (IR). However, evidence for the relationship between TyG-BMI and the incidence of diabetes mellitus remains limited. This study investigated the association between TyG-BMI and diabetes occurrence in Chinese individuals.

Methods

This retrospective study included a cohort of 204978 non-diabetic individuals using data from healthy screening program data in China between 2010 and 2016. The independent and dependent variables are TyG-BMI and incident of diabetes, respectively. Cox proportional hazards regression analysis was used to evaluate hazard ratios (HRs) and 95% confidence intervals (95% CIs) for the relationship between TyG-BMI and incident diabetes. Generalized additive models were used to identify non-linear relationships. Subgroup analysis helped better understand other factors that may affect the association between TyG-BMI and diabetes to identify potential special populations. And the data were downloaded from the DATADRYAD website.

Result

Our study indicated that the incidence of diabetes increases with the rise of TyG-BMI (HR = 1.023, 95%CI(1.022, 1.024)) after adjusting age, gender, SBP, DBP, TC, HDL, LDL, ALT, AST, Scr, smoking status, drinking status, family history. There was a nonlinear relationship between TyG-BMI and the incidence of diabetes, and the inflection point was 232.416. The effect size and confidence interval of the left and right sides of the inflection point were 1.029 (1.027, 1.031), 1.016 (1.014, 1.018), P for interaction < 0.0001. Subgroup analysis showed that the correlation was stronger in the population aged 20–30 (P for interaction < 0.0001, HR 1.029, 95%CI:1.024 to 1.035),and the same trend was found in the following populations: age 30–40(HR = 1.032), age 40–50(HR = 1.029), HDL (high group) (HR = 1.024), SBP<140(HR = 1.025), DBP<90(HR = 1.024), current drinker(HR = 1.031), and ever drinker(HR = 1.032).

Conclusion

This study demonstrated that increased TyG-BMI was positively correlated with incident diabetes in Chinese. TyG-BMI and incident diabetes had non-linear relationship. Before and after TyG-BMI equals 232.416, the risk of diabetes increased by 2.9% and 1.6%, respectively, when TyG-BMI increased one unit.

Background

Diabetes has become a critical worldwide healthy problem with high prevalence. The latest International Diabetes Federation (IDF) Diabetes Atlas (9th edition) indicated that about 463 million adults aged 20–79 suffered from diabetes in the world in 2019[1]. It was estimated that by 2045, the number of diabetes

patients would reach 700.2 million[1]. China has the largest number of diabetic patients. Diabetes mellitus(DM) and its complications have resulted in a severe economic burden of mortality and disability. Thus, Early identification and prediction of diabetes are crucial.

Type 2 diabetes(T2DM) is more common among obese individuals than nonobese individuals[1]. Insulin resistance (IR) and the consequences of compensatory hyperinsulinemia are vital pathological mechanisms of diabetes mellitus and obesity[2]. Thus, recognition of IR before the manifestation of clinical diabetes mellitus is of paramount importance.

Recently, triglyceride glucose body mass index(TyG-BMI), which combines triglyceride(TG), fasting plasma glucose(FPG), and obesity status, has been considered to identify IR more reliably than TyG.[3, 4] Triglycerideglucose (TyG) index, which is estimated using the formula Ln(fasting triglycerides(mg/dl)× fasting blood glucose(mg/dl)/2), is an alternative for identifying insulin resistance in apparently healthy subjects[5–9]. Some studies revealed the TyG index was relevant with a high risk of diabetes. TyG-BMI = TyG × BMI[3]. Body mass index (BMI) is an easily detectable, inexpensive, and non-invasive measurement parameter closely related to IR. Ectopic obesity is the biggest risk factor for type 2 diabetes[10]. A Chinese study indicates that BMI is also independently related to the higher risk of diabetes among young people[11]. A Korean study suggests that triglyceride glucose-body mass index is a simple and clinically useful proxy for insulin resistance in non-diabetic individuals[11]. At present, there are few articles about the relationship between TyG-BMI and diabetes.

In this study, we performed a secondary data analysis based on previously published data. In that paper, the author investigated the association of body mass index and age with incident diabetes [11]. On this secondary analysis, TyG-BMI was used as an independent variable, and outcome variables and other covariates are consistent with those in the original research. The purpose of this study was to explore the association of TyG-BMI with incident diabetes.

Methods

Study population and design

In this population-based cohort analysis of a medical program established by the Rich Healthcare Group in China between 2010 and 2016, we investigated the effect of TyG-BMI on incident diabetes. Data were downloaded from the DATADRYAD website (www.datadryad.org), allowing others to use the database for free. In keeping with the terms of service, this research cites data packets shared by Chen Ying et al.[11]. The database materials included the following variables: 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, Serum urea nitrogen(BUN), serum creatinine (Scr), aspartate aminotransferase (AST), alanine aminotransferase (ALT), systolic blood pressure (SBP), diastolic blood pressure (DBP), incident diabetes at follow up and follow-up time. The authors declared that they had relinquished

copyright and relevant ownership of the database in the original paper. As for ethics approval, the study was a retrospective analysis approved by the rich healthcare group review committee.

The original study enrolled 685,277 participants ≥ 20 years old with at least two visits covering the period 2010–2016 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 filtered. Subjects with the following conditions were excluded: (1) missing information about weight, height, gender, fasting plasma glucose value at baseline; (2) extreme BMI values (< 15 kg/m^2 or > 55 kg/m^2); (3) visit intervals less than 2 years; (4)participants were diagnosed with diabetes at baseline and with undefined diabetes status at follow-up. Finally, in the original study, Ying Chen et al.[11] kept 211,833 participants. We excluded missing values of baseline TG(n = 4,887) and zero values of baseline TG(n = 860) from the analysis cohort for further research. And then, TyG-BMI was calculated as the formula BMI×Ln(fasting triglycerides(mg/dl)×fasting blood glucose(mg/dl)/2). We excluded outliers of TyG-BMI(< means minus three standard deviation (SD) or > means plus three SD) (n = 1,108). Finally, a sum of 204978 participants was selected in our study. Figure 1 depicted the participants' selection process.

Data Collection And Measurements

The original database contained participants' clinical history and lifestyle factors based on a standardized questionnaire regarding demographic characteristics, lifestyle factors, personal medical history, and family history of chronic disease. Trained staff measured height, weight, and blood pressure. Body weight was measured in light clothing with no shoes to the nearest 0.1 kg. Height was measured to the nearest 0.1 cm. BMI was derived from weight in kilograms divided by height in meters squared. Standard mercury sphygmomanometers measured blood pressure. Fasting venous blood samples were collected after at least a 10 hours fast at each visit. TG, TC, LDL-C, HDL-C and Plasma glucose levels were measured on an autoanalyzer (Beckman 5800). Plasma glucose levels were measured by the glucose oxidase method. The formula of the TyG index was Ln(fasting triglycerides(mg/dl)×fasting blood glucose(mg/dl)/2)).The target-independent variable is TyG-BMI, which equals the BMI×TyG index. The dependent variable is incident diabetes, which was defined as fasting plasma glucose ≥ 7 mmol/L, and/or self-reported during follow-up. As this is a retrospective cohort study, it reduced the possibility of selection bias and observation bias.

Statistical analysis

The continuous variable of the normal distribution was represented by mean with standard deviation (SD), and the continuous variable of non-normal distribution was replaced by median with interquartile range (IQR). Categorical variables were expressed as frequencies and percentages. For the handling of missing values, missing continuous variables were replaced with a mean or median depending on the distribution. Missing categorical variables could be a new categorical group. Stratified by TyG-BMI index quartiles, statistical differences of the groups were described with one-way ANOVA (normal distribution),

Kruskal Wallis H (skewed distribution) test, and chi-square test (categorical variables). To explore the relationship between TyG-BMI and incident DM, univariate and multivariate Cox proportional hazard models were applied and adjusted hazard ratios (HRs) with 95% confidence intervals (CIs). According to the recommendation of the STROBE statement, We used three models: crude model; model I adjust for: Age, Gender, SBP, DBP, Smoking Status, Drinking Status, Family History; model II adjust for: Age, Gender, SBP, DBP, Smoking Status, Drinking Status, Family History, TC, HDL, LDL, ALT, AST, Scr. Sensitivity analysis was used to ensure the robustness of data analysis. The TyG-BMI was converted into a categorical variable and calculated the P for trend to perform the linear trend tests. We used the Cox proportional hazards regression model with cubic spline functions to identify non-linear relationships. In addition, If there was obvious in a smoothed curve, the recursive method automatically calculates the inflection point. The associations of TyG-BMI with incident diabetes in subgroups were also studied using a stratified linear regression model and likelihood ratio test to find modifications and interactions. The subgroups were classified by age (20 to < 30, 30 to < 40, 40 to < 50, 50 to < 60, 60 to < 70, ≥70), gender (male vs. female), HDL(low, middle, high, not recorded), LDL(low, middle, high, not recorded), SBP(< 140, ≥ 140), DBP(< 90, ≥ 90), Smoking status(current smoker, ever smoker, never smoker, not recorded), Drinking status(current drinker, ever drinker, never drinker, not recorded), Family history of diabetes(no, yes). Survival estimates and cumulative event rates were compared using the Kaplan–Meier method by using the time-to-first event for each endpoint.

All of the analyses were performed with the statistical software package R (http://www.R-project.org, The R Foundation) and Empower-Stats (http://www.empowerstats.com, X&Y Solutions, Inc., Boston, MA). Significance was accepted at a two-tailed $P < 0.05$.

Result

Baseline characteristics of the study participants

Of the 211,833 subjects recruited in the former study, 204,978 participants were included in the current analysis (described in Fig. 1). The mean age of the population was 42.2 ± 12.7 years old, and 45.17% of participants were women. The mean year of follow-up was 3.1 ± 0.9 years, and 4093 participants happened diabetes during follow-up. The mean TyG-BMI was 158.7 ± 32.4, and the mean FPG, BMI, TG were 88.6 ± 10.9 mg/dl, 23.3 ± 3.3 kg/m^2 and 24.2 ± 18.6 mg/dl respectively. Individuals in the highest TyG-BMI group (Q4) were generally older than those in the lowest TyG-BMI group (Q1) and had higher BMI, FPG, TG, SBP, DBP, TC, ALT, SCR values. What's more, with the increase of TyG-BMI value, the incidence of diabetes increased gradually. (Q1: 0.23% vs. Q2: 0.62% vs. Q3: 1.74% vs. Q4: 5.35%). Compared with the Q1 group, the Q4 group had lower HDL levels, higher AST and LDL levels, higher rates of smoking, drinking, family history. As shown in Table 1.

Table 1
The Baseline Characteristics of participants

TyG-BMI	Q1(≤167.01)	Q2(167.01 to ≤ 191.53)	Q3(191.53 to ≤ 219.26)	Q4(≥219.26)	P-value
Participants	51245	51244	51244	51245	
Age(years)	36.65 ± 10.06	41.26 ± 12.13	44.79 ± 13.08	46.16 ± 13.11	< 0.001
BMI(kg/m^2)	19.45 ± 1.36	21.98 ± 1.20	24.11 ± 1.32	27.21 ± 2.14	< 0.001
FPG(mmol/L)	4.68 ± 0.53	4.84 ± 0.55	4.98 ± 0.58	5.17 ± 0.63	< 0.001
TG(mmol/L)	0.67 (0.52–0.86)	0.91 (0.70–1.18)	1.25 (0.96–1.65)	1.90 (1.40–2.62)	< 0.001
TyG-BMI	151.98 ± 10.59	179.21 ± 7.07	204.83 ± 7.94	244.14 ± 19.76	< 0.001
SBP(mmHg)	110.87 ± 13.45	116.16 ± 14.96	121.63 ± 15.68	127.36 ± 16.40	< 0.001
DBP(mmHg)	69.34 ± 9.12	72.00 ± 9.74	75.54 ± 10.30	79.63 ± 11.02	< 0.001
TC(mmol/L)	4.36 ± 0.79	4.60 ± 0.85	4.82 ± 0.88	5.05 ± 0.92	< 0.001
ALT(U/L)	13.00 (10.30,17.20)	15.90 (12.00-21.90)	20.00 (15.00-28.60)	28.00 (19.30–41.70)	< 0.001
Scr(umol/L)	63.93 ± 13.20	68.29 ± 15.49	72.58 ± 14.84	75.36 ± 15.64	< 0.001
Gender					< 0.001
Male	14983 (29.24%)	24120 (47.07%)	33452 (65.28%)	39551 (77.18%)	
Female	36262 (70.76%)	27124 (52.93%)	17792 (34.72%)	11694 (22.82%)	
Family history					< 0.001

Values are n(%) or mean ± SD

BMI Body mass index, FPG Fasting plasma glucose, TG Triglyceride, TyG-BMI = BMI×Ln(fasting triglycerides (mg/dl)× fasting blood glucose(mg/dl)/2), SBP Systolic blood pressure, DBP Diastolic blood pressure, TC Total cholesterol, ALT Alanine aminotransferase, Scr Serum creatinine, HDL-C High-density lipid cholesterol, LDL-C Low-density lipid cholesterol, AST Aspartate aminotransferase.

TyG-BMI	Q1(≤167.01)	Q2(167.01 to ≤ 191.53)	Q3(191.53 to ≤ 219.26)	Q4(219.26)	P-value
NO	50327 (98.21%)	50095 (97.76%)	50187 (97.94%)	50179 (97.92%)	
YES	918 (1.79%)	1149 (2.24%)	1057 (2.06%)	1066 (2.08%)	
HDL(mmol/L)					< 0.001
Low	4321 (8.43%)	7255 (14.16%)	11440 (22.32%)	15213 (29.69%)	
Middle	8289 (16.18%)	10160 (19.83%)	10449 (20.39%)	9178 (17.91%)	
High	14117 (27.55%)	11538 (22.52%)	8407 (16.41%)	5957 (11.62%)	
Not record	24518 (47.84%)	22291 (43.50%)	20948 (40.88%)	20897 (40.78%)	
LDL(mmol/L)					< 0.001
Low	13027 (25.42%)	10258 (20.02%)	8164 (15.93%)	7193 (14.04%)	
Middle	8693 (16.96%)	10309 (20.12%)	10299 (20.10%)	9935 (19.39%)	
High	5080 (9.91%)	8594 (16.77%)	12194 (23.80%)	13712 (26.76%)	
Not record	24445 (47.70%)	22083 (43.09%)	20587 (40.17%)	20405 (39.82%)	
AST(U/L)					< 0.001
Low	10327 (20.15%)	8482 (16.55%)	6057 (11.82%)	3722 (7.26%)	
Middle	7088 (13.83%)	7635 (14.90%)	7815 (15.25%)	6243 (12.18%)	
High	3699 (7.22%)	5490 (10.71%)	7956 (15.53%)	11777 (22.98%)	

Values are n(%) or mean ± SD

BMI Body mass index, FPG Fasting plasma glucose, TG Triglyceride, TyG-BMI = BMI×Ln(fasting triglycerides (mg/dl)× fasting blood glucose(mg/dl)/2), SBP Systolic blood pressure, DBP Diastolic blood pressure, TC Total cholesterol, ALT Alanine aminotransferase, Scr Serum creatinine, HDL-C High-density lipid cholesterol, LDL-C Low-density lipid cholesterol, AST Aspartate aminotransferase.

TyG-BMI	Q1(≤167.01)	Q2(167.01 to ≤ 191.53)	Q3(191.53 to ≤ 219.26)	Q4(≥219.26)	P-value
Not record	30131 (58.80%)	29637 (57.84%)	29416 (57.40%)	29503 (57.57%)	
Smoking status					< 0.001
Current smoker	1282 (2.50%)	2161 (4.22%)	3248 (6.34%)	4841 (9.45%)	
Ever smoker	298 (0.58%)	507 (0.99%)	768 (1.50%)	893 (1.74%)	
Never smoker	11551 (22.54%)	11271 (21.99%)	11017 (21.50%)	10307 (20.11%)	
Not record	38114 (74.38%)	37305 (72.80%)	36211 (70.66%)	35204 (68.70%)	
Drinking status					< 0.001
Current drinker	108 (0.21%)	209 (0.41%)	386 (0.75%)	615 (1.20%)	
Ever drinker	1059 (2.07%)	1850 (3.61%)	2572 (5.02%)	3234 (6.31%)	
Never drinker	11964 (23.35%)	11880 (23.18%)	12075 (23.56%)	12192 (23.79%)	
Not record	38114 (74.38%)	37305 (72.80%)	36211 (70.66%)	35204 (68.70%)	
Values are n(%) or mean ± SD					
BMI Body mass index, FPG Fasting plasma glucose, TG Triglyceride, TyG-BMI = BMI×Ln(fasting triglycerides (mg/dl)× fasting blood glucose(mg/dl)/2), SBP Systolic blood pressure, DBP Diastolic blood pressure, TC Total cholesterol, ALT Alanine aminotransferase, Scr Serum creatinine, HDL-C High-density lipid cholesterol, LDL-C Low-density lipid cholesterol, AST Aspartate aminotransferase.					

Univariate Analysis

The results of the univariate analysis were shown in Table 2. Table 2 showed that men were more likely to develop diabetes than women, and age, BMI, FPG, TG, TyG-BMI, SBP, DBP, TC, LDL, ALT, AST, SCR, smoking, drinking, and family history were all positively associated with incident diabetes.

Table 2
The results of univariate analysis

	Statistics	HR (95%CI) P value
Age	42.216 ± 12.703	1.067 (1.065, 1.069) <0.00001
Gender		
Male	112106 (54.692%)	Ref
Female	92872 (45.308%)	0.498 (0.465, 0.534) <0.00001
BMI	23.186 ± 3.241	1.256 (1.245, 1.267) <0.00001
FPG	4.919 ± 0.602	10.572 (10.109, 11.057) <0.00001
TG	1.330 ± 0.982	1.281 (1.268, 1.294) <0.00001
Family history		
NO	200788 (97.956%)	Ref
YES	4190 (2.044%)	1.741 (1.487, 2.037) <0.00001
TyG-BMI	195.037 ± 36.149	1.026 (1.026, 1.027) <0.00001
SBP	119.002 ± 16.360	1.038 (1.037, 1.040) <0.00001
DBP	74.128 ± 10.788	1.045 (1.043, 1.048) <0.00001
TC	4.707 ± 0.897	1.422 (1.380, 1.465) <0.00001
HDL		
Low	38229 (18.650%)	Ref
Middle	38076 (18.576%)	0.840 (0.766, 0.921) 0.00021
High	40019 (19.524%)	0.751 (0.683, 0.826) <0.00001
Not record	88654 (43.250%)	0.570 (0.526, 0.616) <0.00001
LDL		
Low	38642 (18.852%)	Ref
Middle	39236 (19.142%)	1.127 (1.019, 1.247) 0.02050
High	39580 (19.309%)	1.659 (1.510, 1.822) <0.00001
Not record	87520 (42.697%)	0.782 (0.714, 0.858) <0.00001
ALT	23.736 ± 21.748	1.004 (1.004, 1.005) <0.00001
AST		

	Statistics	HR (95%CI) P value
Low	28588 (13.947%)	Ref
Middle	28781 (14.041%)	1.412 (1.230, 1.620) <0.00001
High	28922 (14.110%)	2.668 (2.354, 3.025) <0.00001
Not record	118687 (57.902%)	1.332 (1.186, 1.496) <0.00001
Scr	70.043 ± 15.446	1.006 (1.005, 1.007) <0.00001
Smoking status		
Current smoker	11532 (5.626%)	Ref
Ever smoker	2466 (1.203%)	0.763 (0.591, 0.986) 0.03850
Never smoker	44146 (21.537%)	0.440 (0.388, 0.499) <0.00001
Not record	146834 (71.634%)	0.584 (0.526, 0.650) <0.00001
Drinking status		
Current drinker	1318 (0.643%)	Ref
Ever drinker	8715 (4.252%)	0.462 (0.335, 0.638) <0.00001
Never drinker	48111 (23.471%)	0.457 (0.340, 0.612) <0.00001
Not record	146834 (71.634%)	0.483 (0.362, 0.645) <0.00001

In Fig. 2, the cumulative risk of incident diabetes Kaplan Meier curves stratified by TyG-BMI showed that the cumulative risk of diabetes increased gradually with increasing TyG-BMI. There was a significant difference in diabetes risk between the TyG-BMI quartile groups (log-rank test P < 0.0001).

The Multivariate Analysis Of Tyg-bmi With Dm Risk

To evaluate group differences in the association between TyG-BMI and incident diabetes, we applied Cox proportional hazards models, and Table 3 showed the unadjusted and adjusted models. In crude model, TyG-BMI had a positive correlation with diabetes incidence (HR = 1.026, 95% confidence interval (CI):1.026 to 1.027, P < 0.00001). We could draw the same conclusion in model I(minimally adjusted model,adjusted age, gender, SBP, DBP, smoking status, drinking status, family history) and model II(fully adjusted model,adjusted age, gender, SBP, DBP, smoking status, drinking status, family history, TC, HDL, LDL, ALT, AST, SCR). Model I (HR = 1.022, 95% CI: 1.021 to 1.023, P < 0.00001), model II(HR = 1.023, 95% CI: 1.022 to 1.024, P < 0.00001), respectively. We also performed a sensitivity analysis taking TyG-BMI as a categorical variable (quartile) at the same time and calculating P for trend. The result was consistent with that of TyG-BMI as a continuous variable (trend P < 0.00001). In the fully adjusted model (model II),

the risk of diabetes in the Q4 group increased by 10.261 times compared to the Q1 group, and the trend in the quartile was significant (trend P < 0.00001).

Table 3
Relationship between TyG-BMI and the incident of diabetes in different models

Variable	Crude model (HR,95%CI,P)	Model I (HR,95%CI,P)	Model II (HR,95%CI,P)
TyG-BMI	1.026 (1.026, 1.027) < 0.00001	1.022 (1.021, 1.023) < 0.00001	1.023 (1.022, 1.024) < 0.00001
TyG-BMI(quartile)			
Q1	Ref	Ref	Ref
Q2	2.967 (2.405, 3.660) < 0.00001	2.020 (1.636, 2.495) < 0.00001	2.049 (1.659, 2.532) < 0.00001
Q3	8.089 (6.675, 9.801) < 0.00001	4.195 (3.450, 5.102) < 0.00001	4.437 (3.644, 5.403) < 0.00001
Q4	23.876 (19.854, 28.714) < 0.00001	10.562 (8.730, 12.779) < 0.00001	11.261 (9.277, 13.668) < 0.00001
P for trend	< 0.00001	< 0.00001	< 0.00001
Data in the table: HR:hazard ratio,CI:confidence, Ref: reference, P value *P < 0.05 **P < 0.01 ***P < 0.001			
outcome variable: diabetes			
exposure variable: TyG-BMI□TyG-BMI(quartile)			
Crude model adjust for: None			
Adjust I model adjust for: Age, Gender, SBP, DBP, Smoking status, Drinking status, Family history			
Adjust II model adjust for: Age, Gender, SBP, DBP, Smoking status, Drinking status, Family history, TC, HDL, LDL, ALT, AST, Scr			
Cox model Time variable: Follow up			

The Analyses Of The Non-linear Relationship

Because TyG-BMI was a continuous variable, we identified the nonlinear relationship between TyG-BMI and diabetes incidence rate (adjusted age, gender, SBP, DBP, smoking status, drinking status, family history, TC, HDL, LDL, ALT, AST, SCR) by using the generalized additive model(GAM). In addition, there was an inflection point of TyG-BMI calculated by a two-piecewise linear regression model, and the inflection point was 232.416. The association between TyG-BMI and incident diabetes was positive on

either side of the inflection point. The positive potency was slightly weaker on the right side(HR = 1.016, 95%CI: 1.014 to 1.018, P < 0.0001) of the inflection point than on the left(HR = 1.029, 95%CI: 1.027 to 1.031, P < 0.0001). (Table 4,Fig. 3).

Table 4
The result of two-piecewise linear regression model

	incident of diabetes (HR,95%CI, P)
Fitting model by standard linear regression	1.023 (1.022, 1.024) < 0.0001
Fitting model by two-piecewise linear regression	
Inflection point of TyG-BMI	232.416
< 232.416	1.029 (1.027, 1.031) < 0.0001
> 232.416	1.016 (1.014, 1.018) < 0.0001
P for log likelihood ratio test	< 0.001
CI: Confidence interval	
We adjusted Age, Gender, SBP, DBP, TC, HDL, LDL, ALT, AST, SCR, Smoking status, Drinking status, Family history.	

The Results Of Subgroup Analyses

Table 5 was the subgroup analysis for the correlation between TyG-BMI and diabetes incidence to explore other risks. The participants were divided into subgroups according to age, gender, HDL, LDL, SBP, DBP, smoking status, drinking status, and family history of diabetes. The association between TyG-BMI and incident diabetes was stable in family history, smoking status, and gender of patients (all P values for interaction 0.05). In contrast, We observed a number of interactions, including age, HDL, LDL, SBP, DBP, Drinking status (all P values of interaction < 0.05). The relationship between TyG-BMI and diabetes was stronger in people with age 20–30(HR 1.029, 95%CI :1.024 to 1.035), age 30–40(HR 1.032, 95%CI :1.029 to 1.034), age 40–50(HR 1.029, 95%CI :1.027 to 1.031), HDL(high group) (HR = 1.024, 95%CI: 1.022 to 1.026), SBP<140(HR = 1.025, 95%CI:1.024 to 1.027), DBP<90(HR = 1.024, 95%CI:1.023 to 1.025), current drinker(HR = 1.031, 95%CI: 1.022 to 1.041) and ever drinker(HR = 1.032, 95%CI: 1.027 to 1.037). In addition, the relationship between TyG-BMI and diabetes risk was weaker in the people with age 60–70 (HR 1.015, 95%CI :1.013 to 1.017), age ≥ 70(HR 1.013, 95%CI :1.011 to 1.016), HDL(low group) (HR = 1.020, 95%CI: 1.018 to 1.021), LDL(middle group) (HR = 1.022, 95%CI: 1.020 to 1.024), LDL(high group) (HR = 1.021, 95%CI: 1.019 to 1.023), SBP ≥ 140(HR = 1.017, 95%CI:1.015 to 1.019), DBP ≥ 90(HR = 1.018, 95%CI:1.016 to 1.021) and never drinker (HR = 1.022, 95%CI: 1.020 to 1.024).

Table 5
Effect size of TyG-BMI on diabetes in prespecified and exploratory subgroups

Characteristic	No. of participants	Effect size(HR,95%CI,P) P for interacion
Age(years)	27301	<0.0001
20 to < 30	80043	1.029 (1.024, 1.035) < 0.0001
30 to < 40	43888	1.032 (1.029, 1.034) < 0.0001
40 to < 50	29252	1.029 (1.027, 1.031) < 0.0001
50 to < 60	17278	1.023 (1.021, 1.025) < 0.0001
60 to < 70	7216	1.015 (1.013, 1.017) < 0.0001
≥70		1.013 (1.011, 1.016) < 0.0001
Gender		0.9252
Male	112106	1.023 (1.022, 1.024) < 0.0001
Female	92872	1.023 (1.021, 1.024) < 0.0001
HDL(mmol/L)		0.0012
Low	38229	1.020 (1.018, 1.021) < 0.0001
Middle	38076	1.023 (1.021, 1.026) < 0.0001
High	40019	1.024 (1.022, 1.026) < 0.0001
Not recorded	88654	1.024 (1.023, 1.026) < 0.0001
LDL(mmol/L)		0.0222
Low	38642	1.023 (1.021, 1.025) < 0.0001
Middle	39236	1.022 (1.020, 1.024) < 0.0001
High	39580	1.021 (1.019, 1.023) < 0.0001
Not recorded	87520	1.024 (1.023, 1.026) < 0.0001
SBP(mmHg)		<0.0001
<140	185128	1.025 (1.024, 1.027) < 0.0001
≥140	20958	1.017 (1.015, 1.019) < 0.0001
DBP(mmHg)		<0.0001
<90	189459	1.024 (1.023, 1.025) < 0.0001

Note 1:Above model adjusted for Age, Gender, SBP, DBP, TC, HDL, LDL, ALT, AST, SCR, Smoking status, Drinking status, Family history. Note 2: In each case, the model is not adjusted for the stratification variable

Characteristic	No. of participants	Effect size(HR,95%CI,P) P for interacion
≥90	16627	1.018 (1.016, 1.021) < 0.0001
Smoking status		0.1151
Current smoker	11532	1.025 (1.022, 1.028) < 0.0001
Ever smoker	2466	1.029 (1.021, 1.036) < 0.0001
Never smoker	44146	1.023 (1.021, 1.025) < 0.0001
Not recorded	146834	1.022 (1.021, 1.023) < 0.0001
Drinking status		0.0002
Current drinker	1318	1.031 (1.022, 1.041) < 0.0001
Ever drinker	8715	1.032 (1.027, 1.037) < 0.0001
Never drinker	48111	1.022 (1.020, 1.024) < 0.0001
Not recorded	146834	1.022 (1.021, 1.023) < 0.0001
Family history of diabetes		0.1543
No	200788	1.023 (1.022, 1.024) < 0.0001
Yes	4190	1.020 (1.016, 1.024) < 0.0001
Note 1:Above model adjusted for Age, Gender, SBP, DBP, TC, HDL, LDL, ALT, AST, SCR, Smoking status, Drinking status, Family history. Note 2: In each case, the model is not adjusted for the stratification variable		

Discussion

In this China's large retrospective cohort study, we found that after adjusting for many confounding factors (age, gender, SBP, DBP, TC, HDL, LDL, ALT, AST, SCR, smoking, SBP), there was a positive nonlinear correlation between TyG-BMI and risk of diabetes. The inflection point value was 232.416, which was consistent in the direction before and after the inflection point, but the effect value was not completely consistent ([left (HR: 1.029, 95% CI: 1.027–1.031, P < 0.0001)]; Right (HR: 1.016, 95% CI: 1.014–1.018, P < 0.0001)].The subgroup analysis showed that the association between TyG-BMI and diabetes risk were stronger in the following groups: age 20–30(HR = 1.029, 95%CI:1.024 to 1.035), age 30–40(HR = 1.032, 95%CI:1.029 to 1.034), age 40–50(HR 1.029, 95%CI:1.027 to 1.031), high HDL(HR = 1.024, 95%CI: 1.022 to 1.026), SBP<140(HR = 1.025, 95%CI:1.024 to 1.027), DBP<90 (HR = 1.024, 95%CI:1.023 to 1.025), current drinker(HR = 1.031, 95%CI: 1.022 to 1.041), and ever drinker(HR = 1.032, 95%CI: 1.027 to 1.037).

Metabolic disorders, such as obesity, hyperglycemia, hypertension, dyslipidemia, and hyperinsulinemia, are the pathological basis of cardiovascular and cerebrovascular diseases and diabetes. In developing type 2 diabetes, decreased β cell function and insulin resistance are the main events[12]. Adipose tissue

is a complex and highly active metabolic and endocrine organ[13]. Elevated blood glucose and lipid levels have toxic effects on beta cells and interfere with normal glucose metabolism. Insulin resistance triggers hyperinsulinemia, and hyperinsulinemia, in turn, causes insulin resistance[2]. It is generally accepted that insulin resistance is closely related to the risk of type 2 diabetes. Clinically, the gold standard of insulin resistance is the glucose clamp test, which is inconvenient and expensive. Although homeostasis model assessment of insulin resistance (HOMA-IR) has a wide range of clinical applications, its application is limited due to its relatively high cost and low repeatability. Simental-Mendía et al.[3] Proposed the concept of the TyG index, which indicated that the TyG index could be used as an alternative index of insulin resistance in healthy subjects. Many studies have shown that the TyG index is a good alternative marker of insulin resistance.[4, 14–17] Compared with the HOMA-IR index, the TyG index has higher sensitivity in recognizing insulin resistance[15]. TyG index is regular and easy to get, including FBG and TG, which have been associated with diabetes risk[8, 9, 14, 18]. In addition to the TyG index, the relationship between obesity and diabetes is also well documented. The prevalence of type 2 diabetes mellitus is rapidly increasing, in parallel with the current obesity epidemic. The incidence rate of type 2 diabetes is lower in non-obese patients[19]. BMI is a simple, economical, and useful indicator of general obesity. A cross-sectional study of the Taiwan population shows that TyG-BMI (a combination of TyG index and BMI) is an effective marker for early recognition of insulin resistance[3]. A recent study involving 511 individuals indicated that TyG-BMI was a stronger predictor of IR than TyG-WC[3]. In a Nigerian cross-sectional study[20], in all 473 participants, TyG-BMI shows larger AUC for metabolic syndrome detection (0.838, 95% CI: 0.802–0.870) than TyG index (0.796, 95% CI: 0.757– 0.831). After adjusting for gender, age, smoking, SBP and DBP, only the TyG index and TyG-BMI significantly predicted metabolic syndrome in men[20]. However, a Korean retrospective study involving 11,149 people showed that TyG-BMI was superior to the other parameters(TyG index, TyG-WC, TyG-WHtR) in predicting insulin resistance[21]. These conclusions are similar to ours. Firstly, consistent with previous studies, TyG-BMI was positively correlated with the incidence of diabetes. Then we further analyzed and discovered the curvilinear relationship. After adjusting for confounding factors in our study, the association between TyG-BMI and incident diabetes was nonlinear by using two piecewise linear regression models. The inflection point of GAM was 232.416 after adjusting for potential confounding factors (age, gender, SBP, DBP, TC, HDL, LDL, ALT, AST, SCR, smoking, SBP). We found that the inflection point had a stronger relationship on the left side of the inflection point. Therefore, controlling TyG-BMI is more valuable for reducing the risk of diabetes under the inflection point.

Our study has some strength: (1).To our knowledge, this is the first study to assess the association between TyG-BMI and incident diabetes in the Chinese population; (2). Compared with other researches, our sample size is relatively larger, which can better represent the Chinese people; (3). This study was a retrospective cohort study, which reduced selection bias and observation bias; (4). We found the non-linear relationship and made a deeper discussion, and there are also more confounding factors for adjustment; (5). To make the results more robust, TyG-BMI was treated both as a continuous and categorical variable.

The study also has some potential limitations: (1). The data was from the Rich Healthcare Group in China, representing the Chinese population, and couldn't be extended to other races and particular groups like pregnant women and children. (2). This research was based on a secondary analysis of published data, variables were limited to the original study's data, some other important variables such as hip circumference, medication history, hemoglobin A1C, physical activity, dietary factors were not included. (3). The incidence of diabetes may underestimate because of the study's diabetes definition, which did not conduct a 2-hour oral glucose tolerance test. But for such a large cohort, It is a vast project to improve participants' oral glucose tolerance test. (4). The study did not differentiate diabetes types. But these conclusions may be more applicable to type 2 diabetes which accounts for approximately 90ariablesdiabetes patients. (5). According to TyG-BMI, we only measured it at baseline, not measured over time. In the future, we can consider more variables and a longer follow-up with a more refined method.

Conclusion

The association between TyG-BMI and incident diabetes is positive and nonlinear after correcting the related confounding factors. The inflection point was 232.416. On the left side of the inflection point, the relationship between TyG-BMI and diabetes is the most significant.

Abbreviations

BMI
Body mass index; TyG:Triglycerideglucose index;TyG-BMI:triglyceride glucose-body mass index; IR:insulin resistance; HRs:hazard ratios; 95%CIs:95% confidence intervals; IDF:International Diabetes Federation; DM:Diabetes mellitus; T2DM:Type 2 diabetes; TG:Triglyceride; FPG:fasting plasma glucose; LDL-C:low-density lipoprotein cholesterol; HDL-C:high-density lipoprotein cholesterol; TC:total cholesterol; BUN:serum urea nitrogen; Scr:serum creatinine; AST:aspartate aminotransferase ; ALT:alanine aminotransferase; SBP:systolic blood pressure; DBP:diastolic blood pressure. GAM:Generalized additive models; SD:standard deviation. IQR:interquartile range.

Declarations

Authors' contributions

Fan Yang and Xiaohan Ding contributed to the study concept and design, researched and interpreted the data and drafted the manuscript. Zhuangsen CHEN, Yan Liao, Miaoling CHEN researched data and reviewed the manuscript. Weili YAO and Qian LIANG oversaw the progress of the project, contributed to the discussion and reviewed the manuscript. Xinyu WANG and Haofei HU are the guarantors of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. All authors read and approved the final the manuscript.

Acknowledgements

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Availability of data and materials

Data can be downloaded from ‘DATADRYAD’ database (www.Datadryad.org).

Consent for publication

Not applicable.

Ethics approval and consent to participate

In the previously published article [11], Ying Chen, et al. has clearly stated that: the study was conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from all Participants.

Funding

This study was also supported in part by the International Cooperative Research Project of Shenzhen Municipal Science and Technology Innovation Council (accounts GJHZ20180416161481462).

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Figures

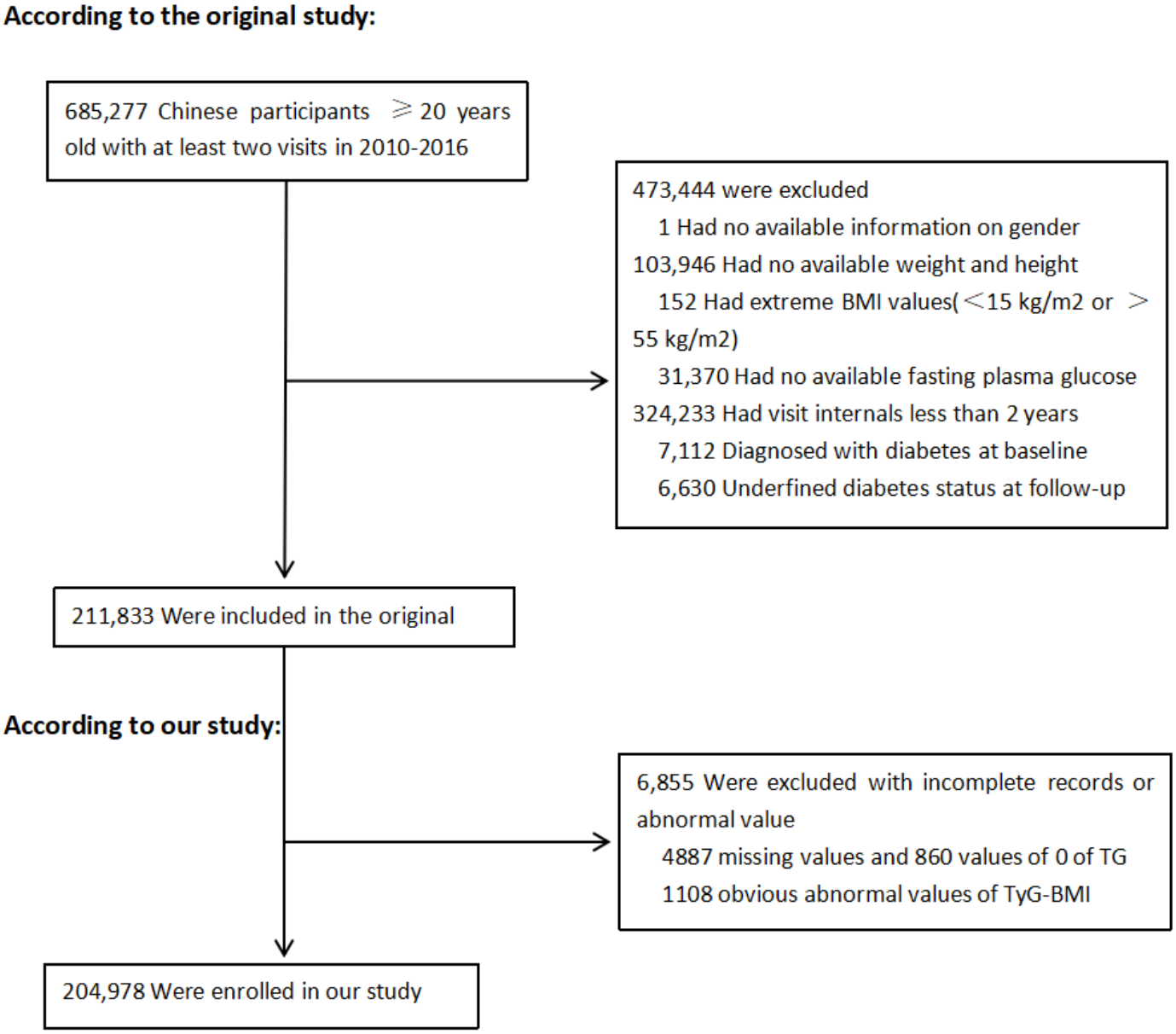

Figure 1

Flowchart of study population

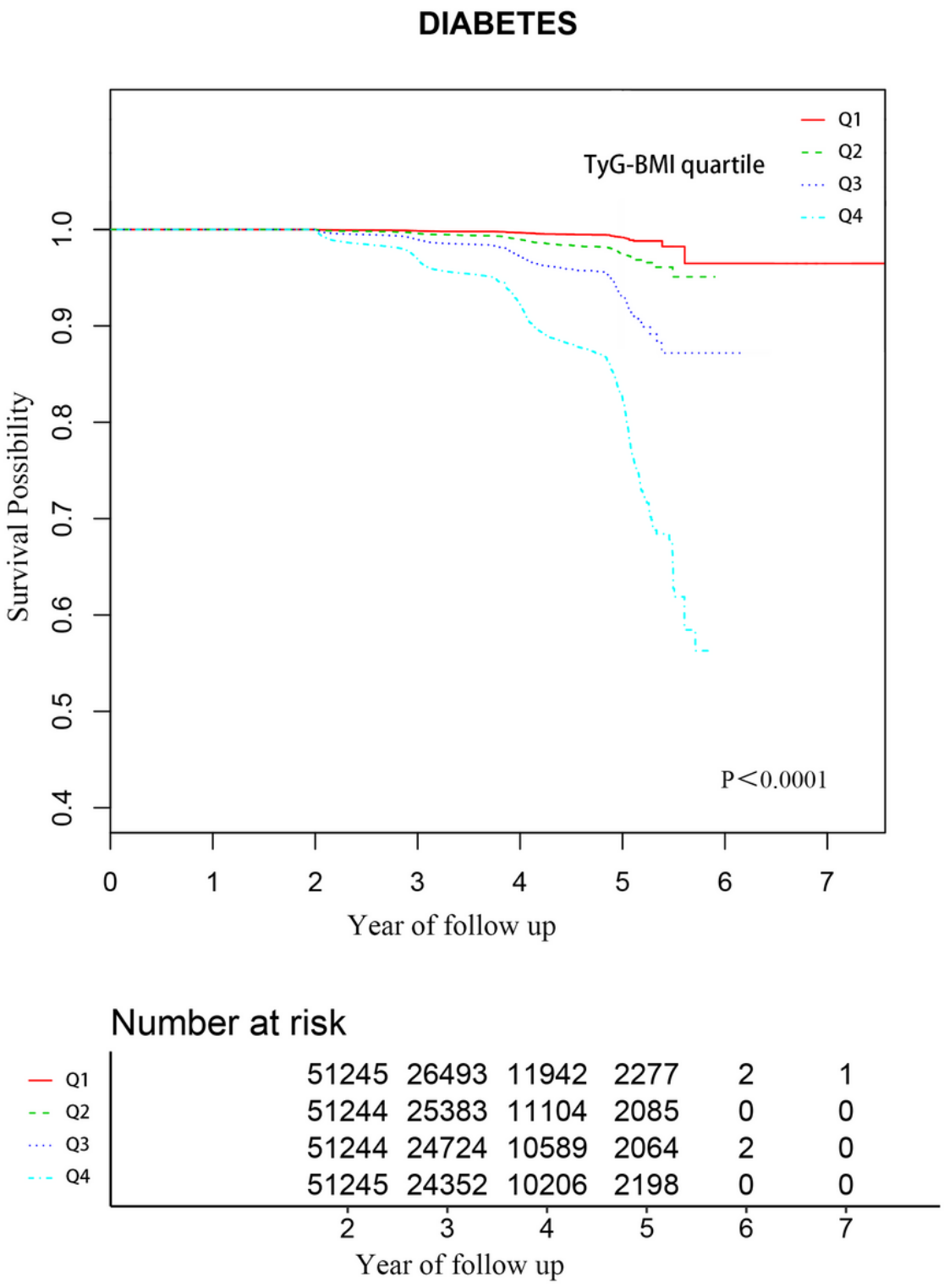

Figure 2

Kaplan–Meier event-free survival curve. Kaplan–Meier analysis of incident of diabetes based on TyG-BMI quartiles (logrank, P < 0.0001).

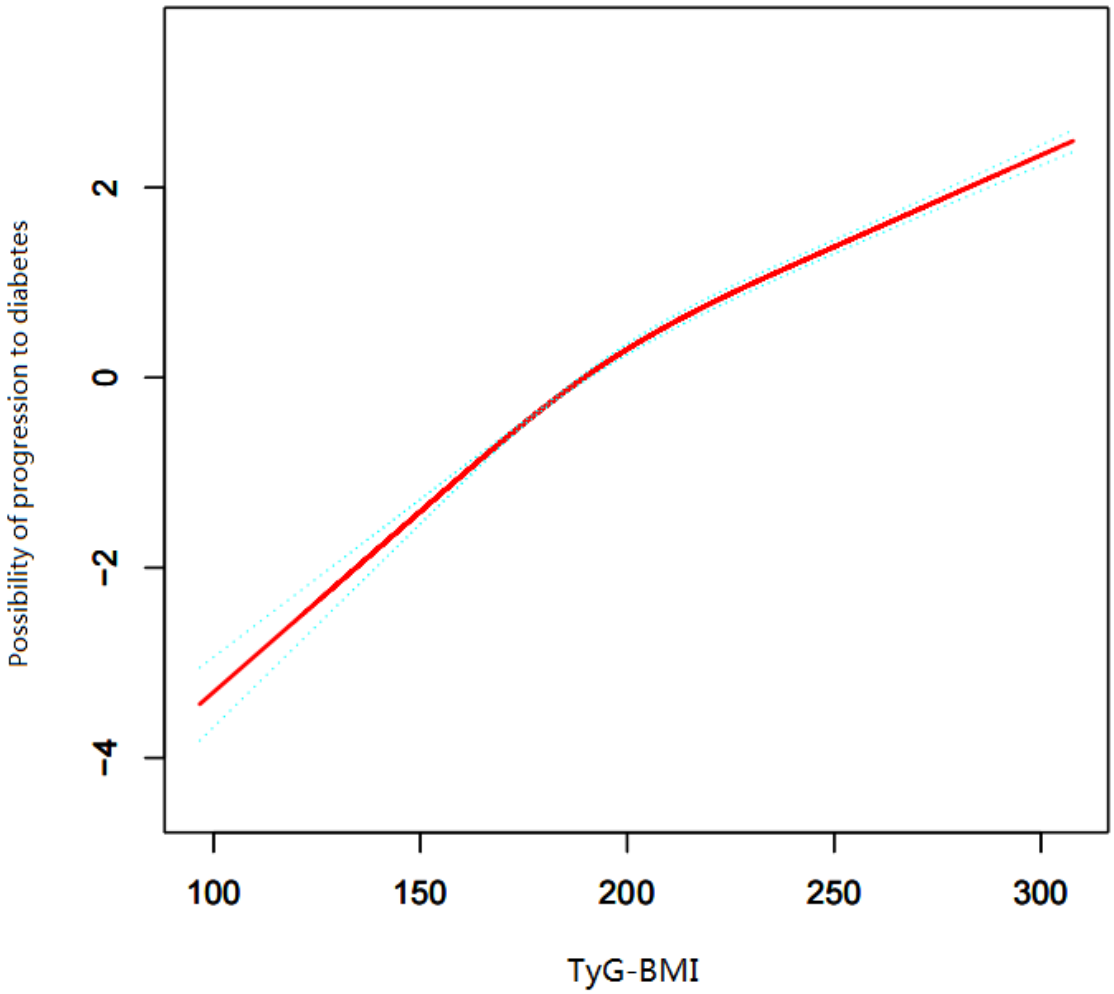

Figure 3

The non-linear relationship between TyG-BMI and incident of diabetes after adjusting for Age, Gender, SBP, DBP, Smoking Status, Drinking Status, Family History, TC, HDL, LDL, ALT, AST, SCR.