The association of serum gamma-glutamyltransferase and the incidence of type 2 diabetes mellitus based on propensity score matching: a retrospective observational cohort study

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Abstract

Background: Previous studies reported that gamma-glutamyltransferase (GGT) may play an important role in the development of diabetes. The purpose of this study is to demonstrate that GGT is an independent risk factor for diabetes and to explore whether the association between GGT and the incidence of diabetes is affected by age and gender in the general Japanese population.

Methods: This study is a retrospective observational cohort study. The study included 15464 men and women with an average age of 43.71 years from the Japanese health checkup program at Murakami Memorial Hospital from 2004 to 2015. The serum gamma-glutamyl transferase was stratified by quintiles. Patients were stratified by gender and age.

Results: After adjusting for potential confounders, each additional standard deviation (SD) of GGT increases the risk of diabetes by 6%. The hazard ratio (HR) is 1.06 and the confidence interval (CI) is (1.02, 1.16). Participants in the fourth to fifth quintiles (Q4-5, ≥ 16 U / L) had a higher risk of diabetes than the third quintile of GGT (Q1-3) (HR: 1.40, 95 % CI: 1.05-1.86). Compared with the GGT of Q1-3, among men and women aged 40 to 50, the GGT of Q4-5 increased the odds of diabetes by 31% and 13%.

Conclusions: GGT is positively correlated with the incidence of diabetes in the Japanese population. Especially in people aged 40-50y, the higher the GGT, the higher the risk of developing diabetes.

Background

With the development of the economy, the improvement of people's living standards and changes in lifestyles, the prevalence of diabetes is increasing year by year in China and worldwide [1]. An estimate released by the International Diabetes Organization, in 2030, people with T2DM will reach 552 million[2]. As a chronic disease, type 2 diabetes mellitus can cause significant series of complications and bring a huge economic burden on society[3]. Therefore, early screening and prevention of type 2 diabetes mellitus are essential.

Serum gamma-glutamyltransferase (GGT), is an enzyme that is mainly responsible for the catabolism of the antioxidant glutathione outside the cell and is currently considered to be a sign of oxidative stress [4]. Serum GGT is considered to be a sign of endogenous fat accumulation and has a close relationship with the liver [5]. Compared with other liver markers such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), and bilirubin, GGT is still one of the main predictors of type 2 diabetes mellitus[6, 7]. A prospective study reported that even within the normal range of serum GGT, the dose-response relationship is associated with the occurrence of type 2 diabetes mellitus[8]. Some studies have shown that GGT can also independently predict the progression of type 2 diabetes mellitus[9–13]. A previous study found that among subjects with higher GGT, age was more closely related to diabetes [13]. Studies have found that men have a closer influence on the relationship between GGT and diabetes[14].

In this study, after adjusting risk factors and controlling confounding factors, we studied the relationship between GGT and type 2 diabetes. Besides, we further explored the correlation between different serum GGT levels and type 2 diabetes mellitus after stratification by age and gender.

Methods

Study design and participants

We downloaded the raw data from the "Dryad Digital Repository" website. The website can use the original data of published papers for free without infringing on the rights of the original author. We cited the following data packages: the Dryad data package [15]. Data from: Ectopic fat obesity presents the greatest risk for incident type 2 diabetes: a population-based longitudinal study, Dryad, Dataset, <https://doi.org/10.5061/dryad.8q0p192>. The study protocol was subject to approval by the Ethics Committee of the First Affiliated Hospital of Wenzhou Medical University. Since the downloaded raw data is anonymous, no informed consent is required. All participants filled out questionnaires on demographics. About Japanese standards, the average weekly ethanol intake is divided into the following four groups: no or minimum alcohol consumption per day, < 40 g/week; light, 40–140 grams per week; moderate, 140–280 grams per week or drinking heavily, > 280 g/week[15]. The diagnosis of fatty liver is jointly diagnosed by a trained ultrasound technician and a gastroenterologist. According to the data filled in at the time of admission, the smoking status was divided into 3 categories: never smoke; had smoked in the past but quit smoking; currently smoking. Regular exercise is defined as the type of physical exercise performed more than once a week [16, 17]. More specific details are presented in the original report[15].

Data source

Japanese baseline demographic data was from a medical examination program at Murakami Memorial Hospital (Gifu, Japan). Variables included in the database file were as follows: sex, age, fatty liver, body mass index (BMI), aspartate aminotransferase (AST), waist circumference(WC), body weight, exercise, high-density lipoprotein cholesterol (HDL-C), gamma-glutamyl transferase(GGT), alanine aminotransferase (ALT), total cholesterol (TC), triglyceride (TG), HbA1c, alcohol consumption, smoking status, fasting plasma glucose(FPG), diastolic blood pressure (DBP), systolic blood pressure (SBP).

Outcomes

The outcome of the study population during follow-up (2004–2015) was the development of type 2 diabetes mellitus. Incident type 2 diabetes mellitus was defined as fasting plasma glucose ≥ 7 mmol/L, HbA1c $\geq 6.5\%$ or self-reported.

Statistical analysis

We grouped GGT in quintiles. Continuous variables were expressed as the means $\pm$ standard deviations, and categorical variables were expressed as a frequency or percentages. One-way ANOVA (normal distribution), be Kruskal-Wallis H (skewed distribution) test and chi-square test (categorical variables) were used to determine any significant differences between the means and proportions of the groups. A Cox proportional hazards model was used to determine the association between GGT and the incidence of diabetes. According to the recommendations of the STROBE statement [18], we also show the results of the unadjusted, minimally adjusted analysis, and fully adjusted analysis. After adding covariates to this model, the matching hazard ratio will change by at least 10% and be adjusted. We also tested the interaction effects in different subgroups. A 1: 2 matching protocol was used for matching, with a caliper width equal to 0.05 of the standard deviation of the propensity score. Statistical packages R (version 3.4.3, The R Foundation; <http://www.r-project.org>) was used for statistical analyses.

Results

Baseline Characteristics of participants by GGT quintiles

In this study, a total of 15,464 people enrolled in the study. Male 7034 (45.49%), female 8430 (54.51%), the average age of the population was 43.71 years, the average GGT was 20.31 IU/L, and the average follow-up time was 6.05y. The study population was divided into 5 groups according to the GGT quintiles. As can be seen from Table 1, age, BMI, WC, ALT, AST, body weight, HDL-c, TG, HbA1c, FPG, DBP and SBP were positively correlated with GGT, and the P-value of the trend test was significant. The proportion of fatty liver in GGTQ4-5 was much higher than GGTQ1-3, and this difference was statistically significant. There was also a positive correlation between alcohol intaking and GGT. For the factor of smoking, the proportion of people with high GGT was higher than that of people with low GGT in the current and past smokers. Among non-smokers, there were no differences among the different GGT groups. During the follow-up period, the proportion of patients diagnosed with diabetes was higher in GGTQ5 than in GGTQ1-4. The cumulative incidence of diabetes stratified by GGT quintiles was shown in Fig. 1. It can be seen that the risk of diabetes mellitus in GGTQ5, GGTQ4 was much higher than GGTQ1, GGTQ2, GGTQ3. We classified GGT into GGTQ4-5 (≥ 16 IU/L) and GGTQ1-3 (< 16 IU/L), with GGT16 IU/L as the boundary.

Table 1
Baseline Characteristics of participants by γ -glutamyltranspeptidase quintiles (N = 15464)

Characteristics	Q1	Q2	Q3	Q4	Q5	P value
	< 11.00 IU/L	11.00 to < 12.00 IU/L	12.00 to < 16.00 IU/L	16.00 to < 24.00 IU/L	24.00 to < 399.00 IU/L	
No. of participants	2885	2328	3674	3304	3273	
Age (years)	42.18 $\pm$ 8.49	42.60 $\pm$ 8.65	43.56 $\pm$ 9.18	44.36 $\pm$ 9.00	45.35 $\pm$ 8.66	< 0.001
BMI (kg/m ²)	20.67 $\pm$ 2.40	21.07 $\pm$ 2.66	21.66 $\pm$ 2.88	22.83 $\pm$ 3.12	23.93 $\pm$ 3.21	< 0.001
WC (cm)	70.54 $\pm$ 7.27	72.79 $\pm$ 7.53	75.37 $\pm$ 8.08	79.37 $\pm$ 8.35	82.63 $\pm$ 8.53	< 0.001
ALT (IU/L)	12.86 $\pm$ 5.23	14.48 $\pm$ 5.38	16.94 $\pm$ 6.61	21.67 $\pm$ 9.97	31.91 $\pm$ 23.59	< 0.001
AST (IU/L)	14.96 $\pm$ 4.23	16.10 $\pm$ 4.57	17.32 $\pm$ 5.16	19.12 $\pm$ 6.66	23.56 $\pm$ 14.32	< 0.001
Body Weight (kg)	53.36 $\pm$ 8.15	55.57 $\pm$ 9.29	59.18 $\pm$ 10.26	64.64 $\pm$ 11.17	68.25 $\pm$ 11.51	< 0.001
HDL (mmol/L)	1.59 $\pm$ 0.37	1.56 $\pm$ 0.39	1.49 $\pm$ 0.41	1.37 $\pm$ 0.40	1.33 $\pm$ 0.39	< 0.001
TC (mmol/L)	4.90 $\pm$ 0.83	4.96 $\pm$ 0.82	5.06 $\pm$ 0.83	5.21 $\pm$ 0.87	5.43 $\pm$ 0.86	< 0.001
TG (mmol/L)	0.61 $\pm$ 0.31	0.67 $\pm$ 0.41	0.80 $\pm$ 0.48	1.04 $\pm$ 0.67	1.34 $\pm$ 0.88	< 0.001
HbA1c (mmol/mol)	32.33 $\pm$ 3.49	32.80 $\pm$ 3.36	33.07 $\pm$ 3.39	33.32 $\pm$ 3.51	33.46 $\pm$ 3.70	< 0.001
FPG (mmol/L)	4.95 $\pm$ 0.38	5.02 $\pm$ 0.39	5.14 $\pm$ 0.39	5.27 $\pm$ 0.38	5.37 $\pm$ 0.38	< 0.001
DBP (mmHg)	66.29 $\pm$ 8.90	67.97 $\pm$ 9.32	70.96 $\pm$ 9.93	73.90 $\pm$ 9.98	77.18 $\pm$ 10.36	< 0.001
SBP (mmHg)	107.11 $\pm$ 12.95	109.68 $\pm$ 13.44	113.76 $\pm$ 14.31	117.66 $\pm$ 14.08	122.08 $\pm$ 14.84	< 0.001
Male	2467 (85.51%)	1642 (70.53%)	1751 (47.66%)	743 (22.49%)	431 (13.17%)	< 0.001
Fatty liver	86 (2.98%)	130 (5.58%)	436 (11.87%)	828 (25.06%)	1261 (38.53%)	< 0.001
Exercise	486 (16.85%)	382 (16.41%)	699 (19.03%)	620 (18.77%)	522 (15.95%)	< 0.001

Characteristics	Q1	Q2	Q3	Q4	Q5	P value
	< 11.00 IU/L	11.00 to < 12.00 IU/L	12.00 to < 16.00 IU/L	16.00 to < 24.00 IU/L	24.00 to < 399.00 IU/L	
Alcohol consumption						< 0.001
None	2699 (93.55%)	2062 (88.57%)	2999 (81.63%)	2292 (69.37%)	1753 (53.56%)	
Light	130 (4.51%)	183 (7.86%)	385 (10.48%)	503 (15.22%)	557 (17.02%)	
Moderate	52 (1.80%)	73 (3.14%)	238 (6.48%)	381 (11.53%)	616 (18.82%)	
Heavy	4 (0.14%)	10 (0.43%)	52 (1.42%)	128 (3.87%)	347 (10.60%)	
Smoking status						< 0.001
Never	2340 (81.11%)	1707 (73.32%)	2246 (61.13%)	1475 (44.64%)	1263 (38.59%)	
Past	277 (9.60%)	278 (11.94%)	632 (17.20%)	840 (25.42%)	925 (28.26%)	
Current	268 (9.29%)	343 (14.73%)	796 (21.67%)	989 (29.93%)	1085 (33.15%)	
Year of follow up (years)	7.17(0.45–12.90)	5.15(0.50–12.96)	5.03(0.52–12.94)	5.06(0.53–12.90)	5.50(0.50–12.96)	< 0.001
Diabetes was diagnosed during follow-up (%)	20 (0.7%)	26 (1.1%)	47 (1.3%)	105 (3.2%)	175 (5.3%)	< 0.001

The results of the relationship between GGT and diabetes mellitus

The COX regression analysis model was used to estimate the correlation between GGT and diabetes mellitus. As can be seen from Table 2, in the unadjusted model, there was a positive correlation between GGT and the incidence of diabetes. In Model I, we adjusted gender and age, and we found that there was still a positive correlation between GGT and the incidence of diabetes. In Model II, after adjusting sex, age, fatty liver, BMI, ALT, AST, WC, body weight, exercise, TC, TG, HbA1c, alcohol consumption, smoking status, FPG, DBP and SBP, the risk of diabetes increased by 6% for every SD raised by GGT (per SD increase, HR: 1.06, 95%CI (1.02–1.16), P = 0.042). For sensitivity analysis, we converted GGT to a categorical variable (quintile). In the adjusted II model, compared with GGTQ1, the HR for diabetes in the GGTQ5 group was 1.49 (95%:1.13–2.66, P = 0.047) and GGTQ4 was 1.46 (95%CI:1.07–2.56, P = 0.044). For further analysis,

with GGT16 IU/L as the limit, GGTQ4-5 was classified into one group, and GGTQ1-3 was classified into another group. It was noted that compared to GGTQ1-3 in a fully adjusted model, the HR for Q4-5 diabetes progression was 1.40 (95%, 1.05–1.86, P = 0.021).

Table 2
Effect modification of GGT on incident of diabetes

Exposure	Non-adjusted		Adjust I		Adjust II	
	HR (95%CI)	P value	HR (95%CI)	P value	HR (95%CI)	P value
GGT (IU/L)	1.01 (1.01, 1.01)	< 0.001	1.01 (1.01, 1.01)	< 0.001	1.00 (1.00, 1.01)	0.042
GGT (IU/L) per SD	1.23 (1.18, 1.27)	< 0.001	1.17 (1.12, 1.23)	< 0.001	1.06 (1.02, 1.16)	0.042
Categories						
GGT Q1	1.0		1.0		1.0	
GGT Q2	2.02 (1.13, 3.61)	0.018	1.92 (1.07, 3.46)	0.029	1.34 (0.74, 2.41)	0.334
GGT Q3	2.49 (1.47, 4.20)	< 0.001	2.22 (1.30, 3.79)	< 0.001	0.98 (0.56, 1.71)	0.949
GGT Q4	5.95 (3.68, 9.60)	< 0.001	5.00 (3.00, 8.34)	< 0.001	1.46 (1.07, 2.56)	0.044
GGT Q5	9.27(5.83,14.72)	< 0.001	7.51 (4.54, 12.41)	< 0.001	1.49 (1.13, 2.66)	0.047
Categories						
GGT Q1-Q3	1.0		1.0		1.0	
GGT Q4-Q5	4.27 (3.38, 5.40)	< 0.001	3.50 (2.69, 4.56)	< 0.001	1.40 (1.05, 1.86)	0.021
Adjust I model adjust for sex, age.						
Adjust II model adjust for sex, age, fatty liver, BMI, ALT, AST, WC, body weight, exercise, TC, TG, HbA1c, alcohol consumption, smoking status, FPG, DBP, SBP. CI, confidence interval; SD, standard deviation						

The results of subgroup analyses

After stratification, we analyzed based on the main covariates known to affect diabetes, including sex, age, BMI, smoking status, alcohol consumption, WC, exercise, fatty liver. As shown in Fig. 2, GGTQ4-5 had an increased risk of developing diabetes in all subgroups compared to GGTQ1-3. For further sensitivity analysis, we stratified by age and gender. It was subdivided into 5 groups based on age and 2 groups

based on gender. As can show in Table 3, in the adjusted II model, the HR of GGTQ4-5 was 1.31 (95%CI:1.01–1.71) or 1.13 (95%CI:1.02–1.38) compared to GGTQ1-3 in the 40-50y male or female. In other age groups, the risk of diabetes was not statistically significant. Because the confidence interval for β values spanned 1.

Table 3

Effect modification of GGT (Q4-5 vs. Q1–3) on incident of diabetes, stratified by age and gender.

Age, y	Sex	Unadjusted		Adjusted			
		Q1-Q3 (%)	Q4-Q5 (%)	HR (95%CI)	P value	HR (95%CI)	P value
20to < 30							
	Male	0/251(0%)	0/17(0%)	1.00 (1.00, 1.00)	NS	1.00 (1.00, 1.00)	NS
	Female	1/69(1.45%)	0/74(0%)	0.00 (0.00, Inf)	NS	0.00 (0.00, Inf)	NS
30to < 40							
	Male	15/2039 (0.74%)	2/262 (0.76%)	1.10 (0.67, 1.80)	NS	0.90 (0.50, 1.62)	NS
	Female	6/1154 (0.52%)	47/1720 (2.73%)	1.76 (1.33, 2.34)	< 0.001	1.05 (0.76, 1.45)	NS
40to < 50							
	Male	19/2324 (0.82%)	15/409 (3.67%)	1.77 (1.41, 2.22)	< 0.001	1.31 (1.01, 1.71)	0.046
	Female	15/993 (1.51%)	114/2060 (5.53%)	1.59 (1.33, 1.90)	< 0.001	1.13 (1.02, 1.38)	0.037
50to < 60							
	Male	13/1078 (1.21%)	15/413 (3.63%)	1.57 (1.23, 2.02)	< 0.001	1.17 (0.86, 1.61)	NS
	Female	13/643 (2.02%)	65/1241(5.24%)	1.41 (1.16, 1.72)	< 0.001	1.16 (0.93, 1.45)	NS
>= 60							
	Male	3/163 (1.84%)	5/73 (6.85%)	1.49 (0.93, 2.41)	0.099	1.67 (0.80, 3.49)	NS
	Female	8/168 (4.76%)	17/308 (5.52%)	1.08 (0.82, 1.43)	0.588	1.11 (0.77, 1.60)	NS
Adjust for fatty liver, BMI, ALT, AST, WC, body weight, exercise, TC, TG, HbA1c, alcohol consumption, smoking status, FPG, DBP, SBP.							

The results of propensity score matching

We matched 686 non-diabetic patients and 343 patients diagnosed with diabetes. Their baseline characteristics are presented in Table 4. From the results, we know that diabetes and non-diabetes groups do not have sex, age, fatty liver, BMI, ALT, AST, WC, body weight, exercise, TC, TG, HbA1c, alcohol consumption, smoking status, FPG, DBP, SBP significance. Diabetes patients have higher GGT than non-diabetics. (30.55 ± 26.47 IU/L VS 28.20 ± 22.62 IU/L). The results before matching are presented in Table S1, the diabetic group and the non-diabetic group. All factors had significance.

Table 4
Baseline characteristics of participants stratified by outcome after PSM

	No Diabetes (n = 686)	Diabetes(n = 343)	P value
Age (years)	47.64 ± 9.11	47.10 ± 8.62	NS
BMI (kg/m ²)	24.73 ± 3.37	24.83 ± 3.77	NS
WC (cm)	84.28 ± 9.06	84.52 ± 10.08	NS
ALT (IU/L)	27.41 ± 17.52	30.66 ± 19.46	NS
AST (IU/L)	21.72 ± 10.35	22.18 ± 9.76	NS
Body Weight (kg)	68.52 ± 12.24	69.16 ± 13.22	NS
HDL-c (mmol/L)	1.27 ± 0.38	1.20 ± 0.34	0.038
TC (mmol/L)	5.44 ± 0.89	5.43 ± 0.91	NS
TG (mmol/L)	1.36 ± 0.85	1.50 ± 1.00	NS
HbA1c (mmol/mol)	36.75 ± 3.32	36.49 ± 3.79	NS
FPG (mmol/L)	5.58 ± 0.34	5.59 ± 0.36	NS
DBP (mmHg)	77.07 ± 10.60	77.21 ± 10.12	NS
SBP (mmHg)	122.12 ± 15.67	121.99 ± 15.56	NS
Male	484 (70.6)	262 (76.4)	NS
Fatty liver	381 (55.5)	194 (56.6)	NS
Exercise	109 (15.9)	49 (14.3)	NS
Alcohol consumption			NS
None	473 (69)	243 (70.8)	
Light	80 (11.7)	37 (10.8)	
Moderate	87 (12.7)	33 (9.6)	
Heavy	46 (6.7)	30 (8.7)	
Smoking status			NS
Never	283 (41.3)	140 (40.8)	
Past	162 (23.6)	69 (20.1)	
Current	241 (35.1)	134 (39.1)	

NS, no significance

	No Diabetes (n = 686)	Diabetes(n = 343)	P value
GGT (IU/L)	28.20 ± 22.62	30.55 ± 26.47	0.031
NS, no significance			

Discussion

This study mainly explored the relationship between GGT and type 2 diabetes mellitus. This study confirmed that GGT was an independent risk factor for incident diabetes among participants. Men or female aged 40–50 years with $\text{GGT} \geq 16 \text{ IU/L}$ were more likely to develop diabetes mellitus. Their hazard ratio was 1.31 or 1.13 compared with that of people with $\text{GGT} < 16 \text{ IU/L}$. It is consistent with the results of previous investigations[19, 20].

Previous studies had shown an important role in exploring CRP and type 2 diabetes mellitus, and GGT might be one of the crucial factors to predict type 2 diabetes mellitus[21]. Some scholars mentioned that there was a dose-response relationship between GGT and diabetes mellitus. Increasing GGT concentration in its physiological range was a sensitive and early biomarker for the development of diabetes[12].

Misuzu Fujita[22] studied the effects of smoking, drinking, ALT, BMI, and GGT on the incidence of type 2 diabetes mellitus. We performed subgroup analysis on important covariates such as smoking, drinking, ALT, and BMI [23]. These covariates were found not to affect the relationship between GGT and type 2 diabetes mellitus. The results were in line with previous research [24]. The observed relationship between GGT and diabetes cannot be explained by alcohol or liver dysfunction. We have the following assumptions: 1. It has been suggested that elevated liver enzymes may reflect underlying chronic inflammation and may impair insulin signaling[25, 26]. 2. Serum GGT level is defined as an increase in free radicals. The presence of free radicals and lipid oxidation is considered to represent oxidative stress[27–29]. Meanwhile, oxidative stress may play a major role in the etiology of type 2 diabetes, which can induce insulin resistance and impair insulin secretion[30, 31].

This study has several strengths. First, this is a large longitudinal study to confirm the relationship between GGT and type 2 diabetes mellitus. Second, for sensitivity analysis, subgroup analyses and propensity score matching are performed. Third, this is an observational study that cannot avoid confounding factors. We use strict control of confounding factors to minimize the effects of confounding factors.

There are some limitations to our study. First, it is a secondary study and the inclusion of covariates is restricted, and more confounding factors such as high-calorie dietary habits, insulin resistance, inflammatory factors, women's pregnancy and menopause cannot be included. Second, the population was limited to the Japanese population, and other races were not regarded.

Conclusion

After strict adjustment of other metabolic parameters, GGT is independently associated with type 2 diabetes. Regardless of men and women, between the ages of 40 and 50, the fourth to fifth quintiles of GGT are more likely to have diabetes compared to lower GGT. For other ages, statistical results are not significant. The detection of GGT is easy to obtain in the clinic, and the cost is low. People with a higher risk of diabetes can be screened. Therefore, if there are more prospective studies to confirm our results in the future, our findings can provide a reference for clinical prevention of diabetes and screening of high-risk diabetes patients, especially in the 40–50 age group with higher GGT.

Abbreviations

BMI: body mass index; ALT: alanine aminotransferase; AST: aspartate aminotransferase; DBP: diastolic blood pressure; GGT: gamma-glutamyl transferase; HbA1c: hemoglobin A1c; HDL: high-density lipoprotein; TC: total cholesterol; SBP: systolic blood pressure; DBP: Diastolic blood pressure; FPG: Fasting plasma glucose; CI: confidence interval; SD: standard deviation; HR: hazard ratio.

Declarations

Ethics approval and consent to participate

The study protocol was subject to approval by the Ethics Committee of the First Affiliated Hospital of Wenzhou Medical University. Since the downloaded raw data is anonymous, no informed consent is required.

Consent for publication

Not applicable.

Availability of data and material

The data analyzed in the study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

Not applicable.

Authors' contributions

RJ and SKH designed the study. BYD and ZYJ collected the data. BYD, ZYJ and LYH conducted the statistical analysis. BYD, ZYJ, HC, MXC, QF and RJ analyzed and interpreted the data. All authors wrote, reviewed and edited the manuscript. All authors read and approved the final manuscript.

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Figures

Incidence of diabetes

Figure 1

Kaplan-Meier curves stratified by GGT quintiles.

Figure 2

Forest plots show effect size of GGT on incident diabetes in main subgroups.

Supplementary Files

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