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Correlation between triglyceride-glucose index and diabetic kidney disease risk in adults with type 1 diabetes mellitus

Mengyun Lei[1†], Ping Ling[1†], Yongwen Zhou[1†], Jing Lv[1], Ying Ni[1], Hongrong Deng[1], Chaofan Wang[1], Daizhi Yang[1], Xubin Yang[1*], Wen Xu[1*] and Jinhua Yan[1*]

Abstract

Background The triglyceride-glucose (TyG) index is identified as an alternative indicator of insulin resistance (IR) and is associated with macro- and micro-vascular diseases among patients with type 2 diabetes mellitus. The relationship between the TyG index and IR and its impact on diabetic kidney disease (DKD) remains unclear among adults with type 1 diabetes mellitus(T1DM).

Methods This study comprised a cross-sectional analysis using data from the Guangdong T1DM Translational Medicine Study (GTT) and a longitudinal analysis using data from the type 1 diabetes (T1D) Exchange registry study. Correlation analysis was used to investigate the association between the TyG index and IR. Logistic regression and Cox proportional hazards regression were performed to explore the impact of the TyG index on DKD risk.

Results The GTT Study included 836 adults (216 with DKD and 620 without DKD). A significant correlation existed between the TyG index and the estimated glucose disposal rate (r=-0.64, $p < 0.01$). The TyG index was a risk factor for DKD after confounder adjustment (OR = 1.34, 95% CI:1.03–1.74). The T1D Exchange registry study included 8,771 adults (2,050 with DKD and 6,721 without DKD). After adjusting confounding factors, the TyG index was identified as an independent risk factor for DKD at enrollment, with the highest risk of DKD incidence observed in the highest TyG tertile group (OR = 1.92, 95%CI:1.67–2.20). During a median follow-up of 44.58(21.84, 67.09) months, the risk of developing DKD was increased by 32% at every 1 SD increase of the TyG index over time among participants without DKD at enrollment.

Conclusions The TyG index could be used to assess IR and was identified as an independent risk factor of DKD among adults with T1DM.

†Mengyun Lei, Ping Ling and Yongwen Zhou contributed equally to this work.

*Correspondence:
Xubin Yang
yxbin@mail.sysu.edu.cn
Wen Xu
xwen@mail.sysu.edu.cn
Jinhua Yan
yanjh79@163.com

Full list of author information is available at the end of the article

Keywords Insulin resistance, Diabetic kidney disease, Type 1 diabetes mellitus

Background

Insulin resistance (IR) is a well-known risk factor for macrovascular disease in patients with type 2 diabetes mellitus (T2DM) [1]. The gold standard for evaluating IR remains to measure glucose disposal rate (GDR) using a hyperinsulinemia-euglycemic clamp (HIEC), yet its invasive and complex procedures render it impractical in clinical settings. Therefore, the emerging triglyceride-glucose (TyG) index, calculated by In [fasting triglyceride (TG, mg/dL) *fasting blood glucose (FBG, mg/dL)/2], is more accessible and cost-effective, which has been suggested as one of the reliable surrogate markers of IR [2]. Meta-analyses have shown that the TyG index is associated with an increased risk of both macrovascular and microvascular diseases among patients with T2DM [3–9].

Meanwhile, IR has also been proven to contribute to the development of diabetic kidney disease (DKD) of type 1 diabetes mellitus (T1DM). (10–11) However, the current homeostasis model assessment is inapplicable for patients with T1DM due to a lack of endogenous insulin. The TyG index might be a potential alternative to IR among participants with T1DM, but this is yet to be confirmed. Additionally, the association between TyG and DKD risk in patients with T1DM also remains unknown.

To investigate the relationship of TyG with IR and its impact on DKD risk among adults with T1DM, we conducted cross-sectional and longitudinal analyses using the data from the Guangdong T1DM translational study (GTT study) [12] and the type 1 diabetes(T1D) Exchange clinic registry [13].

Methods

Study design and data source

This study used the baseline data from the GTT study and then used baseline along with follow-up data from the T1D Exchange clinic registry for external verification.

The GTT study recruited patients with T1DM who were enrolled between June 2010 and June 2018 from 16 tertiary hospitals throughout 12 cities in Guangdong, China. The protocol details have been published previously [12]. It was approved by the Ethics Committee of the Third Affiliated Hospital of Sun Yat-sen University (IRB No. [2014] 2–55). Each participant provided written informed consent.

The T1D Exchange clinic registry encompasses 34,013 participants who received routine clinical care at 83 clinic sites across the United States between July 2007 and April 2018. The crucial data were updated annually. Informed consent, criteria for inclusion, and methods for data collection have been previously reported [13]. The present study used the published data from the T1D Exchange clinic registry, which was permitted.

Study participants

The inclusion criteria were as follows: (1) participants with T1DM aged 18 years or older; (2) availability of essential information at enrollment, including lipid profiles, glycated hemoglobin (HbA1c), and DKD-related data [history and laboratory measurements including estimated glomerular filtration rate (eGFR)and urinary albumin-creatinine-ratio (UACR)]; and (3) The lipid profile measurements taken under fasting conditions. The exclusion criteria were: (1) pregnant women; (2) those who had undergone pancreas or islet transplant; and (3) those with a known kidney disease other than DKD.

Data collection

Information at enrollment from both databases was collected from medical records, including social-demographic data (age, gender, education level), anthropometric data[body mass index(BMI, kg/m^2), systolic blood pressure(SBP, mmHg), and diastolic blood pressure(DBP, mmHg)], medical information (duration of T1DM, onset age of T1DM, previous history of DKD and other known kidney disease), and biological indicators [lipid profiles(mg/dL), HbA1c(%), eGFR(ml/min/1.73 m^2), and UACR(mg/g)].

Additionally, waist-to-hip ratio (WHR) was also collected in the GTT study. Ethnicity, annual household income, current smoking status, method of insulin administration (insulin pump or others), continuous glucose monitoring (CGM) use (yes or no), the record of angiotensin-converting enzyme inhibitor (ACEI) or angiotensin receptor antagonist (ARB) use (yes or no), and total daily insulin dose (TDD, u/kg/d) were also available in the T1D Exchange clinic registry. Follow-up data on medical history, eGFR, and UACR from the T1D Exchange clinic registry were also collected.

Definitions

DKD was defined as an eGFR less than 60 ml/min/1.73 m^2 or UACR more than 30 mg/g after excluding other potential causes of kidney injury [14]. BMI was calculated as weight (kg)/height (m)^2. The TyG index was calculated as In[fasting TG (mg/dL) *mean blood glucose (MBG, mg/dL)/2][15]. In this study, HbA1c-derived MBG [MBG (mmol/L)=1.5944*HbA1c (%)-2.594] [16] rather than FBG was used to calculate the TyG index. The eGFR was calculated according to the MDRD equation in the GTT study [17], while the CKD-Epi equation was used in the T1D Exchange clinic registry [18]. In the GTT

study, IR was quantified by the estimated GDR, which was calculated via a previously established formula for adults with T1DM: In GDR = 4.964 − 0.121*HbA1c (%)-0.012*DBP (mmHg)-1.409*WHR [19]. Other potential alternative indicators of IR were also evaluated, including (1) triglyceride glucose-body mass index (TyG-BMI), which was calculated as TyG*BMI (kg/m^2); (2) triglyceride to high-density lipoprotein ratio(TG/HDL), which was calculated as TG (mg/dL) / HDL (mg/dL); (3) metabolic score for insulin resistance (METS-IR), which was calculated as Ln [(2*MBG (mg/dL)) + TG (mg/dL)]*BMI (kg/m^2) / Ln [HDL (mg/dL)] [20].

Statistical analysis

Continuous variables were summarized as mean (standard deviation) or median (interquartile) where appropriate, and categorical variables as frequencies (percentages). Missing data was handled using multiple imputations. Student's t-test, Wilcoxon signed-rank test, and the χ2 test were appropriate when comparing between 2 groups, while the One-Way ANOVA test, the χ2 test, or the Kruskal-Wallis test were used in the comparison among multiple groups as appropriate. Spearman's correlation analysis was used to evaluate the correlation between TyG and IR. Multivariate linear regression was used to explore factors influencing TyG levels. Logistic regression analysis and Cox proportional hazard survival regression were used to investigate the relationship between TyG and the odd ratio (OR) or hazard ratio (HR) of DKD. Kaplan-Meier survival curves were constructed to estimate cumulative incidences of DKD in different TyG tertile groups and compared using log-rank testing. Statistical analysis was performed using SPSS 27.0 (SPSS Inc., Chicago, IL, USA), GraphPad Prism (GraphPad Software, San Diego, CA, USA), and R software version 3.2.5. Statistical significance was defined as two-tailed $p < 0.05$.

Results

The GTT study

Participants characteristics

A total of 836 adults with T1DM were included in the analysis. The median age was 32.15(25.10, 41.00) years, duration of T1DM was 4.25(1.10, 8.30) years, BMI was 20.56(18.82,22.39) kg/m^2, HbA1c was 8.50(7.29,10.62) %, and TG was 84.07(61.95,121.20) mg/dL, respectively. The mean TyG was 9.14 ± 0.67, and the estimated GDR was 6.31 ± 2.05. There were 216 participants with DKD and 620 participants without DKD, baseline characteristics according to different groups were summarized in Table 1, Additional file 1: Table S1.

Table 1 The baseline characteristics of participants stratified by DKD occurrence

	GTT study			T1D Exchange clinic registry		
Variable	**DKD group (*n* = 216)**	**non-DKD group (*n* = 620)**	***P***	**DKD group (*n* = 2050)**	**non-DKD group (*n* = 6721)**	***P***
Age(years)	31.65(24.80, 41.05)	32.35(25.38,40.92)	0.30	45.00(30.00, 59.00)	33.00 (22.00, 49.00)	< 0.01
Gender (male, %)	87(39.19%)	305(49.19%)	0.02	933(45.50%)	3367(50.10%)	0.15
Duration of T1DM (years)	6.05(2.40, 11.55)	3.59(0.78, 7.23)	< 0.01	26.00 (15.00, 38.00)	15.00(8.00, 25.00)	< 0.01
Onset age of T1DM (years)	25.60 (18.18, 33.40)	27.65(21.18,35.50)	< 0.01	13.00 (8.00, 25.00)	15.00(9.00, 26.00)	< 0.01
Education level (n, %)	36(16.22%)	76(12.26%)	0.03	1036(50.50%)	3030(45.10%)	0.73
Primary school or less	136(61.26%)	357(57.58%)		682(33.30%)	2482(36.90%)	
High school	50(22.52%)	187(30.16%)		332(16.20%)	1209(18.00%)	
Associate degree or higher						
SBP (mmHg)	118.40 ± 16.00	112.90 ± 12.06	< 0.01	124.70 ± 15.83	120.90 ± 13.21	< 0.01
DBP (mmHg)	74.73 ± 10.37	71.80 ± 8.09	< 0.01	71.77 ± 9.60	72.53 ± 8.90	< 0.01
BMI (kg/m^2)	20.51 ± 3.01	20.81 ± 2.69	< 0.01	27.17(23.69, 31.17)	25.97(23.20, 29.40)	< 0.01
TC (mg/dL)	181.20(155.91,212.02)	179.65(154.94, 206.40)	0.93	166.06(145.00, 191.17)	167.57(147.00, 190.00)	0.41
TG (mg/dL)	98.67(68.81, 139.82)	79.65(60.18, 114.16)	< 0.01	83.00(60.00, 126.00)	73.00(54.00, 106.00)	< 0.01
LDL-c (mg/dL)	100.58(82.53, 127.51)	99.61(80.69,128.67)	0.87	86.00(70.00, 107.00)	89.00(73.00,108.00)	< 0.01
HDL-c (mg/dL)	52.33 ± 17.63	56.15 ± 16.14	< 0.01	57.00 (46.00, 70.00)	57.00(47.00, 83.00)	0.26
HbA1c (%)	8.55(7.20, 10.95)	8.50(7.30, 10.60)	0.92	7.90 (7.10, 9.00)	7.60(6.90, 8.50)	< 0.01
TyG	9.29 ± 0.70	9.09 ± 0.65	< 0.01	9.02 ± 0.69	8.83 ± 0.62	< 0.01
TyG-BMI	184.77(167.58, 208.30)	186.14(170.96, 204.98)	0.97	364.24(316.37, 425.29)	343.39(305.76, 393.86)	< 0.01
TG/HDL	0.94(0.64, 1.45)	0.82(0.59, 1.20)	< 0.01	1.46(0.92, 2.51)	1.27(0.84, 2.06)	< 0.01
METS-IR	32.15(29.14, 37.32)	31.85(28.77, 35.94)	0.34	41.05(34.93, 49.00)	39.01(34.10, 45.14)	< 0.01

GTT study, Guangdong Type 1 Diabetes Mellitus translational study; DKD, diabetic kidney disease; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; T1DM, type 1 diabetes mellitus; TC, total cholesterol; TG, triglyceride; LDL-c, low-density lipoprotein cholesterol; HDL-c, high-density lipoprotein cholesterol; HbA1c, glycated hemoglobin; TyG, triglyceride glucose index. TyG-BMI, triglyceride glucose-body mass index; TG/HDL, triglyceride to high-density lipoprotein ratio; METS-IR, metabolic score for insulin resistance

Association between TyG index and IR

Spearman's correlation analysis revealed a moderate linear correlation between the TyG index and GDR (r=-0.64, $p<0.01$) (Additional file 1: Figure S1). In contrast, weaker correlations were observed between TyG-BMI, TG/HDL, and METS_IR with GDR, with correlation coefficients of -0.25 ($p<0.01$), -0.14 ($p<0.01$), and −0.27 ($p<0.01$), respectively.

The relationship of the TyG index with DKD incidence

In the base unadjusted model, the TyG index was detected as a risk factor for DKD [OR (95%CI): 1.55(1.24,1.96), $p<0.01$]. In model 1(after adjusting age, onset age of T1DM, gender, education level, duration of T1DM, BMI, and WHR), the significant associations between TyG index and DKD risk remained [OR (95%CI): 1.53 (1.21, 1.96), $p<0.01$]. In model 2(after further adjusting SBP, DBP, TC, LDL-c, and HDL-c), this influence of TyG on DKD incidence was slightly attenuated [OR (95%CI):1.34(1.03,1.74), $p=0.03$] (Table 2).

In the base unadjusted model, neither TyG-BMI (OR=1.00) nor METS-IR (OR=1.02) were significant predictors of DKD (all $p>0.05$). While TG/HDL was identified as a predictor of DKD [OR (95%CI):1.20(1.06,1.37), $p<0.01$], its contribution was less than that of the TyG index. After adjusting for confounding factors, the impact of TG/HDL on DKD risk remained, albeit less pronounced than that of the TyG index.

T1D Exchange clinic registry

Participants characteristics

A total of 8,771 adults with T1DM were included in the analysis. The screening flowchart is described in Additional file 1: Figure S2. The median age was 36.00(23.00, 51.00) years, with a duration of T1DM of 17.00(9.00, 28.00) years, and a BMI of 26.21 (23.30, 29.81) kg/m^2, respectively. At baseline, the median HbA1c was 7.70(7.00, 8.60) %, TG was 75.00(55.00, 110.00) mg/dL, and the TyG index was 8.80 (8.43, 9.25), respectively. The cross-sectional analysis involved 2,050 participants with DKD and 6,721 without DKD. Baseline characteristics according to different groups were summarized in Table 1, Additional file 1: Table S2.

Table 2 Associations between TyG and DKD risk in the logistic regression models in the GTT study

Model	OR (95%CI)	*p*
Base	1.55 (1.24, 1.96)	<0.01
Model 1	1.53 (1.21,1.96)	<0.01
Model 2	1.34 (1.03,1.74)	0.03

Model 1 adjusted for age, onset age of T1DM, gender, education level, duration of T1DM, BMI, and WHR. Model 2 was further adjusted for TC, HDL, LDL, SBP, and DBP

TyG, triglyceride glucose index; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; WHR, waist-to-hip; T1DM, type 1 diabetes mellitus; TC, total cholesterol; LDL-c, low-density lipoprotein cholesterol; HDL-c, high-density lipoprotein cholesterol; OR, odds of ratio; CI, confidence interval

Among the 6,721 participants without DKD initially, 5,439 adults had follow-up data available for longitudinal analysis, with a median follow-up of 44.58(21.84, 67.09) months. The median age was 34.00 (22.00, 49.00) years, duration of T1DM was 15.00(8.00, 25.00) years, HbA1c was 7.60(6.90, 8.40) %, and TG was 72.00(53.00, 104.00) mg/dL, respectively. The mean TyG was 8.80±0.61. As per the tertiles of TyG levels at enrollment, participants were grouped into TyG tertile 1 (<8.56), TyG tertile 2 (8.56–9.08), and TyG tertile 3 (≥9.08). The median duration of T1DM before developing DKD among the three groups was 25.43 (13.85, 37.93) years, 24.72(14.13, 35.28) years, and 20.34(12.86, 30.61) years, respectively. Shorter durations of T1DM at the onset of DKD were observed in the TyG tertile 3 group compared to the TyG tertile 1 group($p=0.02$).

Association between TyG index and IR

Multiple linear regression indicated that Black Non-Hispanic, female, smoking, and higher levels of TC, TDD, BMI, and DBP were associated with higher TyG levels, whereas higher annual household income and education level, insulin pump use, CGM use, higher levels of HDL-c and LDL-c were associated with lower TyG levels ($p<0.05$) (Additional file 1: Table S3).

The relationship of the TyG index with DKD incidence

Cross-sectional analysis

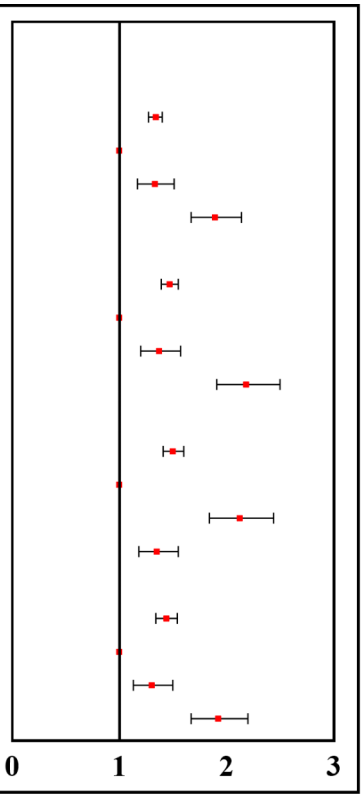
Logistic regression was performed to investigate the impact of baseline TyG levels on the risk of DKD. Models 1 and 2 included covariates consistent with the GTT study except for WHR, which was only available in the GTT study. Model 3 was further adjusted for additional factors, including ethnicity, current smoking status, CGM use, method of insulin administration, annual household income, ACEI/ARB use, and TDD (Additional file 1: Table S4, Fig. 1a). In model 3, the risk of developing DKD was increased by 44% at every 1 SD increase of TyG index, with the highest risk of DKD incidence observed in the highest TyG tertile group [OR (95%CI): 1.30(1.13, 1.50) in TyG tertile 2, and 1.92(1.67, 2.20) in TyG tertile 3, respectively].

Longitudinal analysis

Kaplan–Meier survival curves for the hazard of developing DKD, stratified by the TyG tertile groups, are presented in Fig. 2. Significant differences existed in the hazard of developing DKD among three TyG tertile groups (log-rank test, $p<0.01$). The DKD risk gradually increased with higher TyG, and the group with the highest TyG demonstrated the highest incidence of DKD development.

A.

Variable	OR	95%LCI	95%UCI
Base			
TyG(per 1 SD increase)	1.34	1.27	1.40
TyG ref	1.00	1.00	1.00
TyG tertile 2	1.33	1.17	1.51
TyG tertile 3	1.89	1.67	2.14
Model 1			
TyG(per 1 SD increase)	1.47	1.39	1.55
TyG ref	1.00	1.00	1.00
TyG tertile 2	1.37	1.20	1.57
TyG tertile 3	2.18	1.91	2.50
Model 2			
TyG(per 1 SD increase)	1.50	1.41	1.60
TyG ref	1.00	1.00	1.00
TyG tertile 2	1.35	1.18	1.55
TyG tertile 3	2.12	1.84	2.44
Model 3			
TyG(per 1 SD increase)	1.44	1.34	1.54
TyG ref	1.00	1.00	1.00
TyG tertile 2	1.30	1.13	1.50
TyG tertile 3	1.92	1.67	2.20



B.

Variable	HR	95%LCI	95%UCI
Base			
TyG(per 1 SD increase)	1.34	1.24	1.45
TyG ref	1.00	1.00	1.00
TyG tertile 2	1.44	1.16	1.77
TyG tertile 3	2.02	1.64	2.47
Model 1			
TyG(per 1 SD increase)	1.37	1.26	1.49
TyG ref	1.00	1.00	1.00
TyG tertile 2	1.44	1.16	1.78
TyG tertile 3	2.07	1.67	2.55
Model 2			
TyG(per 1 SD increase)	1.37	1.25	1.50
TyG ref	1.00	1.00	1.00
TyG tertile 2	1.42	1.15	1.76
TyG tertile 3	1.99	1.58	2.49
Model 3			
TyG(per 1 SD increase)	1.32	1.20	1.45
TyG ref	1.00	1.00	1.00
TyG tertile 2	1.36	1.09	1.69
TyG tertile 3	1.84	1.47	2.32

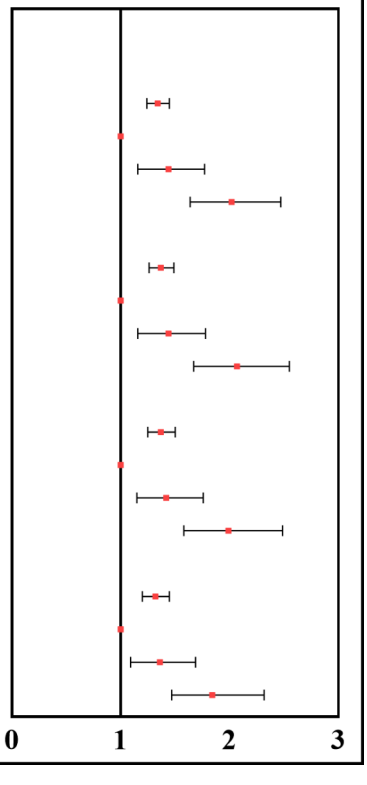


Fig. 1 (See legend on next page.)

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Fig. 1 The relationship between the TyG index and the incidence of DKD. **(a)** cross-sectional analysis using enrollment data from the T1D Exchange clinic registry; **(b)** longitudinal analysis using follow-up data from the T1D Exchange clinic registry. Model 1 adjusted for age at consent, onset age of T1DM, gender, education level, duration of T1DM, and BMI. Model 2 was further adjusted for TC, HDL-c, LDL-c, SBP, and DBP. Model 3 was further adjusted for ethnicity, current smoking status, CGM use, method of insulin administration, TDD, annual household income, and ACEI/ARB use. TyG tertile 1:< 8.56; TyG tertile 2: 8.56–9.08; TyG tertile 3: ≥9.08. TyG, triglyceride glucose index; DKD, diabetic kidney disease; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; T1DM, type 1 diabetes mellitus; TC, total cholesterol; LDL-c, low-density lipoprotein cholesterol; HDL-c, high-density lipoprotein cholesterol; CGM, continuous glucose monitoring; TDD, total daily insulin dose; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor antagonist. OR, odd ratio; HR, hazard ratios; CI, confidence interval

Cox proportional-hazards regression models were built to explore the relationship between TyG and the incidence of DKD (Additional file 1: Table S5, Fig. 1b). The trend of DKD development remained consistent across TyG as categorical values or continuous variables. TyG emerged as a significant independent risk factor for DKD among adults with T1DM, and the HR of a per-SD increase in TyG for DKD was 1.32(1.20,1.45) in the final model 3 after confounder adjustment. This suggested that the risk of developing DKD was increased by 32% at every 1 SD increase of the TyG index. Besides, when comparing against TyG tertile 1 as the reference, the highest tertile of TyG exhibited a hazard ratio ranging from 0.84 to 1.07-fold higher for incidence of DKD [HR (95%CI): 2.02(1.64, 2.47) in the base model, 2.07(1.67,2.55) in model 1, 1.99(1.58, 2.49) in model 2, and 1.84(1.47, 2.32) in model 3, respectively].

Discussion

To our knowledge, this is the first study to investigate the relationship between the TyG index and IR and its impact on DKD risk in adults with T1DM. In the GTT study, there was a moderate relationship between the TyG index and IR, and increased TyG level was closely associated with a higher risk of DKD among Chinese adults with T1DM. Our findings were supported by cross-sectional and longitudinal data from the US T1D Exchange clinic registry, which included a large sample.

The TyG index, initially proposed by Simental-Mendía, L. E. et al., has been widely accepted as a novel, cost-effective, and reliable marker of IR [2]. Previous studies have confirmed TyG levels as an important risk factor for macrovascular complications in patients with or without T2DM [3–9]. While the core pathogenesis of T1DM is insulin deficiency, studies have observed a growing prevalence of IR in patients with T1DM, attributed to long-standing insulin therapy and obesity [19, 21–25]. HIEC is still the prevailing method for assessing IR in patients with T1DM, but various formulas estimating GDR using multiple clinical parameters have been developed as a sensible proxy (19, 24, 26, 27).

The equal applicability of TyG, which has been a well-established IR marker for T2DM [28], remains uncertain among patients with T1DM. The data from the GTT study observed a moderate correlation between TyG and GDR. Due to the absence of WHR to calculate GDR, we failed to verify this relationship in the T1D Exchange clinic registry. Nonetheless, established determinants of IR such as TDD, smoking, BMI, and DBP were associated with elevated TyG levels in the longitudinal cohort from the T1D Exchange clinic registry. These findings confirmed the potential of TyG as a surrogate marker of IR in patients with T1DM. Moreover, the correlation between the TyG index and IR was found to be more robust than that observed for TyG-BMI, TG/HDL, and METS-IR, which have been utilized as alternative indicators of IR in previous studies.

Previous studies found that patients with MetS were more likely to have microvascular complications in T1DM [10, 21, 28–31]. To determine the relationship between TyG and DKD in T1DM, we conducted a cross-sectional analysis using baseline data from the GTT study, further followed by external validation using the T1D Exchange clinic registry. The follow-up data of T1D Exchange also revealed a gradual increase in DKD risk with a higher TyG level after confounder adjustment, and DKD risk was increased by 32% at every 1 SD increase of the TyG index. These findings indicated that TyG was an independent risk factor for DKD among adults with T1DM. Given its accessibility and cost-effectiveness, the TyG index could serve as a valuable tool for primary care physicians in evaluating IR. Besides, the duration of T1DM at the onset of DKD was significantly shorter in the group with the highest TyG tertile compared to the group with the lowest. This suggested that patients with higher TyG levels might experience a shorter DKD-free duration after diagnosis of T1DM. Among alternative markers of IR assessed, the TyG index proved to be the superior predictor of DKD in adults with T1DM.

Our findings underscored the importance of IR in preventing DKD in T1DM. As a crucial component of TyG, managing TG levels deserves attention. Hypertriglyceridemia can trigger the secretion of inflammatory mediators and exert a proapoptotic effect on kidney endothelium both in vitro and in vivo [32]. Animal experiments suggest that fenofibrate can mitigate DKD by enhancing impaired renal tubular fatty acid oxidation, a pathogenic factor of tubulointerstitial fibrosis [33, 34]. The efficacy of fenofibrate intervention in preventing or ameliorating DKD among patients with T2DM remains controversial.[35 – 36] It remains uncertain whether

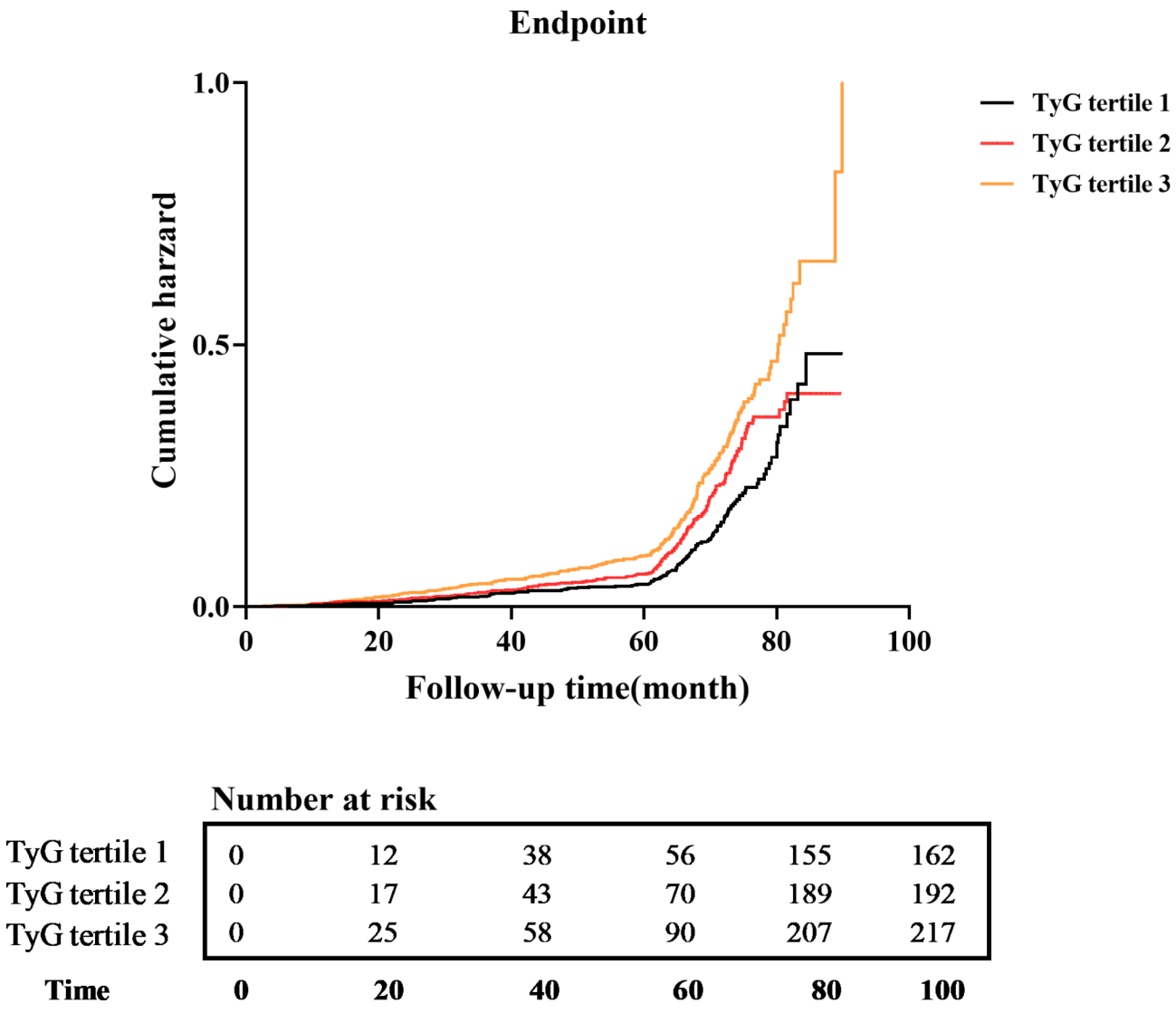

Fig. 2 Kaplan–Meier survival curve-cumulative incidences of DKD in different TyG tertile groups. TyG tertile 1:< 8.56; TyG tertile 2: 8.56–9.08; TyG tertile 3: ≥9.08. TyG index, triglyceride-glucose index; DKD, diabetic kidney disease

lowering TG while optimizing glycemic control can effectively improve DKD among patients with T1DM.

The strengths of our study were as follows: (1) the large sample size; 2) we conducted a cross-sectional analysis among Chinese adults with T1DM and further verified it using a longitudinal cohort from the United States, and the consistency of the outcomes reinforced the reliability of our conclusions; 3) GDR that was used to evaluate IR in the GTT study was calculated via a previously established model using clinical parameters. GDR from the clinical model, though not directly measured, showed a high correlation with the direct method. As a result, it remains still more reliable than other assessment methods.

Of course, there were some limitations in our study: (1) Due to the lack of WHR data, we were unable to use data from the T1D Exchange Clinic Registry to verify the relationship between TyG and GDR further externally; (2) this study only included adults with T1DM, which limits the generalizability of our findings to other subpopulations. Nevertheless, our study revealed that a higher TyG level was associated with an increased risk of DKD; the impact of lowering TyG levels and alleviating IR on DKD still warrants further investigation.

Conclusions

The TyG index could also be used to assess IR and was identified as an independent risk factor of DKD among adults with T1DM. Clinicians should pay attention to IR in this population. Future studies are needed to further investigate the impact of lowering TyG levels and alleviating IR on the prevention of DKD.

Abbreviations

IR	Insulin Resistance
MetS	Metabolic Syndrome
T2DM	Type 2 Diabetes Mellitus
GDR	Glucose Disposal Rate
HIEC	Hyperinsulinemia-Euglycemic Clamp
TyG	Triglyceride Glucose Index
TG	Triglyceride
FBG	Fasting Blood Glucose
T1DM	Type 1 Diabetes Mellitus
DKD	Diabetic Kidney Disease
GTT	Study Guangdong Type 1 Diabetes Mellitus Translational Study
HbA1c	Hemoglobin
GFR	Glomerular Filtration Rate
UACR	Urinary Albumin-Creatinine-Ratio
WHR	Waist-To-Hip Ratio
BMI	Body Mass Index
SBP	Systolic Blood Pressure
DBP	Diastolic Blood Pressure
CGM	Continuous Glucose Monitoring
ACEI	Angiotensin-Converting Enzyme Inhibitor
ARB	Angiotensin Receptor Antagonist
TDD	Total Daily Insulin Dose
MBG	Mean Blood Glucose
OR	Odds of Ratio
HR	Hazard Ratio
HDL-c	High-Density Lipoprotein Cholesterol
TC	Total Cholesterol
LDL-c	Low-Density Lipoprotein Cholesterol
CI	Confidence Interval
TyG-BMI	Triglyceride Glucose-Body Mass Index
TG/HDL	Triglyceride to High-Density Lipoprotein Ratio
METS-IR	Metabolic Score for Insulin Resistance

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13098-024-01468-9.

Supplementary Material 1: Additional file 1: Figure S1. The relationship between the TyG index and GDR in the GTT study. Figure S2. The screening flowchart from the T1D Exchange clinic registry. Table S1. The additional characteristics of participants stratified by DKD from the GTT study. Table S2. The additional characteristics of participants stratified by DKD at baseline from the T1D Exchange clinic registry. Table S3. The significant factors associated with TyG in the multiple linear regression model. Table S4. Associations between TyG and the prevalence of DKD at enrollment using the logistic regression models. Table S5. Associations between TyG and the prevalence of DKD during the follow-up period using Cox proportional-hazards regression models. (575KB, docx)

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Author contributions

MYL, PL, and YWZ: Conduct/data collection and analysis; Write the manuscript. MYL, PL, and YWZ contribute equally to this paper. JL and YN: Data collection; Writing manuscript. HRD, CFW, and DZY: Writing manuscript. JHY, WX, and XBY: Design; Writing manuscript. All authors have read and approved the final manuscript.

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Data availability

The datasets from the GTT study are available upon reasonable request; the T1D Exchange clinic registry datasets are available on the T1D ExHomepage (cdc.gov).

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of The Third Affiliated Hospital of Sun Yat-sen University (IRB No. [2014] 2–55) and has been performed under the guidelines of the Helsinki Declaration. Informed consent was obtained from all individual participants included in the study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]Department of Endocrinology and Metabolism, Guangdong Provincial Key Laboratory of Diabetology, The Third Affiliated Hospital of Sun Yat-sen University, Guangzhou 510630, China

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