


Association of triglyceride-glucose with cardiac hemodynamics in type 2 diabetes

Diabetes & Vascular Disease Research
March-April 2022: 1–10
© The Author(s) 2022
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/14791641221083396
journals.sagepub.com/home/dvr


Chenxi Wang^{1,†}, Zhicong Zhao^{1,†}, Xia Deng¹, Zhensheng Cai¹, Tian Gu¹, Lian Li¹, Chang Guo², Dong Wang¹, Ling Yang¹, Li Zhao¹ and Guoyue Yuan¹ 

Abstract

Purpose: Triglyceride-glucose (TyG) index is a reliable and inexpensive alternative indicator of insulin resistance. Previous studies have shown that elevated TyG index increases the risk of diabetes, coronary heart disease, and other diseases, but the relationship between TyG index and cardiac hemodynamics in patients with type 2 diabetes mellitus (T2DM) is not clear. This study was conducted in patients with T2DM to assess the relationship between TyG and cardiac hemodynamics and its predictive ability for T2DM.

Methods: A total of 647 individuals (348 males and 299 females) were enrolled in this study, including 446 T2DM patients and 201 healthy controls. The clinical data and related laboratory variables were assessed and recorded, and TyG index was calculated. Cardiac hemodynamics was measured by echocardiography. Pearson or Spearman correlation analysis and linear regression analysis were conducted to explore the association between TyG and cardiac hemodynamics. The receiver operating characteristics (ROC) curve was used to evaluate the efficacy of TyG index in the diagnosis of T2DM.

Results: Compared with healthy controls, the systolic blood pressure (SBP), body weight, body mass index (BMI), waist circumference (WC), hip circumference (HC), HOMA-IR, and TyG levels were higher in patients with T2DM. With the increase of TyG, the levels of left ventricular mass index (LVMI), left ventricular mass (LVM), left ventricular end diastolic diameter (LVDd), posterior wall thickness (PWT), and interventricular septum thickness (IVST) were also increased in T2DM individuals. Multivariate linear regression analysis showed that TyG was an independent determinant of LVEF, PWT, IVST, and ejection time (ET) after adjusting for confounding factors. In addition, individuals with visceral obesity had higher TyG and TyG can be used as a predictor of T2DM with an AUC of 0.903 (95% CI:0.879–0.927).

Conclusions: The increase of TyG index is closely related to cardiac hemodynamics of T2DM patients, which is expected to be a simple and practical biological index to predict the changes of cardiac function in patients with T2DM.

Keywords

Triglyceride-glucose index, cardiac hemodynamics, type 2 diabetes, insulin resistance, cardiovascular disease

Introduction

Type 2 diabetes mellitus (T2DM) has become a global public health problem. With the improvement of people's living standards and the change of lifestyle, the prevalence of T2DM is increasing year by year. According to the latest data of the International Diabetes Federation (IDF) in 2019, about 463 million adults worldwide suffer from diabetes, and it is estimated that by 2045, the number of diabetic patients may reach 700 million. The number of deaths resulting from diabetes and its complications in 2019 is

¹Department of Endocrinology and Metabolism, Affiliated Hospital of Jiangsu University, Zhenjiang, China

²Department of Nephrology, Affiliated Hospital of Jiangsu University, Zhenjiang, China

†These authors contributed equally to this work

Corresponding author:

Guoyue Yuan, Department of Endocrinology and Metabolism, Affiliated Hospital of Jiangsu University, 438 Jiefang Road, Zhenjiang 212001, China.

Email: yuanguoyue@ujs.edu.cn



Creative Commons Non Commercial CC BY-NC: This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 License (<https://creativecommons.org/licenses/by-nc/4.0/>) which permits non-commercial use, reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and Open Access pages (<https://us.sagepub.com/en-us/nam/open-access-at-sage>).

estimated to be 4.2 million,¹ among which diabetic macrovascular disease was the leading cause of death in patients with T2DM.² Diabetic macrovascular disease mainly refers to coronary heart disease, cerebrovascular disease, and peripheral artery disease caused by or combined with T2DM, which is the main cause of death and disability of T2DM.³ The occurrence of diabetic macrovascular disease is a complex process involving many factors. Its etiology and pathogenesis are very complicated, which has not been fully elucidated. The main pathological manifestation of diabetic macrovascular disease is atherosclerosis and its sequelae of vascular injury.⁴ Studies have shown that insulin resistance is a high-risk factor in the occurrence and development of atherosclerosis.^{5,6} Therefore, early screening and diagnosis of insulin resistance is of great significance in the detection and treatment of cardiovascular diseases in T2DM patients.

At present, the gold standard of clinical evaluation of insulin resistance is hyper insulinemic-euglycemic clamp (HIEC), but this method requires high cost.⁷ Therefore, a simplified mathematical model triglyceride-glucose index (TyG) was proposed to evaluate insulin resistance.⁸ TyG is a formula for evaluating insulin resistance based on serum triglyceride (TG) levels and fasting plasma glucose (FPG) levels, which was calculated as $\ln [TG (mg/dL) \times FPG (mg/dL)]/2$. This formula has been recognized as a potential tool for diagnosing insulin resistance⁹ and has been proved to have better predictive value than traditional parameters.^{10,11} Existing research in recent years shows that the increase of TyG index is related to the occurrence and development of diabetes,¹² coronary heart disease,¹³ nonalcoholic fatty liver disease,^{14,15} and other diseases,^{16,17} but there are few reports about the relationship between TyG index and cardiac hemodynamics in patients with T2DM. Therefore, the purpose of this study is to explore the correlation between TyG index and cardiac hemodynamics in patients with T2DM and to verify its predictive ability for T2DM, so as to provide possible reference for early prevention, monitoring and treatment of cardiovascular disease in patients with T2DM.

Methods

Study design and patients

A total of 647 individuals were enrolled in this study, including 201 healthy controls and 446 asymptomatic T2DM patients who received diabetes health education in the Department of Endocrinology of Affiliated Hospital of Jiangsu University from June 2019 to February 2020. Among them, there were 348 males and 299 females, ranging from 15 to 76 years old, and the average age was 53 ± 12 years old. T2DM patients all met the diagnostic criteria of diabetes recommended by the World Health

Organization (WHO) in 1999.¹⁸ The following conditions should be excluded for all included patients: (1) patients with incomplete clinical and biochemical data; (2) patients with type 1 diabetes mellitus, special type diabetes mellitus, gestational diabetes mellitus, acute complications of diabetes mellitus and infectious diseases; (3) patients with severe liver or thyroid dysfunction, or with renal diseases caused by urinary tract infection, kidney stones, lupus nephritis, renal malignancy, hypertension, etc; (4) patients with severe cardiovascular diseases such as coronary atherosclerotic heart disease, congestive heart failure, severe arrhythmia, cardiac valve replacement, and cardiac pacemaker; (5) patients with definite familial hyperlipidemia and familial hypertension; (6) patients who have recently used glucocorticoids or antipsychotics; (7) patients with tumor, autoimmune diseases, or hematological diseases. This study was approved by the Ethics Committee of Affiliated Hospital of Jiangsu University, and all individuals' written informed consent was obtained.

Physical examination

All individuals maintained a normal diet and stable exercise, avoided high-fat diet other than daily life, and fasted for 8–12 h the night before the examination. The gender, age, course of T2DM, hypertension, and other general clinical characteristics were collected in the morning. Height, weight, waist circumference (WC), hip circumference (HC), heart rate, and blood pressure (BP) were measured by professionals according to the standard method. Fasting venous blood was collected 4–5 mL and centrifuged at 4000 R/min for 5 min with a centrifugal force of $2860 \times g$, and then serum was collected.

Laboratory measurement

Fasting plasma insulin (FIns) and fasting C-peptide (FC-P) were measured by radioimmunoassay, and fasting plasma glucose (FPG) was measured by glucose oxidase method. Hemoglobin glycosylated (HbA1c) was determined by high performance liquid chromatography (HPLC). The total cholesterol (TC), TG, HDL-C, and LDL-C were measured by enzyme method.

Measurement of triglyceride-glucose and cardiac hemodynamics

$TyG\ index = \ln [TG (mg/dL) \times FPG (mg/dL)]/2$. LVEF was calculated by Teichholz formula. According to the American Society of Echocardiography,¹⁹ two-dimensional echocardiography was used to measure the left atrial diameter, left ventricular end diastolic, left ventricular end diastolic diameter (LVDd), and left ventricular end systolic diameter (LVSd). Left ventricular posterior wall

thickness (PWT) and interventricular septum thickness (IVST) were measured at the end of diastolic period.

Data measurements

The homeostasis model assessment of insulin resistance index (HOMA-IR) was calculated as $FPG (mmol/L) \times FIns (mU/L) / 22.5$.²⁰ Body mass index (BMI) was calculated by height and weight, $BMI = mass(kg) / height(m)^2$. Waist-to-hip ratio (WHR) was calculated by WC and HC. Left ventricular mass index (LVMI) was calculated by this formula¹⁹: $left\ ventricular\ mass(LVM) = 0.80 \times 1.04 \times [(IVST + LvDd + PWT)^3 - LvDd^3 + 0.6(g)]$. $LVMI = LVM / body\ surface\ area (body\ weight^{0.425} \times height^{0.725} \times 0.007184)$.

Statistical analysis

Statistical analysis was performed using SPSS 20.0 (SPSS Inc, Chicago, IL, USA). Categorical variables were expressed as percentages, and continuous variables were expressed as mean \pm standard deviation (SD). Univariate analysis of variance (ANOVA) was used for comparison between groups, and Bonferroni adjusted post-test was performed. According to the TyG index, patients with T2DM were divided into low TyG (Q1) group (TyG < 5.01, $n = 148$), middle TyG (Q2) group ($5.01 \leq TyG < 5.31$, $n = 148$), and high TyG (Q3) group (TyG ≥ 5.31 , $n = 150$). Pearson or Spearman correlation analysis was used to analyze the relationship between variables. Linear regression analysis was performed to determine the

correlation between clinical and laboratory variables with cardiac function parameters. The cardiac hemodynamics were used as the dependent variable and the TyG index as the independent variable to carry out the multivariate linear regression analysis. Four models were set up, unadjusted model did not adjust the confounding factors, model 1 adjusted gender and age; model 2 adjusted gender, age, SBP, DBP, and BMI; and model 3 further adjusted smoking history, drinking history, and diabetes medication history. Moreover, in order to compare the differences of clinical characteristics and cardiac hemodynamics among the groups, SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg were regarded as hypertension group, and the rest of the individuals were regarded as non-hypertension group. The male WHR ≥ 0.9 and female WHR ≥ 0.85 were regarded as visceral obesity group, and the other individuals were regarded as visceral obesity group. All significance tests were performed by two-tailed test, and $p < 0.05$ was considered statistically significant.

Results

Comparison of clinical characteristics between two groups of individuals

A total of 647 individuals were recruited in this study, including 446 patients with T2DM and 201 healthy controls. The age was 53 ± 12 years old and 46.2% of them were female. SBP and DBP were 125.6 ± 17.5 mmHg and 75.6 ± 10.6 mmHg, respectively, and HbA1c was $8.22 \pm$

Table 1. Clinical characteristics according to the prevalence of T2DM.

Characteristic	Normal ($n = 201$)	T2DM ($n = 446$)	p value
Age, years	48.78 \pm 9.32	55.02 \pm 12.62	<0.0001
Sex, male (%)	92 (45.8%)	256 (57.4%)	0.006
TyG index	4.61 \pm 0.26	5.17 \pm 0.37	<0.0001
SBP (mmHg)	120.29 \pm 15.08	128.03 \pm 18.05	<0.0001
DBP (mmHg)	78.26 \pm 11.22	74.43 \pm 10.04	<0.0001
BMI (kg/m ²)	23.69 \pm 3.76	24.72 \pm 3.26	<0.0001
FPG (mmol/L)	5.16 \pm 0.46	10.21 \pm 3.43	<0.0001
FIns (μ U/mL)	7.33 (4.12, 7.94)	9.58 (4.13, 10.98)	0.026
FC-P (ng/ml)	1.90 (1.19, 2.29)	2.41 (1.72, 3.04)	<0.0001
HOMA-IR	1.70 (0.92, 1.85)	4.12 (1.72, 4.84)	<0.0001
HbA1c (%)	5.40 \pm 0.28	9.49 \pm 2.30	<0.0001
TG (mmol/L)	1.39 (0.88, 1.64)	2.54 (1.34, 2.8)	<0.0001
HDL-C (mmol/L)	1.37 \pm 1.00	1.13 \pm 0.39	<0.0001
LDL-C (mmol/L)	2.90 \pm 1.59	2.85 \pm 0.90	0.58

Note: Data are presented as means \pm SD or medians (inter-quantile range (IQR)) for continuous variables and number (percentages) for categorical variables.

Abbreviations: TyG index, Triglyceride-glucose index; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; FPG, fasting plasma glucose; FIns, fasting plasma insulin; FC-P, fasting C peptide; HOMA-IR, homeostasis model assessment-insulin resistance index; HbA1c, glycosylated hemoglobin c; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

2.7%. The clinical characteristics and cardiac hemodynamics of healthy controls and T2DM individuals are shown in Table 1. Analysis of variance showed that comparing with healthy controls, the SBP, BMI, HbA1c, FC-P, Flns, FPG, HOMA-IR, and TyG levels of T2DM patients were higher, while HDL-C levels was relatively lower.

Comparison of clinical characteristics and cardiac hemodynamics according to the tertiles of triglyceride-glucose in type 2 diabetes mellitus individuals

According to the TyG value, all patients with T2DM in the study were divided into three groups: Q1, Q2, and Q3, with 148

Table 2. Clinical characteristics of T2DM patients by tertiles of TyG.

Characteristic	Q1 (TyG < 5.01)	Q2 (5.01 ≤ TyG < 5.31)	Q3 (TyG ≥ 5.31)	p
n	148	148	150	
Age, years	57.97 ± 11.59	55.30 ± 12.36	51.84 ± 13.19	<0.0001
Sex, male (%)	80 (54.1%)	80 (54.1%)	96 (64.0%)	0.133
TyG index	4.79 ± 0.18	5.15 ± 0.08	5.58 ± 0.26	<0.0001
SBP (mmHg)	126.48 ± 19.47	127.56 ± 15.42	130.01 ± 18.91	0.223
DBP (mmHg)	71.99 ± 9.93	74.39 ± 9.51	76.87 ± 10.14	<0.0001
BMI (kg/m ²)	24.05 ± 3.39	24.50 ± 2.99	25.59 ± 3.23	<0.0001
WC (cm)	87.85 ± 9.69	89.48 ± 9.22	92.18 ± 8.97	<0.0001
HC (cm)	95.58 ± 7.10	96.86 ± 6.20	97.56 ± 7.22	0.042
WHR	0.91 ± 0.06	0.92 ± 0.07	0.95 ± 0.08	0.001
FPG (mmol/L)	7.83 ± 2.38	10.43 ± 2.86	12.33 ± 3.35	<0.0001
Flns (μIU/ml)	10.21 (4.05, 11.35)	9.45 (3.71, 10.27)	9.08 (4.52, 11.42)	0.736
FC-P (ng/ml)	2.05 (1.25, 2.80)	2.38 (1.72, 2.96)	2.87 (2.15, 3.26)	<0.0001
HOMA-IR	3.33 (1.32, 3.81)	4.25 (1.74, 4.37)	4.75 (2.42, 6.21)	0.083
HbA1c (%)	8.54 ± 2.25	9.78 ± 2.32	10.14 ± 2.03	<0.0001
ALT (U/L)	21.18 (12.83, 22.53)	23.33 (11.73, 30.22)	28.90 (15.03, 36.00)	<0.0001
AST (U/L)	18.40 (13.18, 20.4)	17.79 (12.00, 21.20)	20.07 (13.00, 23.95)	0.112
TG (mmol/L)	1.27 (0.99, 1.49)	1.94 (1.51, 2.30)	4.39 (2.57, 4.57)	<0.0001
TC (mmol/L)	4.56 ± 1.00	4.86 ± 0.99	5.45 ± 1.22	<0.0001
HDL-C (mmol/L)	1.26 ± 0.36	1.12 ± 0.45	1.01 ± 0.28	<0.0001
LDL-C (mmol/L)	2.68 ± 0.80	2.93 ± 0.82	2.93 ± 1.03	0.021
Heart rate (bpm)	71.62 ± 9.73	73.71 ± 11.2	74.08 ± 11.09	0.106
LVEF (%)	68.07 ± 3.75	66.81 ± 4.00	66.99 ± 3.35	0.007
Internal diameter of aortic root (mm)	29.37 ± 2.93	29.44 ± 2.94	30.04 ± 2.51	0.078
Left atrial diameter (mm)	34.39 ± 3.55	34.39 ± 3.72	34.73 ± 3.36	0.639
LVDd (mm)	44.56 ± 3.45	44.79 ± 3.94	45.58 ± 3.82	0.050
LVSD (mm)	27.87 ± 3.31	28.80 ± 5.13	28.73 ± 3.29	0.086
IVST (mm)	9.83 ± 0.81	9.94 ± 0.89	10.15 ± 0.93	0.007
PWT (mm)	9.68 ± 0.79	9.75 ± 0.84	10.30 ± 2.86	0.005
LVM (g)	147.10 ± 25.32	150.44 ± 29.40	163.63 ± 49.38	<0.0001
LVMI (g/m ²)	86.21 ± 12.13	87.12 ± 15.61	92.10 ± 27.17	0.020
PEP (ms)	103.97 ± 14.63	105.54 ± 14.89	104.45 ± 14.48	0.657
ET (ms)	278.51 ± 24.45	271.25 ± 25.30	265.54 ± 24.55	<0.0001
ET/PEP	2.74 ± 0.49	2.63 ± 0.58	2.60 ± 0.50	0.068

Note: Data are presented as means ± SD or medians (inter-quartile range (IQR)) for continuous variables and number (percentages) for categorical variables.

Abbreviations: TyG index, Triglyceride-glucose index; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; WC, waist circumference; HC, hip circumference; WHR, waist-to-hip ratio; FPG, fasting plasma glucose; Flns, fasting plasma insulin; FC-P, fasting C peptide; HOMA-IR, homeostasis model assessment-insulin resistance index; HbA1c, glycosylated hemoglobin c; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TG, triglyceride; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LVEF, left ventricular ejection fraction; LVDd, left ventricular end diastolic diameter; LVSD, left ventricular end systolic diameter; IVST, interventricular septum thickness; PWT, posterior wall thickness; LVM, left ventricular mass; LVMI, left ventricular mass index; PEP, pre-ejection period; ET, ejection time.

patients in Q1, 148 patients in Q2, and 150 patients in Q3. In the tertiles of TyG index (Table 2), BMI, WC, blood pressure, FPG, HbA1c, HOMA-IR, FC-P, TC, and TG of Q3 group were higher than those of the other two groups. ($p < 0.05$) In terms of cardiac hemodynamics, LVMI, LVM, LVDd, PWT, and IVST levels increased with the increase of TyG value, and the differences were statistically significant. ($p < 0.05$)

Linear regression analysis of triglyceride-glucose and cardiac hemodynamics

The results (Table 3) showed that, as a dependent variable, TyG was independently correlated with LVEF ($p = 0.003$) after

Table 3. Multivariate linear regression analysis between cardiac hemodynamics and TyG.

	Unstandardized coefficients beta	95% CI	<i>p</i>
LVEF			
Unadjusted	-1.358	-2.283-0.434	0.004
Model 1	-1.439	-2.378-0.501	0.003
Model 2	-1.239	-2.222-0.257	0.014
Model 3	-1.248	-2.248-0.248	0.015
LVDd			
Unadjusted	1.310	0.379-2.241	0.006
Model 1	0.949	0.030-1.868	0.043
Model 2	0.493	-0.433-1.418	0.296
Model 3	0.379	-0.559-1.317	0.427
PWT			
Unadjusted	0.589	0.142-1.037	0.010
Model 1	0.585	0.128-1.043	0.012
Model 2	0.455	-0.024-0.933	0.062
Model 3	0.501	0.013-0.989	0.044
IVST			
Unadjusted	0.362	0.144-0.480	0.001
Model 1	0.467	0.254-0.679	<0.0001
Model 2	0.267	0.056-0.478	0.013
Model 3	0.257	0.043-0.471	0.019
LVMI			
Unadjusted	4.722	-0.147-9.591	0.057
Model 1	6.334	1.397-11.272	0.012
Model 2	6.241	1.080-11.402	0.018
Model 3	6.427	1.155-11.700	0.017
ET			
Unadjusted	-15.194	-21.479-8.910	<0.0001
Model 1	-10.491	-16.602-4.379	0.001
Model 2	-8.944	-15.247-2.741	0.005
Model 3	-8.285	-14.589-1.980	0.010

Model 1: adjusted for age, sex;

Model 2: adjusted for SBP, DBP, BMI, WHR in addition to model 1;

Model 3: adjusted for smoking history, drinking history, medical history of diabetes in addition to model 2.

Abbreviations: TyG index, Triglyceride-glucose index; LVEF, left ventricular ejection fraction; LVDd, left ventricular end diastolic diameter; PWT, posterior wall thickness; IVST, interventricular septum thickness; LVMI, left ventricular mass index; ET, ejection time.

gender and age adjustment. After further adjustment with additional confounders including SBP, DBP, BMI, WHR, smoking history, drinking history, and diabetes medication history, TyG remained correlated with LVEF ($p = 0.014$ for model 2 and $p = 0.015$ for model 3). The other hemodynamic parameters were analyzed as dependent variables, and TyG was also an independent determinant of PWT, IVST, LVMI, and ET ($p < 0.05$ for all). In conclusion, TyG is an independent factor determining cardiac hemodynamics in T2DM.

Comparison of clinical characteristics according to the prevalence of hypertension and visceral obesity

The general clinical characteristics and hemodynamic indexes were compared between with or without hypertension and visceral obesity group. The results showed that the individuals with visceral obesity had higher TyG index, DBP, SBP, BMI, ALT, TG, PWT, IVST, LVM, and left atrial diameter than those without visceral obesity, the differences were statistically significant (Table 4). However, TyG index showed no difference between hypertension and non-hypertension group.

Receiver operating characteristics curve analysis of triglyceride-glucose prediction of type 2 diabetes mellitus risk

Figure 1 shows the performance of TyG for predicting the risk of T2DM. The results showed that the area under ROC curve (AUC) predicted by TyG was 0.903 (95%CI: 0.879-0.927) and the difference was considered statistically significant ($p < 0.0001$). When TyG was 4.83, the maximum Youden index was 0.667, so 4.83 was the optimal cut-off value, with a sensitivity of 84.1% and a specificity of 82.6%.

Correlation between triglyceride-glucose and cardiac hemodynamics

As is shown in Supplementary Table 1, TyG was positively correlated with LvDd, LVSD, PWT, IVST, LVM, and aortic root diameter and was negatively correlated with LVEF, ET, and ET/PEP.

Correlation between cardiac hemodynamics and other clinical characteristics

In Supplementary Table 2, we analyzed the correlation between cardiac hemodynamics and general clinical characteristics and the results showed that these hemodynamic parameters were all correlated with WHR ($p < 0.05$). Parameters including LVEF, LVDd, LVSD, LVM, PWT, IVST, and aortic root diameter were positively

Table 4. Clinical characteristics according to the prevalence of visceral obesity.

Characteristic	Non-visceral obesity (n = 86)	Visceral obesity (n = 360)	p value
Age, years	53.21 ± 12.99	55.46 ± 12.51	0.138
Sex, male (%)	59 (68.6%)	197 (54.7%)	0.019
TyG index	5.02 ± 0.35	5.21 ± 0.37	<0.0001
SBP (mmHg)	120.87 ± 15.47	129.74 ± 18.22	<0.0001
DBP (mmHg)	71.28 ± 8.94	75.18 ± 10.16	0.001
BMI (kg/m ²)	21.90 ± 2.40	25.39 ± 3.08	<0.0001
WC (cm)	79.52 ± 7.49	92.31 ± 8.11	<0.0001
HC (cm)	93.81 ± 6.45	97.35 ± 6.82	<0.0001
WHR	0.85 ± 0.05	0.95 ± 0.06	<0.0001
FPG (mmol/L)	9.57 ± 3.26	10.36 ± 3.45	0.055
Flns (μIU/mL)	8.99 (3.28, 10.05)	9.72 (4.48, 11.16)	0.632
FC-P (ng/ml)	2.17 (1.06, 2.43)	2.50 (1.90, 3.09)	0.387
HOMA-IR	3.46 (1.38, 3.94)	4.27 (1.90, 5.10)	0.220
HbA1c (%)	9.17 ± 2.16	9.56 ± 2.33	0.155
ALT (U/L)	21.22 (11.2, 23.00)	25.27 (13.95, 30.78)	0.042
AST (U/L)	17.03 (12.68, 20.15)	19.17 (13.00, 22.28)	0.068
TG (mmol/L)	1.92 (1.04, 2.45)	2.69 (1.46, 2.93)	0.011
TC (mmol/L)	4.75 ± 1.08	5.01 ± 1.14	0.056
HDL-C (mmol/L)	1.24 ± 0.42	1.10 ± 0.37	0.003
LDL-C (mmol/L)	2.73 ± 0.84	2.87 ± 0.91	0.203
Heart rate (bpm)	71.73 ± 10.93	73.46 ± 10.67	0.181
LVEF (%)	67.35 ± 4.40	67.27 ± 3.57	0.865
Internal diameter of aortic root (mm)	29.12 ± 3.03	29.74 ± 2.74	0.064
Left atrial diameter (mm)	32.65 ± 3.37	34.95 ± 3.44	<0.0001
LVDd (mm)	44.37 ± 3.64	45.13 ± 3.78	0.094
LVSD (mm)	28.36 ± 4.15	28.50 ± 3.99	0.779
IVST (mm)	9.60 ± 0.90	10.06 ± 0.86	<0.0001
PWT (mm)	9.52 ± 0.89	10.01 ± 1.95	0.026
LVM (g)	142.18 ± 25.99	156.56 ± 38.65	0.001
LVMi (g/m ²)	85.50 ± 15.27	89.22 ± 20.43	0.114
PEP (ms)	108.47 ± 15.06	103.79 ± 14.43	0.011
ET (ms)	272.14 ± 24.50	271.69 ± 25.48	0.886
ET/PEP	2.56 ± 0.42	2.68 ± 0.54	0.070

Note: Data are presented as means ± SD or medians (inter-quartile range (IQR)) for continuous variables and number (percentages) for categorical variables.

Abbreviations: TyG index, Triglyceride-glucose index; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; WC, waist circumference; HC, hip circumference; WHR, waist-to-hip ratio; FPG, fasting plasma glucose; Flns, fasting plasma insulin; FC-P, fasting C peptide; HOMA-IR, homeostasis model assessment-insulin resistance index; HbA1c, glycosylated hemoglobin c; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TG, triglyceride; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LVEF, left ventricular ejection fraction; LVDd, left ventricular end diastolic diameter; LVSD, left ventricular end systolic diameter; IVST, interventricular septum thickness; PWT, posterior wall thickness; LVM, left ventricular mass; LVMi, left ventricular mass index; PEP, pre-ejection period; ET, ejection time.

correlated with DBP, SBP, and BMI ($p < 0.05$). LVM was also significantly correlated with TG ($r = 0.155$, $p = 0.001$) and FPG ($r = 0.125$, $p = 0.009$). LVEF was significantly correlated with TG ($r = -0.110$, $p = 0.020$) and WHR ($r = -0.117$, $p = 0.014$).

Discussion

The results of our study showed that TyG index of T2DM patients was significantly higher than that of healthy

controls, which is consistent with the previous results.^{21,22}

More importantly, this study observed the relationship between TyG index and cardiac hemodynamics in patients with T2DM for the first time. The results showed that BMI, SBP, DBP, and HOMA-IR in Q3 group were higher than those in the other two groups, and TyG index was correlated with cardiac hemodynamics. In addition, this study also found that TyG is closely related to visceral obesity, which is a risk factor of cardiovascular complications in T2DM. These results together indicated that

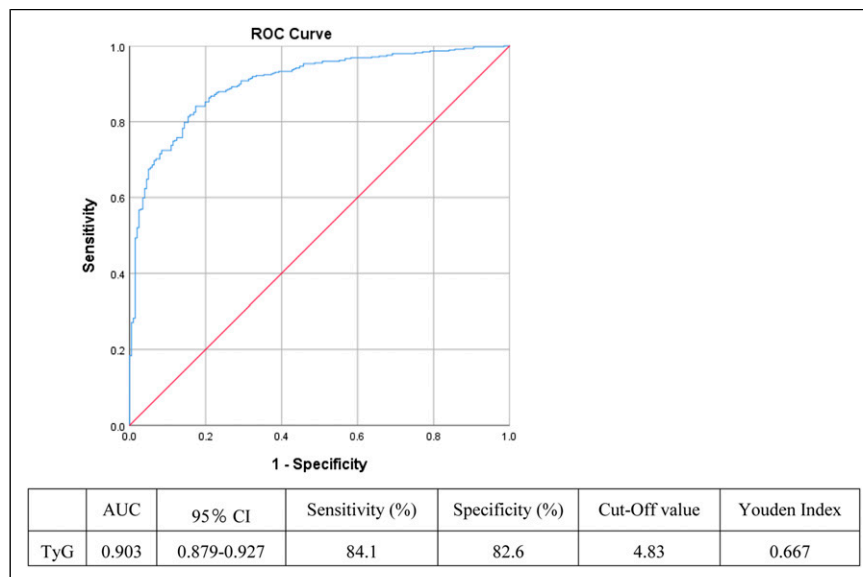


Figure 1. ROC curve analysis of TyG prediction of T2DM risk.

TyG index is significantly associated with the development of cardiovascular risk factors in T2DM patients.

Insulin resistance is one of the earliest metabolic abnormalities leading to T2DM, and it is the key factor of the pathogenesis of T2DM.²³ This study first observed the difference of TyG index between normal people and patients with T2DM. The results showed that compared with healthy controls, HOMA-IR and TyG levels in patients with T2DM were higher, which was consistent with other existing studies.^{24–26} HOMA-IR is calculated based on fasting insulin level and is not suitable for clinical patients who are currently using insulin therapy. Therefore, TyG index may be more suitable as an indicator of metabolic syndrome and T2DM than HOMA-IR or TG/HDL-C.²⁵ It has been found in different studies that TyG index can predict the risk of diabetes. A 6-year follow-up study of 5706 rural Chinese with normal BMI showed that the risk of T2DM rises with the increase of TyG index.¹² A cohort study of metabolic diseases in Korea found that the incidence rate of diabetes increased proportionally with the TyG index quartile. After adjusting for age, gender, BMI, WC, SBP, HDL-C, family history of diabetes, smoking, drinking, and FIns, the risk of diabetes of the highest TyG index quartile was more than four times higher than that of the lowest TyG index quartile. A retrospective analysis conducted by Li et al.²¹ showed that the increased TyG index was independently correlated with the increased risk of diabetes in Chinese adults. The ROC curve of our study also showed that the predictive value of TyG for T2DM risk is 0.903. In conclusion, the TyG index may be a reliable predictor of early risk screening of diabetes, especially in the population

without high-risk factors, such as old age, hypertension, and obesity.²¹

As an indicator of insulin resistance, the relationship between TyG and cardiovascular disease is also widely concerned. Studies have shown that higher TyG index level is associated with poor prognosis in patients with acute ST-segment elevation myocardial infarction,²⁷ higher cardiovascular mortality in patients with peritoneal dialysis,²⁸ and future cardiovascular adverse events in patients with diabetes mellitus and acute coronary syndrome.²⁹ High TyG index is also associated with micro and macrovascular lesions in patients with T2DM.³⁰ Many studies have investigated the relationship between TyG index and the occurrence of cardiovascular events in different patient groups, including non-diabetic and diabetic patients.^{31–33} In patients with T2DM, the TyG index has also been proved to be a better predictor of cardiovascular events than HbA1c.³⁴ Similar studies in South Korea confirmed TyG's independence in describing potential cardiovascular disease.^{35,36} However, few studies have explored the relationship between TyG index and cardiac hemodynamics, which can be used to assess cardiac function and may predict the risk of cardiovascular disease. This study found that TyG was positively correlated with cardiac hemodynamics such as LVDD, LVSD, PWT, IVST, LVM, and aortic root diameter and negatively correlated with LVEF. This result is partly consistent with the study of Chiu,³⁷ in which TyG was considered to be negatively correlated with LVEF in the general population. The inconsistent part is that TyG is not correlated with LVM in that research, while in our study, TyG is positively correlated with LVM. The reasons for this difference may be attributed to different individuals

recruited, different diseases of the tested population, and the influence of drugs used by the individuals. In future clinical practice, patients with T2DM and elevated TyG can be recommended to undergo comprehensive clinical assessment of their cardiovascular risk profile and be considered for echocardiography when necessary. Meanwhile, research exploring the diagnostic performance of TyG index to early detect structural heart disease in people with diabetes is further required.

It is well known that long-term and sustained obesity can significantly increase the incidence of diabetes,³⁸ and obesity, hypertension, and hyperlipidemia play vital role in the occurrence and development of macrovascular complications of T2DM. Chronic hypertension may cause endothelial dysfunction and inflammation, accelerate lipid deposition, and lead to the occurrence and development of atherosclerosis and ventricular hypertrophy.^{39,40} In addition, adipose tissue dysfunction caused by visceral fat accumulation can also produce angiotensin, which may lead to systemic hypertension.⁴¹ Therefore, we further grouped the individuals according to whether there was hypertension or visceral obesity, to explore whether these two factors would affect the value of TyG in T2DM patients. The results showed that TyG was not related to blood pressure, but closely related to visceral obesity. The TyG index, DBP, SBP, TG, PWT, IVST, LVM, and left atrial diameter of visceral obesity individuals were higher than those of non-visceral obesity individuals, the difference was statistically significant. This is consistent with previous findings of our research group. It showed that visceral obesity has a certain impact on exploring the relationship between TyG and hemodynamic index in T2DM patients, which further proved the necessity of adjusting confounding factors such as BMI and WHR in linear regression analysis.

Few studies have discussed the relationship between TyG index and cardiac hemodynamics. The advantage of this study is that we can evaluate the relationship between TyG index and cardiac function by cardiac hemodynamics, which may provide a certain theoretical basis for early diagnosis and intervention of cardiac failure. Meanwhile, the study also has some limitations. First of all, the results of this study are only applicable to patients with early T2DM, because patients with confirmed macro and microvascular diseases have been excluded from the study population according to the exclusion criteria. Second, when comparing healthy controls with T2DM, there was a significant difference in age and gender between the study population—T2DM patients were older and more men. These two factors may have some effects on the differences between groups. Third, because this is a cross-sectional study, we cannot conclude the causal relationship between TyG and cardiac hemodynamics so that

further longitudinal follow-up studies are needed to verify their relationship.

Conclusion

In conclusion, the increase of TyG index is closely related to the cardiac hemodynamics of T2DM patients and is expected to be a new and practical biological indicator for predicting the changes of cardiac function in T2DM patients.

Author Contributions

Guoyue Yuan designed the study; Chenxi Wang, Zhicong Zhao, Xia Deng, Zhensheng Cai, Tian Gu, Lian Li, and Chang Guo participated in acquisition of data; Ling Yang, Dong Wang, and Li Zhao evaluated the literature and edited and revised the manuscript; Chenxi Wang and Zhicong Zhao performed data collation and statistical analysis; Chenxi Wang wrote the first draft of the manuscript. All authors read and approved the final manuscript for publication.

Declaration of conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by the National Natural Science Foundation of China (81870548, 81570721), the Social Development Project of Jiangsu Province (BE2018692), the Natural Science Foundation of Jiangsu Province, China (BK20191222), the Scientific Research Projects of Jiangsu Health and Family Planning Commission (Y2018109), the High Caliber Medical Personnel Foundation of Jiangsu Province (LGY2016053), the Six Talent Peaks Project in Jiangsu Province (2015-WSN-006), the Social Development Project of Zhenjiang City (SH2019041) and the Fifth “169 project” Scientific Research Project of Zhenjiang City, Jiangsu Province.

ORCID iD

Guoyue Yuan  <https://orcid.org/0000-0003-0822-6066>

Supplemental Material

Supplemental material for this article is available online.

References

1. Saeedi P, Petersohn I, Salpea P, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the international diabetes federation diabetes Atlas, 9 edition. *Diabetes Res Clin Pract* 2019; 157: 107843.

2. Gedebjerg A, Almdal T, Berencsi K, et al. Prevalence of micro- and macrovascular diabetes complications at time of type 2 diabetes diagnosis and associated clinical characteristics: A cross-sectional baseline study of 6958 patients in the Danish DD2 cohort. *J Diabetes Complications* 2018; 32: 34–40.
3. Lathief S and Inzucchi S. Approach to diabetes management in patients with CVD. *Trends Cardiovasc Med* 2016; 26: 165–179.
4. Paneni F, Beckman J, Creager M, et al. Diabetes and vascular disease: Pathophysiology, clinical consequences, and medical therapy: Part I. *Eur Heart J* 2013; 34: 2436–2443.
5. Nigro J, Osman N, Dart A, et al. Insulin resistance and atherosclerosis. *Endocr Rev* 2006; 27: 242–259.
6. DeFronzo R. Insulin resistance, lipotoxicity, type 2 diabetes and atherosclerosis: the missing links. The Claude Bernard lecture 2009. *Diabetologia* 2010; 53: 1270–1287.
7. DeFronzo R, Tobin J and Andres R. Glucose clamp technique: a method for quantifying insulin secretion and resistance. *Am J Physiol* 1979; 237: E214–E223.
8. Simental-Mendía L and Guerrero-Romero F. The correct formula for the triglycerides and glucose index. *Eur J Pediatr* 2020; 179: 1171.
9. Locateli J, Lopes W, Simões C, et al. Triglyceride/glucose index is a reliable alternative marker for insulin resistance in South American overweight and obese children and adolescents. *J Pediatr Endocrinol Metab* 2019; 32: 1163–1170.
10. Du T, Yuan G, Zhang M, et al. Clinical usefulness of lipid ratios, visceral adiposity indicators, and the triglycerides and glucose index as risk markers of insulin resistance. *Cardiovasc Diabetol* 2014; 13: 146.
11. Min Park H, Sun Lee H, Lee Y, et al. The triglyceride-glucose index is a more powerful surrogate marker for predicting the prevalence and incidence of type 2 diabetes mellitus than the homeostatic model assessment of insulin resistance. *Diabetes Res Clin Pract* 2021; 180: 109042.
12. Zhang M, Wang B, Liu Y, et al. Cumulative increased risk of incident type 2 diabetes mellitus with increasing triglyceride glucose index in normal-weight people: The rural Chinese cohort study. *Cardiovasc Diabetol* 2017; 16: 30.
13. Park K, Ahn C, Lee S, et al. Elevated TyG index predicts progression of coronary artery calcification. *Diabetes Care* 2019; 42: 1569–1573.
14. Sheng G, Lu S, Xie Q, et al. The usefulness of obesity and lipid-related indices to predict the presence of Non-alcoholic fatty liver disease. *Lipids Health Dis* 2021; 20: 134.
15. Lee S, Kim M, Kang S, et al. Triglyceride glucose index is superior to the homeostasis model assessment of insulin resistance for predicting nonalcoholic fatty liver disease in Korean adults. *Endocrinol Metabolism (Seoul, Korea)* 2019; 34: 179–186.
16. Kim Y, Kim J, Park J, et al. Association between triglyceride-glucose index and gastric carcinogenesis: a health checkup cohort study. *Gastric Cancer* 2022; 25(1): 33–41.
17. Wu T, Fawzy A, Brigham E, et al. Association of triglyceride-glucose index and lung health: A population-based study. *Chest* 2021; 160(3): 1026–1034.
18. Lorenzo C and Haffner S. Performance characteristics of the new definition of diabetes: the insulin resistance atherosclerosis study. *Diabetes Care* 2010; 33: 335–337.
19. Lang R, Badano L, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American society of echocardiography and the European association of cardiovascular imaging. *J Am Soc Echocardiography* 2015; 28: 1–39.
20. Kumashiro N, Erion D, Zhang D, et al. Cellular mechanism of insulin resistance in nonalcoholic fatty liver disease. *Proc Natl Acad Sci USA* 2011; 108: 16381–16385.
21. Li X, Li G, Cheng T, et al. Association between triglyceride-glucose index and risk of incident diabetes: a secondary analysis based on a Chinese cohort study: TyG index and incident diabetes. *Lipids Health Dis* 2020; 19: 236.
22. Park B, Lee H and Lee Y. Triglyceride glucose (TyG) index as a predictor of incident type 2 diabetes among nonobese adults: a 12-year longitudinal study of the Korean Genome and epidemiology study cohort. *Translational Research* 2021; 228: 42–51.
23. Martin B, Warram J, Krolewski A, et al. Role of glucose and insulin resistance in development of type 2 diabetes mellitus: results of a 25-year follow-up study. *Lancet* 1992; 340: 925–929.
24. Lee J, Lim N and Park H. The product of fasting plasma glucose and triglycerides improves risk prediction of type 2 diabetes in middle-aged Koreans. *BMC Endocrine Disorders* 2018; 18: 33.
25. Lee S, Kwon H, Park Y, et al. Predicting the development of diabetes using the product of triglycerides and glucose: The Chungju metabolic disease cohort (CMC) study. *PLoS One* 2014; 9: e90430.
26. Navarro-González D, Sánchez-Iñigo L, Fernández-Montero A, et al. TyG index change is more determinant for forecasting type 2 diabetes onset than weight gain. *Medicine* 2016; 95: e3646.
27. Luo E, Wang D, Yan G, et al. High triglyceride-glucose index is associated with poor prognosis in patients with acute ST-elevation myocardial infarction after percutaneous coronary intervention. *Cardiovasc Diabetol* 2019; 18: 150.
28. Yan Z, Yu D, Cai Y, et al. Triglyceride glucose index predicting cardiovascular mortality in Chinese initiating peritoneal dialysis: A cohort study. *Kidney Blood Press Res* 2019; 44: 669–678.
29. Wang L, Cong H, Zhang J, et al. Triglyceride-glucose index predicts adverse cardiovascular events in patients with diabetes and acute coronary syndrome. *Cardiovasc Diabetol* 2020; 19: 80.
30. Chiu H, Tsai H, Huang J, et al. Associations between triglyceride-glucose index and micro- and macro-angiopathies in type 2 diabetes mellitus. *Nutrients* 2020; 12: 328.
31. Jin J, Cao Y, Wu L, et al. Triglyceride glucose index for predicting cardiovascular outcomes in patients with coronary artery disease. *J Thorac Dis* 2018; 10: 6137–6146.

32. Li S, Guo B, Chen H, et al. The role of the triglyceride (triacylglycerol) glucose index in the development of cardiovascular events: A retrospective cohort analysis. *Sci Rep* 2019; 9: 7320.
33. Sánchez-Íñigo L, Navarro-González D, Fernández-Montero A, et al. The TyG index may predict the development of cardiovascular events. *Eur J Clin Invest* 2016; 46: 189–197.
34. Su W, Chen S, Huang Y, et al. Comparison of the effects of fasting glucose, hemoglobin A, and triglyceride-glucose index on cardiovascular events in type 2 diabetes mellitus. *Nutrients* 2019; 11: 2838.
35. Kim M, Ahn C, Kang S, et al. Relationship between the triglyceride glucose index and coronary artery calcification in Korean adults. *Cardiovasc Diabetol* 2017; 16: 108.
36. Lee S, Ahn C, Lee B, et al. Association between triglyceride glucose index and arterial stiffness in Korean adults. *Cardiovasc Diabetol* 2018; 17: 41.
37. Chiu T, Tsai H, Chiou H, et al. A high triglyceride-glucose index is associated with left ventricular dysfunction and atherosclerosis. *Int J Med Sci* 2021; 18: 1051–1057.
38. Li Y, Teng D, Shi X, et al. Prevalence of diabetes recorded in mainland China using 2018 diagnostic criteria from the American diabetes association: National cross sectional study. *BMJ* 2020; 369: m997.
39. Liu J, Palmieri V, Roman M, et al. The impact of diabetes on left ventricular filling pattern in normotensive and hypertensive adults: The strong heart study. *J Am Coll Cardiol* 2001; 37: 1943–1949.
40. Petrie J, Guzik T and Touyz R. Diabetes, hypertension, and cardiovascular disease: Clinical insights and vascular mechanisms. *Can J Cardiol* 2018; 34: 575–584.
41. Dhalla N, Liu X, Panagia V, et al. Subcellular remodeling and heart dysfunction in chronic diabetes. *Cardiovasc Res* 1998; 40: 239–247.