The Triglyceride-Glucose Index Is Associated With Atherosclerosis in Patients With Symptomatic Coronary Artery Disease

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Abstract

Background

The triglyceride-glucose index (TyG index) has been suggested as a credible surrogate marker of insulin resistance (IR) for many years. Its value in predicting and diagnosing cardiovascular disease has been reported recently. However, few studies have reported that it can be used as a marker for atherosclerosis and coronary artery disease (CAD), which is one of the main causes of cardiovascular-related death. This study will attempt to prove that the TyG index can be a useful marker for predicting atherosclerosis and has diagnostic significance for symptomatic CAD.

Methods

The baseline data of 3059 cardiology patients, as well as their clinical data, biochemical parameters and medical histories, were collected from our clinical cases over the last three years. Further screening resulted in 1581 data points of symptomatic CAD. The TyG index was calculated by the formula $\text{Ln}(\text{fasting triglycerides (mg/dl)} \times \text{fasting blood glucose (mg/dl)}/2)$. CAD was defined as a nonzero Gensini score on coronary angiography. Participants were divided into four groups according to TyG index tertiles.

Results

We evaluated 1581 patients, and the majority were male (41.9%) and elderly (59.5%). Cardiometabolic risk factors were positively associated with the TyG index. Arterial damage, including carotid and coronary damage, was highly associated with the TyG index. After adjustment for sex, age and multiple risk factors, Poisson regression analysis indicated that the prevalence ratios for carotid plaque and coronary stenosis were 1.11 (95% CI 0.55–2.11; $P = 0.01$) and 2.94 (95% CI 0.58–1.50; $P = 0.01$), respectively. Moreover, the TyG index has better diagnostic efficacy for symptomatic CAD than do fasting glucose and triglycerides (AUC TyG = 0.734; AUC fasting glucose = 0.611; AUC triglyceride = 0.717).

Conclusion

The TyG index is a useful marker for predicting atherosclerosis and may be a diagnostic indicator for symptomatic CAD.

Background

Coronary artery disease (CAD) is a leading cause of morbidity and mortality worldwide [1], and in 2015, it led to the deaths of 7.4 million people. Due to the atherosclerosis process, CAD occurs when the coronary arteries are obstructed, which is highly associated with risk factors [2]. CAD can develop slowly and often without symptoms [3] and is classified as asymptomatic CAD. The main manifestation in its

symptomatic phase is angina, defined as chest pain radiating to the shoulders, arms, and jaw [3]. Insulin resistance (IR) has been proven to play an important role in CAD [4]. The triglyceride-glucose (TyG) index, calculated from fasting triglycerides and blood glucose, has been suggested to be a reliable marker instead of IR for metabolic disorders [5, 6].

Recently, the TyG index has been reported to be associated with cardiovascular disease (CVD) risk in apparently healthy individuals [7]. Last year, da Silva et al. [3] published an article on how the TyG index was associated with symptomatic CAD in patients in secondary care. Another article by Zhao et al. [8] showed that an elevated TyG index is associated with a higher risk of arterial stiffness and nephric microvascular damage. There are also some articles studying the effect of the TyG index on the prognosis of cardiovascular diseases [9]. However, the prognostic value of the TyG index in patients with CAD has not been determined [10]. Atherosclerosis is the pathological basis of CAD, among which coronary artery calcification (CAC) is a risk factor for cardiovascular events [11]. In recent years, research on TyG and CAC has also made progress [7]. Therefore, it is necessary to study the relationship between the TyG index and atherosclerosis. Diabetes and hyperlipidaemia are both risk factors for CAD [12, 13], and these two variables have a direct relationship with a high TyG index (based on the formula). In this sense, controlling for these two variables is necessary. Comparing the diagnostic values of fasting glucose and triglyceride levels with the TyG index is another important point [14]. Therefore, the primary objective of the study was to prove that the TyG index has a better diagnostic ability for CAD than either blood glucose or triglyceride alone.

Methods

Population and study design

From 2016 to 2019, we diagnosed and treated approximately 5000 patients with symptomatic CAD, and 3059 of them completed our follow-up for this study. In addition, 1581 of them who had accurate fasting triglyceride and fasting blood glucose results were divided into four groups according to TyG index tertiles. Patients with symptomatic CAD were those with a history of angina, a clinical diagnosis including diagnosis without complementary tests, or a history of a positive stress test, and patients with treated CAD were those with angioplasty/stent/revascularization [15]. We stratified them into four groups: (a) only symptomatic CAD, (b) symptomatic CAD with diabetes (here referred to as T2DM), (c) symptomatic CAD with hyperlipidaemia, and (d) symptomatic CAD with both diabetes and hyperlipidaemia (Hyperlipidaemia was defined as an adult with a fasting serum total cholesterol of more than 5.72 mmol/L and triglycerides of more than 1.7 mmol/L [16]. T2DM was defined as fasting serum glucose $\geq$ 7.0 mmol/L or the 2-h serum glucose of the oral glucose tolerance test $\geq$ 11.1 mmol/L or current use of hypoglycaemic drugs or insulin [10].) Among these patients, 270 underwent coronary artery angiography, and 1290 underwent carotid Doppler ultrasound. These two parts were also divided into four groups according to TyG index tertiles. Ultimately, we can study the relationship between TyG and symptomatic CAD and central and peripheral vascular atherosclerosis.

Data collection

Height and weight were measured, and body mass index (BMI) was calculated as weight divided by height squared. Family history and personal medical history, including diabetes, hypertension and previous cerebrovascular or cerebrovascular diseases, were collected from self-reported medical history. A smoker was defined as a subject who reported having smoked cigarettes regularly over the previous six months. Blood samples were obtained from participants who were in a fasting state in the morning of the exam day. Concentrations of total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) were measured using an automatic biochemistry analyzer (Hitachi 7150, Japan). The TyG index was calculated using the formula $\text{Ln}(\text{fasting triglycerides (mg/dl)} \times \text{fasting blood glucose (mg/dl)})/2$ [17]. The results of carotid colour Doppler ultrasound and coronary angiography were determined by our trained doctors from department of radiology and cardiology the Department of Radiology and Cardiology.

Statistical analysis

Continuous variables were expressed as the mean $\pm$ SD (variables with a normal distribution) or median (variables with a skewed distribution) and the number (percentage) for the categorical variables. Categorical variables were compared by chi square tests. The associations between the TyG index and cardiovascular risk factors were obtained by linear regression. Relationships between the TyG index and different groups of coronary artery angiography and carotid Doppler ultrasound were examined by Poisson regression and adjusted by confounders. The area under the curve (AUC) of the receiver operating characteristic (ROC) curve and a 95% confidence interval (CI) were calculated to compare the diagnostic efficacy of the TyG index with fasting glucose and triglycerides for symptomatic CAD. All statistical analyses were performed using SPSS statistical package, version 23.0 (SPSS, Inc., Chicago, IL, USA) and STATA 13.0. P values of < 0.05 were considered statistically significant.

Results

Baseline characteristics

A total of 1581 patients experienced symptomatic CAD who had accurate TyG results, with a mean age of 68.0 ± 11.4 years, mean BMI of 24.9 ± 3.3 kg/m²; 41.9% were male. The most prevalent was symptomatic CAD with hyperlipidaemia (37.8%), followed by symptomatic CAD with diabetes (30.1%) and only symptomatic CAD (18.7%). Regarding the history of diseases, 35.8% had arterial hypertension, 37.0% had diabetes and 78.2% had dyslipidaemia. Furthermore, 62.8% of the included patients had a family history of CAD, and 33.6% and 31.9% used hypoglycaemic and lipid-lowering medication, respectively.

The patients were stratified according to TyG index. As shown in Table 1, patients in the highest TyG index group presented higher values of BMI, SBP, DBP, TC, LDL-C, LDL-C/HDL-C ratio, TG, blood glucose, smoking rate, and Hb1Ac (%) than those in the lowest TyG index group. Additionally, lower values of HDL-

C and age were present in those in the highest TyG index group. In addition, patients who had diabetes and hypertension were more present in the last group of TyG index.

Table 1
Clinical characteristics of subjects based on the TyG index

Variables	TyG index tertiles				P-value
	T1 (lowest) (n = 395)	T2 (n = 395)	T3 (n = 395)	T4 (highest) (n = 396)	
TyG index	8.06 ± 0.36	8.72 ± 0.12	9.11 ± 0.12	9.76 ± 0.38	< 0.001
Male, sex [%]	185 (46.7)	183 (46.2)	160 (40.4)	150 (37.8)	
Age (years)	70 ± 11.6	68 ± 11.3	68 ± 11.3	67 ± 11.6	< 0.001
BMI (kg/m2)	24.18 ± 3.1	24.39 ± 3.0	25.07 ± 2.9	26.00 ± 3.5	< 0.001
SBP (mmHg)	138.5 ± 21.2	141.0 ± 20.2	139.2 ± 21.2	143.6 ± 21.9	< 0.001
DBP (mmHg)	78.3 ± 11.4	79.9 ± 12.4	78.9 ± 12.1	80.6 ± 12.4	< 0.001
Hypertension [%]	116 (29.4)	131 (33.1)	169 (42.7)	184 (46.5)	
Total cholesterol (mg/dl)	161.1 ± 38.5	173.4 ± 37.4	180.1 ± 17.1	186.2 ± 37.0	< 0.001
HDL-C (mg/dl)	46.7 ± 12.7	45.6 ± 1.1	41.3 ± 1.6	45.6 ± 11.0	< 0.001
LDL-C (mg/dl)	102.8 ± 3.2	115.8 ± 3.3	112.6 ± 5.1	124.4 ± 37.9	< 0.001
LDL-C/HDL-C ratio	2.4 ± 0.8	2.6 ± 0.7	2.8 ± 0.8	2.8 ± 0.8	< 0.001
Triglycerides (mg/dl)	79.5 ± 37.4	116.7 ± 34.9	149.8 ± 38.4	209.3 ± 66.2	< 0.001
Blood glucose (mg/dl)	93.6 ± 29.8	110.5 ± 25.7	128.8 ± 39.7	180.6 ± 11.2	< 0.001
Diabetes [%]	96 (24.2)	159 (40.2)	245 (61.9)	333 (84.1)	
Smoking [%]	119 (30.1)	131 (33.4)	135 (34.1)	159(40.1)	

Data are represented as the mean ± SD or number (%).

BMI body mass index, SBP systolic blood pressure, DBP diastolic blood pressure, HDL-C high-density lipoprotein, LDL-C low- density lipoprotein

Variables	TyG index tertiles				P-value
Hb1Ac (%)	6.2 ± 0.8	6.1 ± 0.7	6.4 ± 1.2	7.2 ± 2.0	< 0.001
Use of lipid-lowering agents [%]	93 (23.4)	131 (33.1)	135 (34.1)	148 (37.4)	
Use of hypoglycaemic agents [%]	77 (19.9)	116 (29.2)	119 (30.1)	219 (55.4)	
Family history of CAD [%]	240 (60.6)	242 (61.2)	246 (62.1)	266 (66.9)	
Data are represented as the mean ± SD or number (%).					
BMI body mass index, SBP systolic blood pressure, DBP diastolic blood pressure, HDL-C high-density lipoprotein, LDL-C low- density lipoprotein					

Cardiovascular risk factors according to quartiles of the TyG index

We also analyzed the association between quartiles of the TyG index (I quart n = 133, II quart n = 767, III quart n = 595, IV quart n = 86) and cardiovascular risk factors. As shown in Table 2, the TyG index was positively associated with BMI, LDL-C, LDL-C/HDL-C ratio and family history of CAD, as well as the presence of diabetes, hypertension and smoking. On the other hand, it was negatively related to age and HDL-C (Additional Table 1) (all P < 0.05).

Table 2
TyG index and cardiovascular risk factors

Variables	I quart	II quart	III quart	IV quart	P-value
	n = 133	n = 767	n = 595	n = 86	
	< 8.00	8.00-8.99	9.00-9.99	≥ 10.00	
Male, sex (%)	64(48.1)	342(44.6)	226(38.0)	34(39.5)	
Age (years)	70.0 ± 12.1	68.6 ± 9.2	67.8 ± 8.9	67.7 ± 11.1	< 0.001
BMI (kg/m ²)	24.0 ± 3.2	24.5 ± 4.1	25.5 ± 2.9	26.2 ± 2.4	< 0.001
Family history of CAD [%]	81 (60.9)	483 (63.0)	377 (63.4)	52 (60.5)	
Smoking [%]	41 (30.8)	248 (32.3)	219 (36.8)	35 (40.7)	
Hypertension [%]	41 (30.8)	281 (36.6)	284 (47.7)	42 (48.8)	
Diabetes [%]	12 (9.0)	294 (38.3)	442 (74.3)	85 (98.8)	
Hyperlipidaemia [%]	38 (28.6)	296 (38.6)	362 (60.8)	76 (88.4)	
HDL-C (mg/dl)	48.4 ± 12.7	45.6 ± 11.4	44.9 ± 10.0	46.5 ± 11.9	< 0.001
LDL-C (mg/dl)	98.6 ± 30.2	111.8 ± 32.5	123.5 ± 39.3	127.7 ± 38.6	< 0.001
LDL-C/HDL-C ratio	2.2 ± 0.8	2.6 ± 0.9	2.8 ± 0.8	2.8 ± 0.9	< 0.001
Events, n (%)	66(49.6)	396(51.6)	320(53.8)	47(54.7)	
Data are represented as the mean ± SD or number (%).					
BMI body mass index, SBP systolic blood pressure, DBP diastolic blood pressure, HDL-C high-density lipoprotein, LDL-C low-density lipoprotein					

Association between TyG index and carotid plaque

Table 3 shows that the fourth TyG index tertile presented a significant association with the higher prevalence of carotid plaque independent of the influence of social variables (sex, age), lifestyle (smoking), clinical history (hypertension, diabetes, family history of CAD and use of medication) [prevalence ratio (PR): 1.11 (95% CI: 0.55–2.11)].

Table 3
Association of the TyG index with the different phases of carotid Doppler ultrasound

Carotid colour Doppler ultrasound (n = 1290)	TyG index tertiles			
	1 (lowest)	2	3	4 (highest)
	PR (95% CI)			
Normal (n = 911)				
Model 1	Ref.	1.00 (0.79–1.28)	1.01 (0.79–1.29)	0.88 (0.61–1.27)
Model 2	Ref.	1.00 (0.82–1.23)	1.00 (0.79–1.28)	0.88 (0.71–1.21)
Model 3	Ref.	1.01 (0.79–1.29)	1.01 (0.78–1.28)	0.90 (0.61–1.26)
Arteriosclerosis (n = 170)				
Model 1	Ref.	0.84 (0.50–1.42)	0.86 (0.50–1.50)	1.48 (0.73–1.92)
Model 2	Ref.	0.84 (0.51–1.39)	0.86 (0.51–1.51)	1.48 (0.73–1.92)
Model 3	Ref.	0.85 (0.55–1.29)	0.86 (0.50–1.50)	1.49 (0.75–1.90)
Arteriosclerosis with Plaque (n = 209)				
Model 1	Ref.	1.14 (0.67–1.94)	1.07 (0.63–1.80)	1.11 (0.53–2.33)
Model 2	Ref.	1.15 (0.66–1.96)	1.07 (0.63–1.80)	1.11 (0.54–2.11)
Model 3	Ref.	1.14 (0.67–1.94)	1.08 (0.70–1.75)	1.11 (0.55–2.11)
Data are the prevalence ratio (95% CI) based on Poisson regression; Italic values show the presence of statistical significance.				

Model 1: crude

Model 2: adjusted by sex and age

Model 3: adjusted by model 2, use of hypoglycaemia, antihypertensive, anticoagulant, stroke, peripheral artery disease, and the presence of any other stage of the disease

Association between TyG index and cardiovascular disease

Table 4 shows that the severity of cardiovascular disease increases with the increase in the TyG index after the Gensini score is greater than twenty. It also shows that the fourth TyG index tertile presented a significant association with a higher prevalence of cardiovascular disease independent of the influence of social variables (sex, age), lifestyle (smoking), clinical history (hypertension, diabetes, family history of CAD and use of medication) [prevalence ratio (PR): 2.94 (95% CI: 0.58–1.50)].

Table 4

Association of the TyG index with the Gensini scores of coronary angiography in the different groups

• Gensini scores of Coronary angiography (n = 270)	TyG index tertiles			
	1 (lowest)	2	3	4 (highest)
	PR (95%CI)			
0 (n = 48)				
Model 1	Ref.	0.34 (0.81–1.42)	0.93 (0.82–1.44)	0.95 (0.85–1.65)
Model 2	Ref.	0.34 (0.81–1.42)	0.93 (0.82–1.45)	0.95 (0.85–1.65)
Model 3	Ref.	0.34 (0.82–1.39)	0.94 (0.84–1.44)	0.95 (0.85–1.65)
(0, 20] (n = 157)				
Model 1	Ref.	0.75 (0.37–1.51)	0.87 (0.44–1.74)	0.65 (0.22–1.95)
Model 2	Ref.	0.76 (0.38–1.50)	0.87 (0.44–1.74)	0.65 (0.23–1.94)
Model 3	Ref.	0.75 (0.37–1.51)	0.87 (0.44–1.74)	0.65 (0.22–1.95)
> 20 (n = 65)				
Model 1	Ref.	1.39 (0.33–1.58)	1.65 (0.40–1.68)	2.95 (0.57–1.52)
Model 2	Ref.	1.39 (0.34–1.57)	1.65 (0.40–1.68)	2.94 (0.58–1.50)
Model 3	Ref.	1.39 (0.34–1.58)	1.66 (0.41–1.68)	2.94 (0.58–1.50)
Data are the prevalence ratio (95% CI) based on Poisson regression; <i>Italic values show the presence of statistical significance.</i>				

Model 1: crude

Model 2: adjusted by sex and age

Model 3: adjusted by model 2, use of hypoglycaemia, antihypertensive, anticoagulant, stroke, peripheral artery disease, and the presence of any other stage of the disease

Diagnostic efficacy of the TyG index for symptomatic CAD

By analysing the diagnostic efficiency of the TyG index in symptomatic CAD based on the ROC curves, Fig. 1 shows that the TyG index has a certain diagnostic value in symptomatic CAD compared with fasting glucose and triglycerides, and the maximum AUC was 0.734. When the critical value was set at 8.97, the sensitivity and specificity of the TyG index in symptomatic CAD diagnosis were 62.40% and 90.00%, respectively.

Discussion

The TyG index has been reported to be positively associated with cardiovascular risk factors [14, 18]. In addition, some studies found that the TyG index was also related to the prevalence of CVD [10, 19]. However, the prognostic value of the TyG index in patients with symptomatic CAD remains undetermined.

In this study, we investigated whether the TyG index was associated with the prevalence of atherosclerosis, which was independent of conventional cardiovascular risk factors. We confirmed the prognostic value of the TyG index in symptomatic CAD. To the best of our knowledge, there are few studies on the relationship between the TyG index and the presence of carotid and coronary atherosclerosis among patients with symptomatic CAD. Furthermore, the TyG index showed higher predictability for symptomatic CAD than did fasting triglycerides and glucose.

The TyG index was first studied as a marker of identifying insulin resistance (IR) with a high sensitivity and specificity [4, 20, 21], which has been proposed as an important cause of cardiovascular disease (CVD) [22]. It was demonstrated that the TyG index was a useful predictor of T2DM, as well as CVD [19, 23, 24]. Moreover, studies showed that the TyG index is associated with the risk of CVD compared to the usual tool for insulin resistance evaluation [25]. Subsequently, several studies verified the relationship between the TyG index and atherosclerosis and CAD.

To date, very few studies have examined the relationship between the TyG index and atherosclerosis. Irace et al. [26] evaluated the association between carotid atherosclerosis and the TyG index after adjustment for traditional cardiovascular risk factors and positive results. Whereafter, Alizargar and Bai [27] reported that the TyG index could predict only CCA-IMT independent of other risk factors. In a recent study, Lambrinoudaki et al. [28] confirmed that the TyG index is associated with carotid atherosclerosis and arterial stiffness mainly in lean postmenopausal women. In the same year, Lee et al. [29] showed an independent relationship between the TyG index and coronary artery stenosis in patients with type 2 diabetes. However, all these studies have limitations, such as using only postmenopausal women or patients with type 2 diabetes.

In the present study, we demonstrated that the TyG index was independently associated with the prevalence of atherosclerosis in patients with symptomatic CAD. We analyzed the carotid artery and coronary artery separately, indicating that the TyG index can predict arteriosclerosis from the peripheral vascular and central vascular aspects.

On the other hand, in recent years, there have been relatively more studies on the relationship between the TyG index and CAD [22, 30, 31]. da Silva et al. [3] reported that the TyG index was positively associated with CAD in the symptomatic phase, independent of social, clinical and food consumption characteristics. However, it did not compare the diagnostic values of fasting glucose and triglyceride levels with the TyG index [14]. Whereafter, Won et al. [32] found that the TyG index is an independent predictor for the progression of CAC, especially in adults without heavy baseline CAD. Recently, Park et al. [33] reported that the TyG index is an independent marker for predicting subclinical CAD in individuals conventionally considered healthy.

On this basis, the predictive and diagnostic value of the TyG index for CAD with clinical symptoms is worth studying.

In this study, on the basis of verifying the relationship between the TyG index and cardiovascular risk factors, we compared the diagnostic efficacy of the TyG index and fasting glucose and triglycerides on symptomatic CAD. We proved that the TyG index has a better diagnostic value for symptomatic CAD. According to the formula of the TyG index, we can see that fasting glucose and triglycerides have a direct impact on the results, but this study verified that the predictive value of the TyG index for symptomatic CAD is much higher than that of the former two.

There were several limitations in the present study. First, the sample size might not be large enough, and the follow-up period might not be long enough. Second, this is a retrospective observational study that has a memory lapse, and the description of symptoms is not accurate. Third, other confounding factors, such as exercise habits and job category, were not included. Thus, we could not adjust for nutritional habits, which can affect blood glucose and triglyceride levels. Last, we verified the relationship only between the TyG index and symptomatic CAD but not subclinical CAD. Thus, it can also be seen from the bar chart that whether there is a relationship between the TyG index and patients without diabetes and hyperlipidaemia still needs to be studied.

Conclusions

The TyG index was positively associated with a higher prevalence of arteriosclerosis, regardless of conventional influencing factors. In addition, The TyG index has better diagnostic efficacy for symptomatic CAD than fasting glucose and triglycerides according to the ROC curve. Based on the findings of this study, the TyG index is a useful marker for predicting atherosclerosis and may be a diagnostic basis for symptomatic CAD in the future. Further prospective large-scale studies are required to clarify the mechanisms of this relationship.

List Of Abbreviations

CAD: Coronary artery disease; CAC: Coronary artery calcification; T2DM: Type 2 diabetes mellitus; TyG index: Triglyceride-glucose index; TC: Cholesterol; TG: Triglyceride; LDL-C: Low-density lipoprotein cholesterol; HDL-C: High-density lipoprotein cholesterol ; NSTEMI: Non-ST-segment elevation acute coronary syndrome; BMI: Body mass index; FBG: Fasting blood glucose; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; HbA1c: Glycosylated hemoglobin A1c; AUC: Area under the curve.

Declarations

Not applicable.

Ethics approval and consent to participate

The study protocol was approved by the Ethics Committee of Tianjin Union Medical Center.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

Funding

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Author contributions

Liping Wei and Xin Qi designed the experiments. Zixian Dong drafted the manuscript. Wenguang Hou, Hao Wu and Yufan Zhang collected data. Jiao Li and Qianqian Zhang analyzed the data and generated the figures. All authors have read and approved the final version of the manuscript.

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Patient consent for publication

Not applicable.

Competing interests

All the authors confirm that they have no competing interests.

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Figures

Figure 1

Analysis of TyG index, fasting glucose and triglyceride diagnostic efficiency in symptomatic CAD