

Triglyceride-glucose index predicts the risk of coronary artery disease in premenopausal women

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Abstract

Background: The triglyceride glucose index (TyG index), a reliable alternative marker of insulin resistance (IR), has been regarded as an independent predictor of cardiovascular disease (CVD). However, the relationship between TyG index and coronary artery disease (CAD) in premenopausal women remains unclear. We aimed to investigate the prognostic value of TyG index in premenopausal women with CAD.

Methods: A total of 158 Chinese female subjects were enrolled in this retrospective study. Clinical data were collected from medical records. The severity of CAD was assessed by coronary angiography. CAD was defined as Coronary artery stenosis $\geq 50\%$ in at least one major coronary artery. Patients were divided into different groups according to their TyG index and whether they had CAD. Multivariate logistic regression model was used to evaluate the relationship between TyG index and CAD.

Results: The patients with high TyG index had a higher risk of CAD than those with low TyG index ($P < 0.01$). The difference was pronounced in the age group of 49 years or older. Multivariate logistic regression analysis showed that the TyG index was an independent risk factor for CAD in premenopausal women (fully adjusted model: OR 2.730, 95%CI 1.102-6.764, $P = 0.030$).

Conclusions: Elevated TyG index is associated with increased risk of CAD in Chinese premenopausal women, suggesting that the TyG index may be used as a marker of CAD risk in premenopausal women in China.

Background

Premenopausal women have not received enough attention due to their low risk of coronary artery disease (CAD). However, the incidence of CAD in those population has a rising prevalence [1]. Studies have shown that there has been a substantial rise in premenopausal women suffering from angina and myocardial infarction over the last few years [2, 3]. Therefore, it is crucial to identify patients who has high risk of developing future CAD so as to timely treatment can be accepted. A rapidly available marker of risk stratification is of great importance to reduce the risk of CAD in premenopausal women.

The development of CAD is affected by many factors such as abnormal blood glucose and dyslipidemia [4, 5]. One test is Insulin resistance (IR), which is more closely associated with abnormalities in glucose and lipid metabolism that ultimately lead to increased coronary atherosclerosis [6, 7]. It has been reported that IR is not only an independent risk factor for CAD [8], but also associated with other CAD risk factors, such as hypertension [9] and obesity [10].

Recently, a novel convenient biomarker of IR, Triglyceride glucose index (TyG index), is superior to homeostasis model assessment of insulin resistance (HOMA-IR) in IR estimation, leading some researchers to carry out a large number of studies on TyG [11, 12]. Previous studies have found that the TyG index plays an essential role in the development of arterial stiffness [13], coronary artery calcification [14], and subclinical or symptomatic CAD [15, 16]. However, to date, there are few studies on the

relationship between TyG index and premenopausal women with CAD. Therefore, to further examine the association between TyG index and CAD in premenopausal women, we evaluate the value of TyG index in Chinese premenopausal women.

Methods

Study population

This was a retrospective cohort study. A total of 185 premenopausal female patients underwent coronary angiography from September 2018 to December 2021 in The First Hospital of Hebei Medical University were enrolled. The menopausal status was defined as absence of menses for at least 12 consecutive months. Major exclusion criteria were as follows: (1) Prior coronary intervention or coronary thrombolysis or coronary artery bypass grafting was performed; (2) Long-term use of drugs that interfere with normal estrogen secretion; (3) Chronic dialysis; (4) Severe hepatic dysfunction; (5) Severe acute infection; (6) Malignant tumor; (7) Suspected familial hypertriglyceridemia [plasma triglyceride (TG) $\geq$ 500 mg/dL (5.65 mmol/L) or more than one first-degree relative with TG $\geq$ 500 mg/dL]; (8) Rheumatic immune disease; (9) Severe psychiatric disorders; (10) Incomplete clinical data. According to the exclusion criteria, 4 patients were excluded for performed with prior coronary intervention; 2 patients were excluded for performed with coronary thrombolysis; 1 patient was excluded for suspected familial hypertriglyceridemia; 2 patients were excluded for treated with chronic dialysis; 3 patients were excluded for diagnosis of rheumatic immune disease; 15 patients lacking complete clinical data, and the detailed population screening process is shown in Fig. 1. Ultimately, a total of 158 patients participated in the study. The study was performed according to the guidelines of the Helsinki Declaration and was approved by the Ethics Committee of The First Hospital of Hebei Medical University. This study was a retrospective study. The study was approved by the Ethics Committee of the First Hospital of Hebei Medical University and informed consent was not required.

Data Collection and definitions

All demographic data, medical history, laboratory indicators, and basic medication information were collected from medical records by trained clinicians. Body mass index (BMI) was calculated by dividing body weight (kg) by the square of height (m^2). Blood pressure was measured in the seated position using a mercury sphygmomanometer, and the mean results of three measurements of systolic blood pressure (SBP) and diastolic blood pressure (DBP) were recorded. The venous blood samples were collected after overnight fasting before coronary angiography. Routine biochemical parameters including lipids, fasting blood glucose (FBG), and renal function. TyG index was defined as $TyG = \ln [\text{fasting triglycerides (mg/dl)} \times \text{fasting glucose (mg/dl)} / 2]$. We used the baseline fasting triglycerides and FBG to calculate the TyG index [17, 18]. Hypertension was defined as SBP $\geq$ 140 mmHg or DBP $\geq$ 90 mmHg, any use of the antihypertensive drug, or a self-reported history of hypertension. Diabetes was defined as FBG $\geq$ 7.0

mmol/L, any use of glucoselowering drugs, or a self-reported history of diabetes. Dyslipidemia was defined as any self-reported history or use of lipid-lowering drugs, total cholesterol (TC) ≥ 5.17 mmol/L.

Angiographic Analysis

Angiographic data were obtained from the cardiac catheterization laboratory records. Coronary angiography was performed by three dedicated interventionists by radial or femoral route depending on the operator's discretion. The assessment of coronary artery was done by three senior-most cardiologists to maintain uniformity and to reduce the inter-observer variability. CAD was defined as coronary artery stenosis $\geq 50\%$ in at least one major coronary artery. The complexity of coronary atherosclerosis was quantified by the Gensini score, which includes both angiographically significant and nonsignificant stenosis [19, 20]. The final Gensini score was expressed as the sum of all the individual coronary artery scores. To aid in the generation of Gensini score, at least 5 different planes of view were obtained for each patient.

Statistical Analysis

Continuous variables were expressed as mean $\pm$ standard deviation when normally distributed and as median (interquartile range) for variables not normally distributed. Comparisons between different groups were analyzed by Student's t-test or Mann-Whitney U test. Categorical variables were expressed as quantities and percentages and were compared by the chi-square test. Univariate logistic regression analysis was performed to identify risk factors of CAD. Multivariable logistic regression analysis was performed to estimate odds ratio (OR) for CAD. The variables with $P < 0.2$ in univariate logistic regression analysis or clinically relevant to CAD were adjusted for different models [21]. The Hosmer-Lemeshow goodness-of-fit test was used to assess calibration. A 2-sided analysis with a P -value < 0.05 was considered significant. All statistical analyses were performed using SPSS version 26.0.

Results

Baseline characteristics of patients in different TyG index groups

None of the 158 premenopausal women had a history of smoking. Patients were divided into two groups by the median TyG index level (8.482): low TyG index group (< 8.482) and high TyG index group (≥ 8.482). The demographic, laboratory and angiographic characteristics of the participants are shown in Table 1. The prevalence of hypertension, diabetes, CAD, dyslipidemia, BMI, left anterior artery (LAD) stenosis, FBG, low-density lipoprotein cholesterol (LDL-C), Uric Acid (UA), Apolipoprotein A1 (ApoA1), Apolipoprotein B (ApoB), TC, TG, antihypertensive agents, antidiabetic agents and Gensini score was significant higher in the high TyG index group. Nevertheless, the patients with high TyG index had a lower high-density lipoprotein cholesterol (HDL-C). There was no significant difference in other baseline characteristics.

Table 1
Comparison of baseline characteristics of patients in different TyG index groups

Items	Total population (n = 158)	TyG index		<i>P</i> value
		Low (< 8.482 , n = 73)	High (≥ 8.482 , n = 73)	
TyG index	8.48 (8.12–8.95)	8.12 (7.97–8.30)	8.95 (8.59–9.28)	< 0.001
Clinical characteristics				
Age, years	48.00 (43.00–51.00)	48.00 (43.00–51.00)	49.00 (44.00–51.00)	0.541
BMI, kg/m ²	26.58 $\pm$ 4.03	25.72 $\pm$ 4.20	27.43 $\pm$ 3.68	0.007
CAD, n (%)	57 (36.08)	18 (22.78)	39 (49.37)	0.001
Diabetes mellitus, n (%)	25 (15.82)	3 (3.80)	22 (27.85)	< 0.001
Hypertension, n (%)	67 (42.41)	27 (34.18)	40 (50.63)	0.036
Dyslipidemia, n (%)	52 (32.91)	17 (21.52)	35 (44.30)	0.002
History of Stroke, n (%)	14 (8.86)	7 (8.86)	7 (8.86)	1.000
Family history of CAD, n (%)	16 (10.13)	5 (6.33)	11 (13.92)	0.114
Family History of Stroke, n (%)	2 (1.27)	1 (1.27)	1 (1.27)	1.000
Vital signs at admission				
SBP, mmHg	130.50 (119.00–144.25)	128.00 (115.00–143.00)	134.00 (121.00–145.00)	0.245
DBP, mmHg	83.23 $\pm$ 11.75	81.61 $\pm$ 11.72	84.85 $\pm$ 11.62	0.083
RHR, beats per minute	74.00 (66.00–83.00)	73.00 (66.00–82.00)	75.00 (66.00–84.00)	0.412
Angiography characteristics				
LM ,n (%)	0 (0.00)	0 (0.00)	0 (0.00)	-

Dates are presented as mean $\pm$ SD, medians with inter quartile ranges or percentage. TyG triglyceride-glucose index, BMI body mass index, CAD coronary artery disease, SBP systolic blood pressure, DBP diastolic blood pressure, RHR resting heart rate, LM left main coronary artery, LAD left anterior descending artery, LCX left circumflex artery, RCA right coronary artery, FBG fasting blood glucose, LDL-C low-density lipoprotein cholesterol, HDL-C high-density lipoprotein cholesterol, TG triglycerides, TC total cholesterol, UA Uric Acid, Lp(a) lipoprotein (a), ApoA1 apolipoprotein A1, ApoB apolipoprotein B.

Items	Total population (n = 158)	TyG index		<i>P</i> value
		Low (< 8.482 , n = 73)	High (≥ 8.482 , n = 73)	
LAD, n (%)	50 (31.65)	15 (18.99)	35 (44.30)	0.001
LCX, n (%)	24 (15.19)	9 (11.39)	15 (18.99)	0.184
RCA, n (%)	22 (13.92)	7 (8.86)	15 (18.99)	0.066
Gensini score	0.00 (0.00–16.00)	0.00 (0.00–10.00)	3.00 (0.00–22.00)	0.009
Laboratory characteristics				
FBG, mmol/L	4.94 (4.59–5.45)	4.79 (4.54–5.08)	5.37 (4.69–6.30)	< 0.001
Creatinine, $\mu\text{mol/L}$	53.35 (48.38–59.80)	52.70 (48.50–58.80)	53.90 (47.90–61.10)	0.188
LDL-C, mmol/L	2.84 ± 0.68	2.68 ± 0.64	2.99 ± 0.69	0.005
HDL-C, mmol/L	1.09 (0.96–1.26)	1.18 (1.06–1.35)	1.01 (0.89–1.15)	< 0.001
TG, mmol/L	1.19 (0.88–1.69)	0.88 (0.71–1.04)	1.69 (1.38–2.13)	< 0.001
TC, mmol/L	4.31 (3.85–5.05)	4.22 (3.75–4.84)	4.65 (4.06–5.41)	0.020
UA, $\mu\text{mol/L}$	280.35 (231.10–342.68)	266.40 (224.10–304.30)	305.50 (246.60–375.50)	0.002
Lp(a), mg/L	147.10 (83.78–341.08)	156.30 (79.50–366.30)	145.80 (87.50–313.80)	0.756
ApoA1, g/L	1.25 (1.15–1.37)	1.26 (1.16–1.38)	1.24 (1.12–1.36)	0.357
ApoB, g/L	0.75 (0.60–0.89)	0.65 (0.53–0.80)	0.81 (0.69–0.95)	< 0.001
Medications at discharge				
Antihypertensive agents, n (%)	34 (21.52)	11 (13.92)	23 (29.11)	0.020

Dates are presented as mean $\pm$ SD, medians with inter quartile ranges or percentage. TyG triglyceride-glucose index, BMI body mass index, CAD coronary artery disease, SBP systolic blood pressure, DBP diastolic blood pressure, RHR resting heart rate, LM left main coronary artery, LAD left anterior descending artery, LCX left circumflex artery, RCA right coronary artery, FBG fasting blood glucose, LDL-C low-density lipoprotein cholesterol, HDL-C high-density lipoprotein cholesterol, TG triglycerides, TC total cholesterol, UA Uric Acid, Lp(a) lipoprotein (a), ApoA1 apolipoprotein A1, ApoB apolipoprotein B.

Items	Total population (n = 158)	TyG index		<i>P</i> value
		Low (< 8.482 , n = 73)	High (≥ 8.482 , n = 73)	
Antidiabetic agents, n (%)	13 (8.23)	3 (3.80)	10 (12.66)	0.043
Lipid-lowering agents, n (%)	3 (1.90)	1 (1.27)	2 (2.53)	1.000
Dates are presented as mean $\pm$ SD, medians with inter quartile ranges or percentage. TyG triglyceride-glucose index, BMI body mass index, CAD coronary artery disease, SBP systolic blood pressure, DBP diastolic blood pressure, RHR resting heart rate, LM left main coronary artery, LAD left anterior descending artery, LCX left circumflex artery, RCA right coronary artery, FBG fasting blood glucose, LDL-C low-density lipoprotein cholesterol, HDL-C high-density lipoprotein cholesterol, TG triglycerides, TC total cholesterol, UA Uric Acid, Lp(a) lipoprotein (a), ApoA1 apolipoprotein A1, ApoB apolipoprotein B.				

Baseline characteristics of patients in different age groups

For further comparison of baseline characteristics, the patients were divided into two groups by the median age level (49): low age group (< 49) and high age group (≥ 49). The baseline characteristics are shown in Table 2. The prevalence of hypertension, dyslipidemia, CAD, resting heart rate(RHR), left anterior artery (LAD) stenosis, right coronary artery (RCA) stenosis, and lipoprotein (a) [LP(a)] were significant higher in the high age group. In addition, we divided the patients into groups according to age and TyG index. Figure 2 shows the high TyG index had a higher risk of CAD than the low TyG index ($P < 0.001$), the difference was pronounced in the age group of 49 years or older.

Table 2
Comparison of baseline characteristics of patients in different age groups

Items	Age		Pvalue
	Low(< 49, n = 82)	High(≥ 49, n = 76)	
Clinical characteristics			
Age, years	44.00 (41.00–47.00)	51.00 (49.00–52.00)	< 0.001
BMI, kg/m ²	26.42 ± 4.28	26.74 ± 3.76	0.620
CAD, n (%)	23 (28.05)	34 (44.74)	0.029
Diabetes mellitus, n (%)	11 (13.41)	14 (18.42)	0.389
Hypertension, n (%)	28 (34.15)	39 (51.32)	0.029
Dyslipidemia, n (%)	20 (24.39)	32 (42.11)	0.018
History of Stroke, n (%)	6 (7.32)	8 (10.53)	0.478
Family history of CAD, n (%)	7 (8.54)	9 (11.84)	0.491
Family History of Stroke, n (%)	1 (1.22)	1 (1.32)	1.000
Vital signs at admission			
SBP, mmHg	128.5 (114.75-143.25)	136.00 (121.00-145.75)	0.089
DBP, mmHg	82.17 ± 12.20	84.37 ± 11.21	0.241
RHR, beats per minute	76.50 (69.50-86.25)	71.00 (64.00–81.00)	0.007
Angiography characteristics			
LM, n (%)	0 (0.00)	0 (0.00)	-
LAD, n (%)	19 (23.17)	34 (44.74)	0.017
LCX, n (%)	10 (12.20)	14 (18.42)	0.276
RCA, n (%)	7 (8.54)	15 (19.74)	0.042
Gensini score	0.00 (0.00-10.50)	2.00 (0.00–16.00)	0.127
Laboratory characteristics			
FBG, mmol/L	4.88 (4.54–5.30)	5.06 (4.64–5.64)	0.055
Dates are presented as mean ± SD, medians with inter quartile ranges or percentage. TyG triglyceride-glucose index, BMI body mass index, CAD coronary artery disease, SBP systolic blood pressure, DBP diastolic blood pressure, RHR resting heart rate, LM left main coronary artery, LAD left anterior descending artery, LCX left circumflex artery, RCA right coronary artery, FBG fasting blood glucose, LDL-C low-density lipoprotein cholesterol, HDL-C high-density lipoprotein cholesterol, TG triglycerides, TC total cholesterol, UA Uric Acid, Lp(a) lipoprotein (a), ApoA1 apolipoprotein A1, ApoB apolipoprotein B.			

Items	Age		P value
	Low(< 49, n = 82)	High(≥ 49, n = 76)	
Creatinine, μmol/L	52.65 (48.48–59.13)	53.70 (48.23–60.10)	0.777
LDL-C, mmol/L	2.80 ± 0.66	2.88 ± 0.71	0.481
HDL-C, mmol/L	1.09 (0.95–1.26)	1.12 (0.96–1.27)	0.884
TG, mmol/L	1.19 (0.83–1.61)	1.21 (0.91–1.89)	0.333
TC, mmol/L	4.22 (3.82–4.95)	4.67 (3.89–5.41)	0.160
UA, μmol/L	285.10 (228.85–348.55)	272.55 (232.60–341.20)	0.671
Lp(a), mg/L	137.15 (69.05–241.45)	183.45 (95.83–486.05)	0.022
ApoA1, g/L	1.25 (1.15–1.36)	1.24 (1.15–1.37)	0.740
ApoB, g/L	0.74 (0.57–0.84)	0.75 (0.62–0.92)	0.411
TyG index	8.41 (8.08–8.76)	8.53 (8.16–9.02)	0.113
Medications at discharge			
Antihypertensive agents, n (%)	14 (17.07)	20 (26.32)	0.158
Antidiabetic agents, n (%)	5 (6.10)	8 (10.53)	0.311
Lipid-lowering agents, n (%)	1 (1.22)	2 (2.63)	0.947
Dates are presented as mean ± SD, medians with inter quartile ranges or percentage. TyG triglyceride-glucose index, BMI body mass index, CAD coronary artery disease, SBP systolic blood pressure, DBP diastolic blood pressure, RHR resting heart rate, LM left main coronary artery, LAD left anterior descending artery, LCX left circumflex artery, RCA right coronary artery, FBG fasting blood glucose, LDL-C low-density lipoprotein cholesterol, HDL-C high-density lipoprotein cholesterol, TG triglycerides, TC total cholesterol, UA Uric Acid, Lp(a) lipoprotein (a), ApoA1 apolipoprotein A1, ApoB apolipoprotein B.			

Evaluation of Factors Associated with the TyG Index

Univariate logistic regression analysis showed that TyG index, age, BMI, diabetes mellitus, hypertension, SBP, DBP, RHR, HDL-C, Lp(a), ApoB, antihypertensive agents and antidiabetic agents were potential risk factors for CAD in Table 3 ($P < 0.2$). These potential risk factors were adjusted in the multivariate logistic regression analysis model. After adjustment, Table 4 showed the TyG index was an independent predictor of the CAD in premenopausal women in 3 different adjusted models.

Table 3
Univariate logistic regression model analysis of risk factors predicting CAD

Items	OR	95%CI	Pvalue
TyG index dichotomy	3.304	1.664–6.563	0.001
Age	1.077	1.006–1.153	0.034
BMI	1.065	0.982–1.155	0.130
Diabetes mellitus	4.941	1.972–12.378	0.001
Hypertension	2.710	1.389–5.287	0.003
Dyslipidemia	1.166	0.587–2.316	0.662
History of Stroke	1.368	0.450–4.159	0.581
Family History of CAD	0.560	0.172–1.825	0.336
Family History of Stroke	1.786	0.110-29.104	0.684
SBP	1.020	1.001–1.038	0.035
DBP	1.030	1.001–1.060	0.042
RHR	0.977	0.949-1.05	0.108
Creatinine	1.005	0.971–1.041	0.761
LDL-C	1.195	0.741–1.927	0.464
HDL-C	0.381	0.096–1.512	0.170
TC	1.097	0.787–1.530	0.585
UA	1.002	0.998–1.005	0.325
Lp(a)	1.002	1.001–1.003	0.005
ApoA1	0.579	0.134–2.498	0.463
ApoB	2.802	0.585–13.412	0.197
Antihypertensive agents	2.867	1.318–6.236	0.008
Antidiabetic agents	4.547	1.332–15.518	0.016
Lipid-lowering agents	3.636	0.322–41.013	0.296
TyG triglyceride-glucose index, BMI body mass index, CAD coronary artery disease, SBP systolic blood pressure, DBP diastolic blood pressure, RHR resting heart rate, LDL-C low-density lipoprotein cholesterol, HDL-C high-density lipoprotein cholesterol, TC total cholesterol, UA Uric Acid, Lp(a) lipoprotein (a), ApoA1 apolipoprotein A1, ApoB apolipoprotein B.			

Table 4
Association between the TyG index and CAD

Low TyG index group				High TyG index group		
	OR	95%CI	Pvalue	OR	95%CI	Pvalue
Model 1	Reference	-	-	3.228	1.639–6.596	0.001
Model 2	Reference	-	-	2.521	1.198–5.306	0.015
Model 3	Reference	-	-	2.730	1.102–6.764	0.030
Model 1: adjusted for age.						
Model 2: adjusted for model1, BMI, Diabetes mellitus, Hypertension.						
Model 3: adjusted for model2, HDL-C, Lp(a), ApoB, RHR, SBP, DBP, Antihypertensive agents, Antidiabetic agents.						
TyG triglyceride-glucose index, CAD coronary artery disease, BMI body mass index, RHR resting heart rate, SBP systolic blood pressure, DBP diastolic blood pressure, HDL-C high-density lipoprotein cholesterol, Lp(a) lipoprotein (a), ApoB apolipoprotein B.						

Discussion

To our knowledge, this is the first study to examine the relationship between TyG index and CAD in premenopausal women. It is the first time to confirm that TyG index is an independent risk factor for CAD in premenopausal women. We also find the high TyG index had a higher risk of CAD than the low TyG index and the difference was pronounced in the age group of 49 years or older.

Cardiovascular diseases, especially CAD, are one of the leading causes of death in women, and they have received extensive attention both in China and abroad [22]. However, among these risk factors, type 2 diabetes contributes importantly to cardiovascular disease, because it is highly prevalent and adjusted calculate hazard ratios (HRs) with diabetes were: 2.00 (95% CI 1.83–2.19) for CAD [23, 24]. Before type 2 diabetes is diagnosed, IR can be present for years, thereby increasing insulin and glucose concentrations [25, 26]. IR has been shown to be superior to other cardiovascular risk factors in predicting CAD risk in previous studies, such as in a standardized meta-analysis researchers found that the relative risk of cardiovascular disease was higher for an increase of one standard deviation in HOMA-IR compared to an increase of one standard deviation in fasting glucose or fasting insulin concentration [27]. In a study of type 1 diabetes, researchers study showed that decreased insulin sensitivity in these subjects is a real cardiovascular risk factor and contributes to the onset of early atherosclerosis [28]. Hanley AJ et al found a significant association between HOMA-IR and risk of CAD [29]. And a previous prospective study showed that IR per se calculated by homeostasis model assessment is an independent risk factor for major cardiovascular events [30].

In this light, IR is a crucial mechanism for CAD and is an independent risk factor for CAD [31]. According to some previous studies, there is an association between IR and CAD. First, IR promotes the progression of CAD by inducing glucose metabolism imbalance, altering systemic lipid metabolism, and causing endothelial dysfunction [32]. Second, IR increases sympathetic nerve activity and leads to increased catecholamine secretion, which increases myocardial oxygen consumption [33, 34]. Third, IR facilitates atherothrombosis through increased cellular synthesis of plasminogen activator inhibitor-1 (PAI-1) and fibrinogen and reduced production of tissue plasminogen activator [35]. In the pathogenesis of atherosclerosis, IR-mediated impairment of endothelial function was earliest found. The relationship between IR and endothelial function is closely associated with metabolic actions of phosphatidylinositol 3-kinase (PI3K)-dependent signaling pathways and mitogenactivated protein kinase (MAPK)-dependent insulin signaling [36, 37]. IR is typically defined as decreased sensitivity or responsiveness to metabolic actions of insulin. Endothelial insulin resistance is typically accompanied by reduced PI3K-NO pathway and an intact or heightened MAPK-ET-1 pathway [38]. As a result, nitric oxide production is reduced and enhanced production of ET-1 in endothelium [39]. The involvement of these factors leads to vulnerable and obstructive atherosclerosis in coronary vessels [40]. Recently, the TyG index, a product of fasting serum triglycerides and glucose, has been suggested as a surrogate marker for the assessment of IR [17, 18]. This index has the advantage of being applicable in clinical practice since both triglyceride and glucose concentrations are inexpensive and routinely measured [17]. Some clinical studies have shown that the TyG index is better for the prediction of IR than HOMA-IR [41]. Previous studies have shown that the TyG index has a positive correlation with IR, similar to the insulin-mediated glucose uptake or hyperinsulinemic-euglycemic clamp test [17]. The mechanism of TyG in predicting atherosclerosis may be related to IR-mediated endothelial dysfunction, systemic inflammation, oxidative stress and vascular remodeling [42–44]. Thus the TyG index may be a useful tool to predict arterial stiffness and CAD. Therefore, we believe that the predictive effect of TyG index on CAD should be interpreted as IR reflected by TyG index. A study of Iranians showed that TyG index was significantly associated with the risk of CAD, especially in younger populations [45]. A retrospective cohort study of older than 60 years showed that participants in the top quartile of TyG index had a 72% higher risk of CAD events than the rest of the population [46]. Presently, more and more premenopausal women had CAD. Traditional opinion considered that men were easily suffered from CAD and young premenopausal women never had CAD, which contribute the inadequate concern for premenopausal women with abnormal chest pain especially atypical angina symptom. The present study, which included premenopausal women, is the first to confirm that TyG index is an independent risk factor for an increased risk of CAD in premenopausal women. The TyG index can be used as a convenient and inexpensive predictor of the CAD, providing a basis for primary prevention in young women.

The present study also had several limitations. Firstly, the sample size might be not large enough. Secondly, owing to a shortage of records insulin concentration data, we could not compare the predictive value of TyG index with those of HOMA-IR and the hyperinsulinaemic euglycaemic clamp test for the development of CAD. Thirdly, we did not enrolled men or postmenopausal women in the study. Future studies are needed to evaluate the specific relation between three different population. Moreover, the TyG

index seems to be significantly affected by diet and ethnic group [47, 48]. Thus, the findings from the current study are difficult to generalize to all countries and ethnic groups. Finally, although other potential cardiac risk factors were adjusted for, we still cannot exclude the possibility of residual or unassessed confusion.

Conclusion

Our study showed that the TyG index is an independent risk factor for CAD in Chinese premenopausal women. The high TyG Index had a higher risk of CAD than the low TyG Index, the difference was pronounced in the age group of 49 years or older.

Abbreviations

TyG
Triglyceride-glucose
IR
Insulin resistance
CAD
coronary artery disease
TG
triglyceride
BMI
Body mass index
SBP
systolic blood pressure
DBP
diastolic blood pressure
RHR
resting heart rate
LM
left main coronary artery
LAD
left anterior descending artery
LCX
left circumflex artery
RCA
right coronary artery
FBG
fasting blood glucose
LDL-C

low-density lipoprotein cholesterol
HDL-C
high-density lipoprotein cholesterol
TG
Triglycerides
TC
total cholesterol
UA
Uric Acid
Lp(a)
lipoprotein (a)
ApoA1
apolipoprotein A1
ApoB
apolipoprotein B
HRs
calculate hazard ratios
HOMA-IR
homeostasis model assessment of insulin resistance
PAI-1
plasminogen activator inhibitor-1
PI3K
phosphatidylinositol 3-kinase
MAPK
mitogenactivated protein kinase
NO
nitric oxide
ET-1
endothelin-1

Declarations

Ethics approval and consent to participate

The study was performed according to the guidelines of the Helsinki Declaration and has been approved by the ethics committees at the First Hospital of Hebei Medical University, China (reference number 20200511). This study was a retrospective study. The study was approved by the Ethics Committee of the First Hospital of Hebei Medical University and informed consent was not required.

Consent for publication

No published individual participant data were reported that would require consent from the participants.

Availability of Data and Material (ADM)

Due to the small amount of data in this study and the fact that we will collect further data for subsequent studies, the datasets generated and/or analysed during the current study are not publicly available but are available from the corresponding author on reasonable request.

Competing interests

The authors have no relevant financial or non-financial interests to disclose. The authors have no conflicts of interest to declare that are relevant to the content of this article. All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript. The authors have no financial or proprietary interests in any material discussed in this article.

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Author Contributions

All authors contributed substantially to the acquisition and interpretation of data. All authors contributed to manuscript writing, revised the manuscript critically for important intellectual content and approved the final version for publication. Qifeng Guo and Ying Zhan coordinated the writing of the manuscript and are responsible for the integrity of the work as a whole.

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Figures

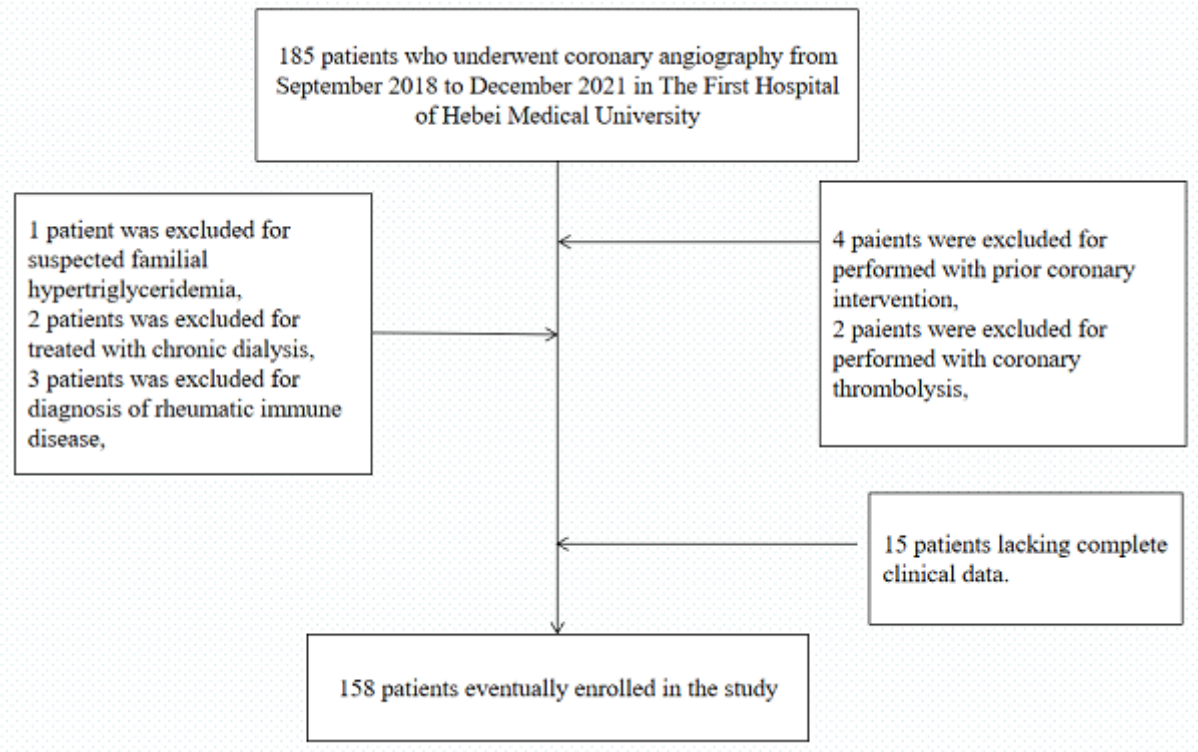


Figure 1

Flowchart of the study population enrollment

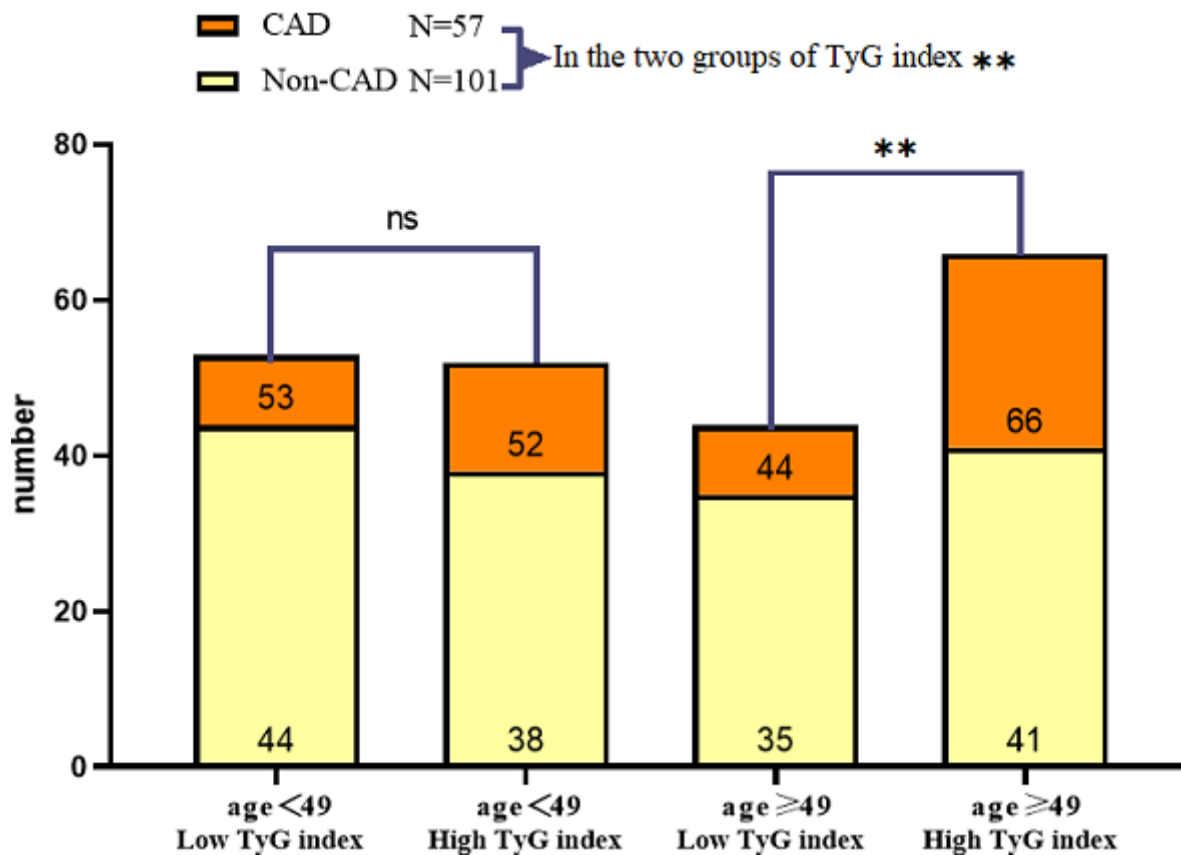


Figure 2

Final inclusion by age and TyG index. Patients were divided into two groups by the median TyG index level (8.482): low TyG index group (<8.482) and high TyG index group (≥ 8.482). The patients were divided into two groups by the median age level (49): low age group (<49) and high age group (≥ 49). We combined different age groups with different TyG groups and divided them into 4 groups on average, which were age <49 and the low TyG index group, age <49 and the high TyG index group, age ≥ 49 and the low TyG index group, age ≥ 49 and the high TyG index group. Age <49 and the low TyG index had a total of 53 patients, of whom 44 did not have CAD. Age <49 and the high TyG index group had a total of 52 patients, of whom 38 did not have CAD. Age ≥ 49 and the low TyG index group had a total of 44 patients, of whom 35 did not have CAD. Age ≥ 49 and the high TyG index group had a total of 66 patients, of whom 41 did not have CAD. We performed statistical analysis on the occurrence of CAD in the same age group with different TyG groups. We dichotomized TyG in the entire study population for statistical analysis of coronary heart disease. TyG, triglyceride-glucose index; CAD, coronary artery disease. ns $P \geq 0.05$, * $P < 0.05$ and ** $P < 0.01$