The correlation of Triglyceride-glucose index with premature coronary heart disease and multivessel disease: a novel risk factor?

Ao Wei
Tianjin Chest Hospital
Jingjing Liu
Tianjin Chest Hospital
Le Wang
Tianjin Chest Hospital
Senshuang Zheng
University of Groningen, University Medical Centre Groningen
Hongliang Cong (hongliangcong@126.com)
Tianjin Chest Hospital

Research Article

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Abstract

Background

For a decade, the global burden of coronary heart disease (CHD) has increased in the young population. To identify the characteristics and to determine the risk factors of premature CHD and multivessel disease (MVD) patients.

Methods

A total of 2846 patients were enrolled in this retrospective, cross-sectional study. Premature CHD is defined as men < 45 years and women < 55 years. Demographic and clinical data were collected from the database of patient medical records. Logistic regression models were applied to analyse the risk factors of premature CHD and MVD.

Results

Most traditional factors and the TyG index between premature and mature CHD patients were not statistically significant. A significantly higher rate of dyslipidaemia was found in female premature CHD patients (OR = 1.412, 95%CI:1.029–1.936). In the crude models, female patients with the highest TyG index level were more likely to have premature MVD (OR = 2.065, 95%CI:1.426–2.991) or mature MVD (OR = 1.837, 95%CI:1.104–3.056) than those with the lowest TyG index group instead of premature single-vessel disease. Among male patients, the same trend was observed in mature MVD of CHD (OR = 2.272, 95%CI:1.312–3.937). The significance of the TyG index was not revealed in the multivariate analyses; however, hypertension, diabetes, obesity, smoking, OMI, and Lp(a) showed a positive association with MVD.

Conclusion

Dyslipidaemia should be used as an effective factor for the prediction and prevention of premature CHD in women. The TyG index could be a simple auxiliary indicator to be applied in population-based cardiovascular disease screening for the initial identification of vascular disease severity.

1 Introduction

Cardiovascular diseases (CVDs) are the leading cause of death worldwide [1]. Coronary heart disease (CHD), an atherosclerotic disease which is the principal burden of CVDs, caused 9.14 million deaths, accounting for 16.2% of all deaths globally [2]. In China, it was estimated that over 11 million patients are currently suffering from CHD [3]. Although more than half of new cases are in people aged over 70, researchers observed that the incidence has risen in younger people [4–6]. The latest data showed that 17.9% of new cases were in people under 55 years old, and 12.3% of deaths were in people under 60 years nationally [7].

Across several guidelines and studies, premature CHD has been defined as males < 55 or < 45 years and females < 65 or < 55 years [8, 9]. Compared with mature CHD, patients with premature CHD usually have more acute coronary syndrome (ACS), worse prognosis, and a higher burden of disease [10, 11]. Prior studies have noted several risk factors for atherosclerosis and CHD, including male gender, obesity, diabetes, smoking, dyslipidaemia, hypertension, and insulin resistance (IR) [4, 12–14]. In addition, Singh et al., Panwar et al., and Zhou et al. revealed the correlation

between premature CHD and familial hypercholesterolemia, apolipoprotein B, and homocysteine respectively [6, 15, 16]. As a novel marker of IR, the triglyceride-glucose (TyG) index has been widely used in recent cardiovascular studies [17–21]. It has been observed that an increased TyG index is associated with a higher risk of CVD, artery calcification, and major adverse cardiovascular events [18, 21]. Furthermore, Wang et al. reported the relevancy of multivessel disease (MVD) of CHD and high TyG index, and worse outcomes were found in the MVD than in single-vessel disease (SVD) [21–23].

Few studies have investigated the differences between the patient characteristics with premature and mature CHD, as well as the correlation of TyG index and traditional risk factors with premature CHD and the vascular disease severity. This study, therefore, aims to identify the characteristics of premature CHD patients and to determine the risk factors of premature CHD and MVD. This may help to improve the prevention and diagnosis of premature CHD and to reduce the burden of the disease.

2 Materials And Methods

2.1 Study design and population

We applied a single-centre, retrospective, cross-sectional study. The patients enrolled in the study were females < 60 and males < 50 years old who had received their first diagnosis of CHD in Tianjin Chest Hospital between 2014 and 2017. An instance of CHD was defined as (a) coronary angiography showing any coronary artery stenosis ≥ 50% of the diameter, or (b) the patient had typical symptoms, changes in cardiac biomarker level and electrocardiographic evidence [24]. The classification of CHD was according to the 10th Revision of the International Classification of Diseases (ICD-10). Four types of CHD were considered in this study, namely stable angina (SA, ICD-10-CM code I20.8), unstable angina (UA, ICD-10-CM code I20.0), non-ST-segment elevation myocardial infarction (NSTEMI, ICD-10-CM code I21.4), and ST-segment elevation myocardial infarction (STEMI, ICD-10-CM code I21.0, I21.1, I21.2, I21.3). Patients with a history of CHD, or history of percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) were excluded, as were those without independent behavioural and cognitive abilities. A total of 2846 patients were included in the analysis. The age for premature CHD was determined as < 45 years for male patients and < 55 years for female patients [8]. This study adhered to the Declaration of Helsinki and was approved by the Medical Ethics Committee of Tianjin Chest Hospital (No. 2018XKZ23). All patients enrolled in this study provided verbal informed consent.

2.2 Data collection

Demographic and clinical data were obtained from the database of patient medical records maintained in the Tianjin Chest Hospital by trained clinicians. We extracted the baseline data of the patient's first diagnosis. The data collection consisted of information on sociodemographic characteristics (age, gender), behaviour (smoking), disease history (hypertension, diabetes), family history of CHD, clinical and serum biochemical indicators (body mass index (BMI), left ventricle ejection fraction (LVEF), haemoglobin (Hb), fasting blood glucose (FBG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglyceride (TG), lipoprotein (a) (Lp(a)), C-reactive protein (CRP), creatinine (Cre)), and the disease characteristics ((SVD or MVD), old myocardial infarction (OMI), types of CHD).

2.3 Definitions

Hypertension and diabetes were determined by the attending physician combining the patient's self-report, clinical presentation, and results of resting blood pressure measurements or oral glucose tolerance test (OGTT). BMI was

calculated by applying weight (kg)/height (m^2). BMI ≥ 24.0 is overweight and obesity, and BMI < 24.0 is underweight and normal [25]. The diagnosis of dyslipidaemia was based on the 2016 Chinese guideline for the management of dyslipidaemia in adults. Hypercholesterolaemia with TC ≥ 5.2 mmol/L, hyperglyceridaemia with TG ≥ 1.7 mmol/L, mixed hyperlipidaemia with TC ≥ 5.2 mmol/L and TG ≥ 1.7 mmol/L, and HDL-C deficiency with HDL-C < 1.0 mmol/L were defined as dyslipidaemia [26]. MVD was defined as at least 2 vessels with ≥ 50% stenosis [27]. TyG index was calculated using ln[(fasting triglyceride (mg/dL) × fasting blood glucose (mg/dL)/2] [28]. The patients were divided into quartiles by TyG index: quartile 1 (TyG index ≤ 8.5711), quartile 2 (8.5711 < TyG index ≤ 8.9731), quartile 3 (8.9731 < TyG index ≤ 9.3975), and quartile 4 (TyG index > 9.3975). BMI, smoking, hypertension, diabetes, dyslipidaemia, and family history were considered as traditional risk factors for CHD.

2.4 Statistical analysis

The age for premature CHD was different between male and female patients, and the analysis also showed that the differences in several variables between the genders were statistically significant (Supplementary Materials, Table S1). Thus, all data analyses were stratified by gender. Descriptive statistics were used, including mean ± standard deviation for continuous variables, median and inter-quartile range (IQR) for non-normally distributed continuous variables, and frequencies for categorical variables. Sociodemographic and clinical characteristics were compared between premature and mature CHD groups by the t-test, analysis of variance or Mann-Whitney U test for continuous variables, and Chi-square test for categorical variables. Binary logistic regression analyses were applied to reveal the characteristics and determinants of premature CHD compared with mature CHD; multinomial logistic regression analyses were applied to identify the correlation between the risk factors and the onset age of MVD and SVD in CHD. The crude models (model 1) used the quartile of the TyG Index as the only independent variable; potential risk factors were then included in model 2. The variables with a significance of < 0.2 in the univariate analyses and which are considered relevant in clinical practice were incorporated in the multivariate regression analyses. Additionally, the multicollinearity test was carried out between the included variables, and those with a variance inflation factor > 10 were excluded. The results of the regression analysis were presented with estimated odds ratios (ORs) and 95% confidence intervals (CIs). A two-sided *P*-value of < 0.05 was considered statistically significant. Statistical analysis was performed using SAS 9.4 (SAS Institute Inc., Cary, NC, USA) and IBM SPSS Statistics, version 23.0 for Windows.

3 Results

3.1 Characteristics of patients

Of the 2846 patients, 1449 were female (50.9%) and 1397 were male (49.1%), with an average age of 51.8 ± 3.7 and 41.1 ± 4.2 years, respectively. There were 1093 cases of premature CHD in women (75.4%), and 1068 cases in men (76.4%). Patient characteristics are listed by gender in Supplementary Materials (Table S1). The female group had fewer patients with MVD (52.6% vs. 61.2%), smoking (19.4% vs. 73.9%), dyslipidaemia (64.4% vs. 84.8%), ≥ 3 traditional risk factors (25.7% vs. 46.1%), and old myocardial infarction (3.9% vs. 11.0%) compared with the male group, while more patients had hypertension (65.3% vs. 55.9%) and diabetes (30.0% vs. 22.1%). It was also apparent that the females showed significantly lower levels of TyG Index (8.89 vs. 9.06), TG (1.56 vs. 1.95), CRP (1.51 vs. 2.46), and Cre (56.0 vs. 77.0), and a higher level of LVEF (62.0 vs. 59.0) than the males.

Determinants of premature CHD and TyG index

Among our enrolled patients, men were younger for both premature and mature CHD compared with women. The average ages of premature CHD in female and male patients were 50.7 ± 3.6 and 39.7 ± 4.0, respectively. In the univariate analysis, the clinical characteristics of male patients in the premature and mature CHD groups were similar except for age and FBG, and there was no statistical difference. Significantly higher FBG was shown in the mature group compared to the premature group (5.54 vs. 5.34). For female patients, the proportion of patients diagnosed with hypertension or diabetes in the mature group was higher than that in the premature CHD group (Hypertension: 71.3% vs. 63.3%; Diabetes: 34.3% vs. 28.5%). Also, there were higher level of Lp(a), CRP and Cre in mature patients than in premature patients (Lp(a): 33.0 vs. 25.3; CRP: 1.97 vs. 1.43; Cre: 57.0 vs. 56.0) (Table 1).

Table 1
Baseline characteristics of premature and mature CHD by gender.

Variables	**Female**			**Male**		
Premature (n = 1093)	Mature (n = 356)	*P* value	Premature (n = 1068)	Mature (n = 329)	*P* value	
Age, years	50.7 ± 3.6	55.3 ± 0.5	**< 0.001**	39.7 ± 4.0	45.3 ± 0.5	**< 0.001**
BMI, kg/m^2	25.9 ± 2.6	25.7 ± 2.6	0.410	25.8 ± 2.7	26.0 ± 2.6	0.432
Obesity, n (%)	841 (76.9)	269 (75.6)	0.593	811 (75.9)	256 (77.8)	0.484
Smoking, n (%)	212 (19.4)	69 (19.4)	0.995	803 (75.2)	230 (69.9)	0.057
Hypertension, n (%)	692 (63.3)	254 (71.3)	**0.006**	584 (54.7)	197 (59.9)	0.097
Diabetes, n (%)	312 (28.5)	122 (34.3)	**0.041**	232 (21.7)	77 (23.4)	0.521
Dyslipidaemia, n (%)	687 (65.5)	206 (61.1)	0.146	862 (85.0)	263 (84.0)	0.672
Family history of CHD, n (%)	220 (20.1)	73 (20.5)	0.878	210 (19.7)	69 (21.0)	0.603
≥ 3 traditional risk factors, n (%)	262 (25.0)	94 (27.9)	0.286	472 (46.5)	140 (44.7)	0.572
Diagnosis, n (%)			0.515			0.746
SA	110 (10.1)	37 (10.4)		97 (9.1)	26 (7.9)	
UA	819 (74.9)	277 (77.8)		538 (50.4)	173 (52.6)	
NSTEMI	45 (4.1)	11 (3.1)		103 (9.6)	35 (10.6)	
STEMI	119 (10.9)	31 (8.7)		330 (30.9)	95 (28.9)	
ACS, n (%)	983 (89.9)	319 (89.6)	0.858	971 (90.9)	303 (92.1)	0.509
OMI, n (%)	41 (3.8)	16 (4.5)	0.531	121 (11.3)	32 (9.7)	0.416
MVD, n (%)	530 (52.5)	176 (52.9)	0.905	617 (60.7)	193 (62.9)	0.500

* MVD: multivessel disease, BMI: body mass index, SA: stable angina, UA: unstable angina, NSTEMI: non-ST-segment elevation myocardial infarction, STEMI: ST-segment elevation myocardial infarction, ACS: acute coronary syndrome, OMI: old myocardial infarction, TyG Index: triglyceride-glucose index, LVEF: left ventricle ejection fraction, Hb: haemoglobin, FBG: fasting blood glucose, TC: total cholesterol, LDL-C: low density lipoprotein cholesterol, HDL-C: high-density lipoprotein cholesterol, TG: triglyceride, Lp(a): lipoprotein (a), CRP: C-reactive protein, Cre: creatinine.

Variables	Female			Male		
TyG Index	8.88 (8.49, 9.30)	8.90 (8.49, 9.31)	0.663	9.05 (8.64, 9.45)	9.11 (8.73, 9.54)	0.060
	8.95 ± 0.69	8.96 ± 0.67		9.12 ± 0.70	9.19 ± 0.71	
LVEF, %	62.0 (58.0, 65.0)	62.0 (58.0, 65.0)	0.341	58.0 (52.0, 62.0)	59.0 (54.0, 63.0)	0.187
	61.1 ± 6.7	60.8 ± 6.8		56.5 ± 8.8	57.2 ± 8.1	
Hb, g/L	129.0 (121.0, 137.0)	129.0 (121.0, 137.0)	0.444	150.0 (142.0, 158.0)	149.0 (141.0, 156.0)	0.121
	128.1 ± 13.2	129.0 ± 11.0		149.8 ± 12.5	148.3 ± 14.2	
FBG, mmol/L	5.40 (4.90, 6.79)	5.47 (4.89, 7.03)	0.666	5.34 (4.74, 6.41)	5.54 (4.86, 7.07)	**0.003**
	6.43 ± 2.64	6.47 ± 2.62		6.12 ± 2.52	6.47 ± 2.52	
TC, mmol/L	4.70 (3.98, 5.39)	4.71 (3.97, 5.57)	0.434	4.63 (3.90, 5.37)	4.52 (3.78, 5.56)	0.815
	4.77 ± 1.13	4.85 ± 1.18		4.72 ± 1.20	4.75 ± 1.30	
LDL-C, mmol/L	3.07 (2.40, 3.73)	3.09 (2.41, 3.83)	0.365	3.05 (2.39, 3.74)	3.01 (2.30, 3.81)	0.709
	3.12 ± 1.00	3.18 ± 1.03		3.13 ± 1.06	3.13 ± 1.14	
HDL-C, mmol/L	1.14 (0.97, 1.35)	1.13 (0.98, 1.33)	0.788	0.90 (0.77, 1.05)	0.93 (0.80, 1.07)	0.105
	1.17 ± 0.29	1.17 ± 0.30		0.93 ± 0.22	0.95 ± 0.23	
TG, mmol/L	1.57 (1.12, 2.18)	1.56 (1.12, 2.24)	0.865	1.93 (1.35, 2.69)	1.96 (1.41, 2.61)	0.691
	1.86 ± 1.31	1.83 ± 1.10		2.37 ± 1.94	2.46 ± 2.38	

* MVD: multivessel disease, BMI: body mass index, SA: stable angina, UA: unstable angina, NSTEMI: non-ST-segment elevation myocardial infarction, STEMI: ST-segment elevation myocardial infarction, ACS: acute coronary syndrome, OMI: old myocardial infarction, TyG Index: triglyceride-glucose index, LVEF: left ventricle ejection fraction, Hb: haemoglobin, FBG: fasting blood glucose, TC: total cholesterol, LDL-C: low density lipoprotein cholesterol, HDL-C: high-density lipoprotein cholesterol, TG: triglyceride, Lp(a): lipoprotein (a), CRP: C-reactive protein, Cre: creatinine.

Variables	Female			Male		
Lp(a), mg/L	25.3 (10.0, 68.4)	33.0 (10.7, 93.1)	**0.043**	18.6 (7.1, 55.0)	19.8 (7.1, 62.2)	0.551
	57.0 ± 75.5	71.1 ± 91.3		43.1 ± 59.6	45.5 ± 59.0	
CRP, mg/L	1.43 (0.61, 3.79)	1.97 (0.74, 4.18)	**0.041**	2.59 (0.97, 6.58)	2.05 (0.83, 5.31)	0.054
	5.05 ± 19.05	5.39 ± 15.04		9.45 ± 24.70	8.36 ± 22.62	
Cre, μmol/L	56.0 (50.0, 62.8)	57.0 (50,0, 65,0)	**0.011**	77.0 (69.0, 85.0)	77.0 (69.0, 87.0)	0.451
	57.0 ± 12.4	58.7 ± 12.3		78.4 ± 16.1	79.3 ± 16.1	

* MVD: multivessel disease, BMI: body mass index, SA: stable angina, UA: unstable angina, NSTEMI: non-ST-segment elevation myocardial infarction, STEMI: ST-segment elevation myocardial infarction, ACS: acute coronary syndrome, OMI: old myocardial infarction, TyG Index: triglyceride-glucose index, LVEF: left ventricle ejection fraction, Hb: haemoglobin, FBG: fasting blood glucose, TC: total cholesterol, LDL-C: low density lipoprotein cholesterol, HDL-C: high-density lipoprotein cholesterol, TG: triglyceride, Lp(a): lipoprotein (a), CRP: C-reactive protein, Cre: creatinine.

Considerable differences were evident in hypertension, dyslipidaemia, Lp(a) and Cre between premature and mature CHD female patients in the multivariate regression models. Female patients with hypertension were more likely to develop mature CHD than those without hypertension (premature CHD: OR = 0.665, 95%CI:0.505–0.877). The Lp(a) (premature CHD: OR = 0.998, 95%CI:0.996–0.999) and Cre (premature CHD: OR = 0.989, 95%CI:0.979–0.998) levels in the female mature CHD group were higher than those in the premature CHD group. Compared with female patients without dyslipidaemia, those with dyslipidaemia (OR = 1.412, 95%CI:1.029–1.936) were significantly more likely to have premature CHD. Among males with mature CHD, there were a greater number of patients in quartile 4 of the TyG index than in quartile 1 (premature CHD: OR = 0.536, 95%CI: 0.338–0.850) (Table 2).

Table 2
Multivariate analysis on the characteristics and determinants of premature CHD compared with mature CHD.

Variables	Model1		Model2	
	OR(95%CI)	*P* value	OR(95%CI)	*P* value
Female				
TyG Index		0.835		0.793
Quartile 1	1		1	
Quartile 2	0.984(0.705, 1.373)	0.786	0.939(0.659,1.337)	0.681
Quartile 3	0.982(0.697, 1.383)	0.806	0.864(0.576,1.296)	0.763
Quartile 4	0.862(0.612, 1.215)	0.361	0.793(0.500,1.258)	0.382
Obesity			1.051(0.781,1.415)	0.742
Smoking			0.968(0.705,1.329)	0.841
Hypertension			0.665(0.505,0.877)	**0.004**
Diabetes			0.843(0.620,1.145)	0.274
Dyslipidaemia			1.412(1.029,1.936)	**0.033**
Family history of CHD			0.947(0.694,1.293)	0.733
Lp(a)			0.998(0.996,0.999)	**0.005**
CRP			1.001(0.994,1.007)	0.877
Cre			0.989(0.979,0.998)	**0.021**
Male				
TyG Index		0.141		0.065
Quartile 1	1		1	
Quartile 2	0.755(0.503,1.132)	0.924	0.708(0.463,1.083)	0.868
Quartile 3	0.709(0.478,1.053)	0.502	0.613(0.392,0.958)	0.282
Quartile 4	0.634(0.430,0.934)	0.079	0.536(0.338,0.850)	**0.033**
Obesity			0.907(0.663,1.241)	0.541
Smoking			1.317(0.987,1.757)	0.061
Hypertension			0.874(0.670,1.140)	0.321
Diabetes			1.028(0.742,1.425)	0.867
Dyslipidaemia			1.491(0.990,2.244)	0.056

* CHD: coronary heart disease, TyG Index: triglyceride-glucose index, Lp(a): lipoprotein (a), CRP: C-reactive protein, Cre: creatinine.

Variables	Model1		Model2	
	OR(95%CI)	*P* value	OR(95%CI)	*P* value
Family history of CHD			0.923(0.665,1.281)	0.632
Lp(a)			0.999(0.997,1.001)	0.418
CRP			1.003(0.997,1.008)	0.398
Cre			0.997(0.989,1.005)	0.485
* CHD: coronary heart disease, TyG Index: triglyceride-glucose index, Lp(a): lipoprotein (a), CRP: C-reactive protein, Cre: creatinine.				

The indicators associated with TyG index are showed in Supplementary Materials (Table S2 and Table S3). The TyG index levels were positively associated with diabetes (female: β = 0.606, $P < 0.001$; male: β = 0.556, $P < 0.001$), dyslipidaemia (female: β = 0.665, $P < 0.001$; male: β = 0.703, $P < 0.001$), and haemoglobin (Hb) (female: β = 0.005, $P < 0.001$; male: β = 0.004, $P = 0.007$), and negatively correlated with Lp(a) (female: β=-0.001, $P < 0.001$; male: β=-0.001, $P < 0.001$) regardless of gender. Female patients with obesity (β = 0.073, $P = 0.028$) had a higher TyG index level. Unlike female patients, male patients with a higher CRP level (β = 0.002, $P = 0.022$) and without OMI (β=-0.119, $P = 0.033$) or a family history of CHD (β=-0.128, $P = 0.003$) generally had a higher TyG index.

3.2 Factors in the onset age of MVD and SVD

The characteristics of different onset ages of MVD and SVD in CHD are presented in Supplementary Materials (Table S4 and Table S5). In the crude models, female patients with the highest TyG index level were more likely to have premature MVD (OR = 2.065, 95%CI:1.426–2.991), or mature MVD (OR = 1.837, 95%CI:1.104–3.056) than those in the lowest TyG index group, instead of premature SVD. Among male patients, the same trend was also observed in mature MVD of CHD (OR = 2.272, 95%CI:1.312–3.937) (Table 3). The significance of the TyG index was also not shown in the multivariate analyses. Patients with premature and mature MVD had a higher proportion of hypertension, OMI, and higher Lp(a) levels than those with premature SVD. In addition, obesity and lower Hb levels in male patients, and smoking, diabetes, and higher CRP levels in female patients were common risk factors for premature and mature MVD, taking premature SVD as a reference. Nevertheless, the differences in characteristics between the patients with premature SVD and mature SVD were not significant (Fig. 1).

Table 3
Crude models on the risk factors of the onset age of MVD and SVD

Variables	Premature MVD of CHD	*P* value	Mature SVD of CHD	*P* value	Mature MVD of CHD	*P* value
Female	n = 530		n = 157		n = 176	
Model 1						
TyG Index						
Quartile 1	1		1		1	
Quartile 2	0.905(0.643,1.275)	0.570	0.956(0.582,1.572)	0.608	0.966(0.596,1.567)	0.889
Quartile 3	1.273(0.901,1.798)	0.171	1.142(0.688,1.895)	0.859	1.156(0.707,1.892)	0.564
Quartile 4	2.065(1.426,2.991)	**< 0.001**	1.670(0.982,2.841)	0.058	1.837(1.104,3.056)	**0.019**
Male	n = 617		n = 114		n = 193	
Model 1						
TyG Index						
Quartile 1	1		1		1	
Quartile 2	1.057(0.720,1.551)	0.778	1.177(0.624,2.222)	0.614	1.492(0.833,2.672)	0.178
Quartile 3	1.104(0.757,1.609)	0.608	1.184(0.633,2.215)	0.597	1.704(0.967,3.003)	0.065
Quartile 4	1.110(0.762,1.619)	0.586	1.107(0.588,2.086)	0.752	2.272(1.312,3.937)	**0.003**

* CHD: coronary heart disease, SVD: single-vessel disease, MVD: multivessel disease, TyG Index: triglyceride-glucose index.

4 Discussion

We compared the clinical characteristics of premature CHD with mature CHD patients and explored the risk factors for the vascular disease severity in premature and mature CHD. Our results showed that female patients in the premature group had a higher rate of dyslipidaemia than those in the mature group, and the TyG index was also not a useful marker for premature CHD. When including the TyG index only, female patients with MVD and male patients with mature MVD were more likely to have higher levels than those with premature SVD. Additionally, significantly higher rates of hypertension, diabetes, OMI, smoking (female), obesity (male), and higher levels of Lp(a) and CRP (female) were observed in patients with MVD, considering traditional risk factors and other clinical indicators.

One important finding was that the differences in most characteristics between premature and mature CHD patients were not statistically significant. Also, among the few statistically significant risk factors, the proportions and levels were higher in mature patients than in premature patients. Only dyslipidaemia was found the opposite trend for female patients. Several previous studies have explored the association between risk factors and onset age of CHD. Our finding is similar to that of Mohammad et al. who found that premature CHD patients had higher rates of hyperlipidaemia and family history of CHD than mature patients [14]. However, this is inconsistent with the results of Zhou et al., who found that the rates of family history of hypertension, diabetes and the levels of BMI, TG, TC and LDL-C in the premature CHD group were higher than those in the mature group [6]. Both studies found more patients with MVD among the mature CHD group than in the premature group, which was not observed in our study [6, 14]. One explanation for the divergence in the results is that the studies enrolled different populations and sample sizes. In addition, our study added stratified analyses by gender and included new risk factors for CHD, such as TyG index, Lp(a), CRP, and Cre for multivariate analysis. All of the above may contribute to the discrepancies seen with the previous study.

The higher rate of hypertension and higher levels of Lp(a), Cre, and TyG index in mature CHD may be explained by the fact that the prevalence of hypertension as well as the level of Lp(a), Cre, and TyG index rose with elevated age [4, 29–31] The onset of CHD in women comes later than in men by 7–10 years because of the role of endogenous estrogen in enhancing vascular relaxation and improving blood lipids and blood coagulation [32, 33]. However, CHD mortality is higher in women than in men because of this late onset [34]. This study observed a higher incidence of dyslipidaemia in premature CHD female patients, which is consistent with the findings of Penida et al [35]. This reveals that general practitioners and clinicians should pay more attention to the early prevention of dyslipidaemia in women at a young age, and patients with dyslipidaemia should regularly participate in cardiovascular disease screening.

IR is defined as a sensitivity reduction in insulin-dependent cells' response to insulin [36]. It induces an imbalance in glucose metabolism and leads to dyslipidaemia and lipid triad, which each contribute to CVD and atherosclerotic plaque generation [37]. The TyG index proposed by Simental-Mendia et al. could be useful as a simple and reliable surrogate to measure IR in clinical practice [28]. Compared with traditional indices for predicting IR, HOMA-IR, the TyG index is easier to obtain and has higher sensitivity [18, 21, 28]. Also, Kim et al., Park et al., and Su et al. identified that an increased TyG index is associated with a raised risk of CHD [18, 20, 38]. In our study, no difference was found in the TyG index between the premature and mature CHD groups in univariate analyses, while the multivariate analyses showed that more male patients with premature CHD had a lower level of TyG index. The TyG index thus did not present superiority in predicting premature CHD. Furthermore, the TyG index was positively associated with diabetes, dyslipidaemia, Hb, obesity, and CRP, which is partly consistent with the results of Jin et al. and Wang et al. [17, 19, 21]. The main explanation for this correlation is that most of these factors are components of metabolic syndrome and IR [19].

In this study, the TyG Index was used as one of the markers of CHD vascular disease severity, which was reflected by whether the patients had SVD or MVD. Although it is not claimed that MVD of CHD is more severe than SVD, a published study identified that patients with MVD are more likely to experience complications with diabetes, renal insufficiency, and a history of myocardial infarction compared with those with SVD [39]. Also, Part et al. and Lopes et al. found that MVD was associated with a worse prognosis than SVD [22, 40]. Therefore, prevention of MVD risk factors and early prediction of the number of diseased vessels could reduce the risk and burden of CHD through appropriate interventions [2]. Our finding that patients with MVD of both premature and mature CHD generally had more patients with the highest TyG index than those with premature SVD is consistent with that of Mao et al. [19].

The correlation between the TyG index and vascular disease severity disappeared after adjusting for traditional CHD risk factors; however, other risk factors such as hypertension, diabetes, obesity, smoking, OMI, and Lp(a) showed a positive association with vascular disease severity. This may be because the TyG index is associated with cardiometabolic risk factors, which have a stronger effect on the vascular disease severity than the TyG index in our models [19]. This suggests that the TyG index should be added as one of the risk factors for CHD or CVD screening, and could be used as an auxiliary indicator for identifying vascular disease severity.

5 Strengths And Limitations

To our knowledge, this study is the first to fully explore the correlation between the risk factors and the onset age of CHD and vascular disease severity, and also to include the TyG index as a potential risk factor. Compared with previously published studies, this study has a larger sample size, and all the patients enrolled were of a younger age, which aptly reflects the real clinical characteristics of patients with premature CHD. However, this study has several limitations. First, the distribution of characteristics between patients in the premature and mature groups was similar due to the young age of the entire study population. Second, this study only collected the baseline data of patients at the time of attendance and did not conduct follow-up; therefore, the correlation between onset age and risk factors of CHD and disease progression and prognosis cannot be explored. Third, OGTT was requested only in patients with diabetic symptoms, which may lead to a missed diagnosis of diabetics. Fourth, the family history of CHD relied on self-reports from patients, which tends to lead to information bias.

6 Conclusions

The similarity of most characteristics in our study between the premature and mature CHD groups suggests that these risk factors cannot be used to determine whether or not patients would experience CHD at an early age. The TyG index was also not a useful indicator for premature CHD. However, we identify that dyslipidaemia should be used as an effective indicator for the prediction and prevention of premature CHD in women in public health strategies. The TyG index may prove to be a simple and accessible auxiliary indicator to be applied in population-based cardiovascular disease screening for the initial identification of vascular disease severity. Finally, an aggressive management and prevention strategy for diabetes, hypertension, obesity, OMI, and Lp(a), along with smoking cessation, are effective measures to reduce MVD of CHD. Further studies could quantify the cut-off value of the TyG index in predicting premature CHD and MVD.

Abbreviations

CVD: Cardiovascular disease; CHD: Coronary heart disease; ACS: Acute coronary syndrome; IR: insulin resistance; TyG index: Triglyceride-glucose index; MVD: Multivessel disease; SVD: Single-vessel disease; SA: Stable angina; UA: Unstable angina; NSTEMI: Non-ST-segment elevation myocardial infarction; STEMI: ST-segment elevation myocardial; infarction; PCI: Percutaneous coronary intervention; CABG: Coronary artery bypass grafting; BMI: Body mass index; LVEF: Left ventricle ejection fraction; Hb: Haemoglobin; FBG: Fasting blood glucose; TC: Total cholesterol; LDL-C: Low-density lipoprotein cholesterol; HDL-C: High-density lipoprotein cholesterol; TG: Triglyceride; Lp(a): Lipoprotein (a); CRP: C-reactive protein; Cre: Creatinine ; OMI: Old myocardial infarction; OGTT: Oral glucose tolerance test; IQR: Inter-quartile range; OR: Odds ratio; CI: Confidence interval.

Declarations

Ethics approval and consent to participate: This study adhered to the Declaration of Helsinki and was approved by the Medical Ethics Committee of Tianjin Chest Hospital (No. 2018XKZ23). All patients enrolled in this study provided verbal informed consent.

Consent for publication: Not applicable.

Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests.

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Authors' contributions: HC and AW contributed to conception and design of the study. AW, JL, and LW collected, cleaned, and coded the study data. HC supervised the research process. AW and LW performed the statistical analysis. AW and JL wrote the first draft of the manuscript. LW and SZ wrote sections of the manuscript. All authors contributed to manuscript revision, read, and approved the final version. All authors agreed to the published the manuscript.

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Figures

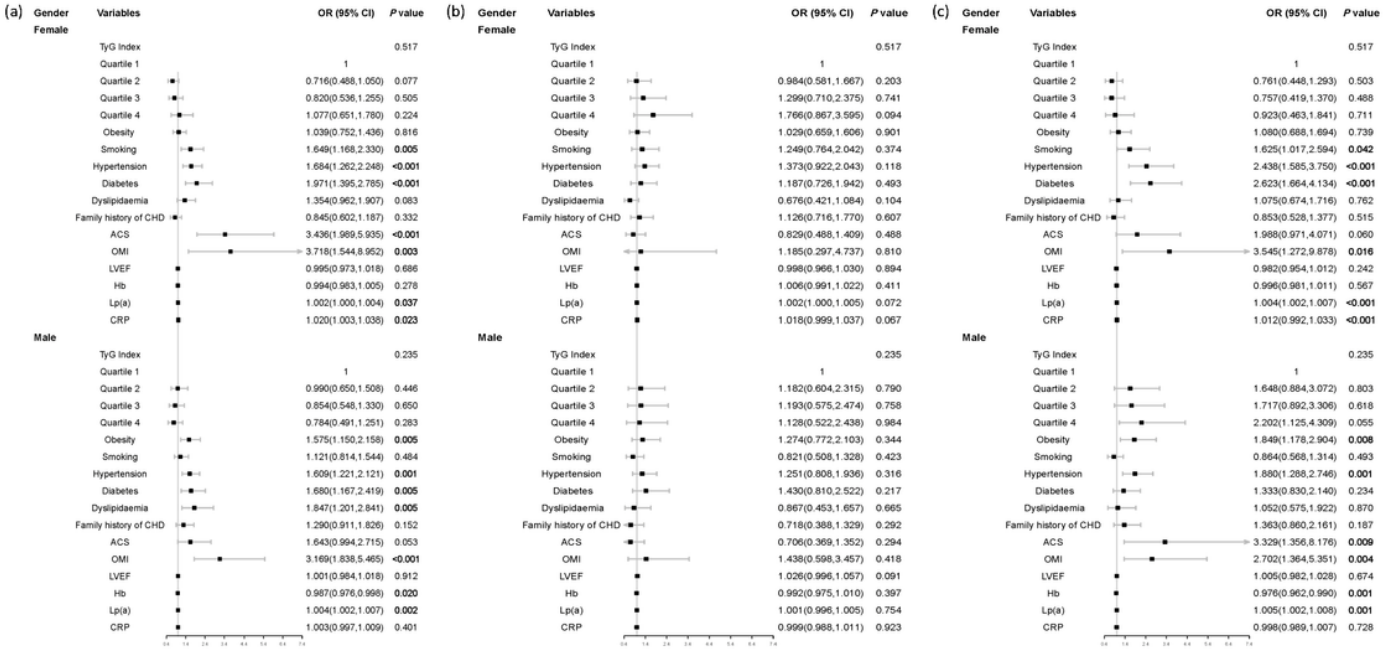

Figure 1

Multivariate analysis on the risk factors of the onset age of MVD and SVD in CHD compared with premature SVD of CHD.

* (a) Premature MVD of CHD; (b) Mature SVD of CHD; (c) Mature MVD of CHD

CHD: coronary heart disease, SVD: single-vessel disease, MVD: multivessel disease, TyG Index: triglyceride-glucose index, ACS: acute coronary syndrome, OMI: old myocardial infarction, LVEF: left ventricle ejection fraction, Hb: haemoglobin, Lp(a): lipoprotein (a), CRP: C-reactive protein.

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