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BMJ Open Correlation of triglyceride–glucose index and dyslipidaemia with premature coronary heart diseases and multivessel disease: a cross-sectional study in Tianjin, China

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ABSTRACT

Objectives Over the past decade, the incidence and global burden of coronary heart disease (CHD) have increased in the young population. We aimed to identify patient characteristics and risk factors for premature CHD, including single-vessel disease (SVD) and multivessel disease (MVD).

Design Retrospective, cross-sectional study.

Setting Demographic and clinical data of patients with CHD were collected from the patient medical records of a tertiary hospital in Tianjin, China, between 2014 and 2017.

Participants A total of 2846 patients were enrolled in the study.

Primary and secondary outcome measures Premature CHD, which is the primary outcome, was defined as men <45 years and women <55 years. MVD, which is the secondary outcome, was defined as at least two vessels with ≥50% stenosis. Logistic regression models were applied to analyse the characteristics and risk factors of premature CHD and MVD.

Results Most of the characteristics between patients with premature and mature CHD were not statistically significant. A significantly higher dyslipidaemia prevalence was found in female patients with premature CHD (OR=1.412, 95% CI: 1.029 to 1.936). In the crude model, instead of premature SVD, premature (OR=2.065, 95% CI: 1.426 to 2.991) or mature (OR=1.837, 95% CI: 1.104 to 3.056) MVD was more common in female patients with the highest triglyceride–glucose (TyG) index quartile than those with the lowest TyG index quartile. In male patients, the same trend was observed for mature MVD (OR=2.272, 95% CI: 1.312 to 3.937). The significance of the TyG index was not revealed in multivariate analyses; however, hypertension, diabetes, obesity, smoking, old myocardial infarction and lipoprotein (a) showed a positive association with MVD.

Conclusions Dyslipidaemia should be considered as an effective factor for the prediction and prevention of premature CHD in women. The TyG index can be a simple auxiliary indicator that can be used in population-based cardiovascular disease screening for the early identification of vascular disease severity.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ The study identified the correlation between the risk factors and the onset age of coronary heart disease (CHD) and vascular disease severity, and included the triglyceride–glucose index as a potential risk factor.
- ⇒ We have a relatively larger sample size, and all the patients enrolled were of a younger age, which reflects the real characteristics of patients with premature CHD.
- ⇒ We only collected the baseline data of patients at the time of attendance and did not explore the correlation of onset age and risk factors of CHD with disease progression and prognosis.

INTRODUCTION

Cardiovascular diseases (CVDs) are the leading cause of death worldwide.¹ Coronary heart disease (CHD), an atherosclerotic disease, is the principal burden of CVDs. It has caused 9.14 million deaths, accounting for 16.2% of all deaths globally in 2019.² In China, it is estimated that over 11 million patients currently suffer from CHD.³ Although more than half of new cases have occurred in people over age 70, researchers have observed that incidence has risen in younger people also.^{4–6} The latest nationwide data showed that 17.9% of new cases occurred in people under age 55, and 12.3% of deaths occurred in people under age 60.⁷

According to several guidelines and studies, premature CHD has been defined as CHD in males aged <55 or <45 and females aged <65 or <55.^{8,9} Compared with mature CHD, patients with premature CHD are usually more likely to present acute coronary syndrome, worse prognosis and a higher burden of disease.^{10,11} Prior studies have identified several risk factors for atherosclerosis and CHD, including male sex, obesity, diabetes,

smoking, dyslipidaemia, hypertension and insulin resistance (IR).^{4 12–14} In addition, Zhou *et al*, Panwar *et al* and Singh *et al* revealed the correlation between premature CHD and familial hypercholesterolaemia, apolipoprotein B and homocysteine, respectively.^{6 15 16} Regarding IR, homeostasis model assessment for IR (HOMA-IR) and triglyceride/high-density lipoprotein cholesterol (TG/HDL-C) ratio have been proposed as predictors.^{17 18} As a novel IR marker, the triglyceride–glucose (TyG) index has been widely used in recent cardiovascular studies.^{19–23} An increased TyG index is associated with a higher risk of CVD, artery calcification and major adverse cardiovascular events.^{20 23} Furthermore, Wang *et al* reported the association between multivessel disease (MVD) of CHD and a high TyG index, and worse outcomes were found in MVD than in single-vessel disease (SVD) of CHD.^{23–25}

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

METHODS

Study design and population

This was a single-centre, retrospective, cross-sectional study. Patients enrolled in the study were all patients who had received their first diagnosis of CHD at Tianjin Chest Hospital between 2014 and 2017. A CHD case was defined as (a) coronary angiography showing any coronary artery stenosis $\geq 50\%$ in diameter or (b) the patient had typical symptoms, changes in cardiac biomarker levels and electrocardiographic evidence.²⁶ The classification of CHD was based on the 10th revision of the International Classification of Diseases (ICD-10). Four types of CHD were considered in this study: 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 codes I21.0, I21.1, I21.2 and I21.3). Patients with a history of CHD, percutaneous coronary intervention or coronary artery bypass grafting were excluded, patients lacked independent behavioural and cognitive abilities as well. In total, 2846 patients were included in the analysis. The age for premature CHD was determined to be <45 years for male patients and <55 years for female patients.⁸

Data collection

Demographic and clinical data were obtained from the database of patient medical records maintained at the Tianjin Chest Hospital by trained clinicians. We extracted the baseline data of patients' first diagnoses. The data collection consisted of information on sociodemographic

characteristics (age, sex); behaviour (smoking); disease history (hypertension, diabetes); family history of CHD; clinical and plasma 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), HDL-C, triglyceride (TG), lipoprotein (a) (Lp(a)), C reactive protein (CRP), creatinine (Cre)); disease characteristics (premature or mature; SVD or MVD); old myocardial infarction (OMI); and types of CHD (SA, UA, NSTEMI, STEMI). Before the plasma biological test, the patients were requested to fast for at least 8 hours.

Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

Definitions

Hypertension and diabetes were determined by the attending physician by combining the patient's self-report, clinical presentation and the results of resting blood pressure measurements or the oral glucose tolerance test (OGTT). BMI was calculated as weight (kg)/height (m²). Individuals with a BMI of ≥ 24.0 kg/m² are considered overweight and obese, and those with a BMI of <24.0 kg/m² are considered underweight and normal.²⁷ 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.²⁸ MVD was defined as the presence of at least two vessels with $\geq 50\%$ stenosis.²⁹ The TyG index was calculated as $\ln((\text{fasting triglyceride (mg/dL)} \times \text{FBG (mg/dL)})/2)$.³⁰ The patients were divided into quartiles according to the TyG index: quartile 1 (TyG index ≤ 8.5711), quartile 2 ($8.5711 < \text{TyG index} \leq 8.9731$), quartile 3 ($8.9731 < \text{TyG index} \leq 9.3975$) and quartile 4 (TyG index > 9.3975). The TG/HDL ratio was calculated as TG (mmol/L)/HDL (mmol/L). BMI, smoking, hypertension, diabetes, dyslipidaemia and family history were considered traditional risk factors for CHD.

Statistical analysis

The age for premature CHD differed between male and female patients, and the differences in several variables between sexes were statistically significant (online supplemental table 1). Therefore, all data analyses were stratified by sex. Missing data due to incomplete patient medical records were not interpolated and included in the analysis. Descriptive statistics were used, including mean \pm SD for continuous variables, median and IQR for non-normally distributed continuous variables and frequencies for categorical variables. Sociodemographic and clinical characteristics were compared between the

premature and mature CHD groups using the t-test, analysis of variance or Mann-Whitney U test for continuous variables and χ^2 test for categorical variables. Binary logistic regression analysis was applied to reveal the characteristics and determinants of premature CHD compared with mature CHD, and multinomial logistic regression analysis was applied to identify the correlation between risk factors and age of onset of MVD and SVD in CHD. Mature CHD and premature SVD were the reference groups in regression analyses, respectively. The crude model (model 1) used the quartile of the TyG index as the only independent variable; potential risk factors were then included in model 2. Variables with a significance of <0.2 in the univariate analyses, which are considered relevant in clinical practice, were incorporated into the multivariate regression analyses. Additionally, the multicollinearity test was performed between the included variables, and those with a variance inflation factor >10 were excluded. The results of the regression analysis are presented as estimated OR and 95% CI. A two-sided p value of <0.05 was considered statistically significant. Statistical analyses were performed using SAS (V.9.4) and IBM SPSS Statistics for Windows (V.23.0).

RESULTS

Characteristics of patients

Of the 2846 patients, 1449 were women (50.9%) and 1397 were men (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 sex in the online supplemental 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 OMI (3.9% vs 11.0%) than the male group. In contrast, the female group had more patients with hypertension (65.3% vs 55.9%) and diabetes (30.0% vs 22.1%) than the male group. The female group showed significantly lower the TyG index (8.89 vs 9.06), TG/HDL ratio (1.38 vs 2.13), 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 male group.

Determinants of premature CHD and TyG index

The average ages of the female and male patients with premature CHD were 50.7 ± 3.6 and 39.7 ± 4.0 , respectively. In the univariate analysis of the whole population, the mature CHD group contained more patients with hypertension (65.8% vs 59.0%) and diabetes (29.1% vs 25.2%) and a higher FBG level (5.50 vs 5.37) than the premature CHD group. There was no statistical difference between the clinical characteristics of male patients in the premature and mature CHD groups, except for FBG levels. The FBG levels were significantly higher in the mature CHD group than in the premature CHD group (5.54 vs 5.34). The female patients diagnosed with hypertension

or diabetes were more in the mature CHD group than that in the premature CHD group (hypertension: 71.3% vs 63.3%, diabetes: 34.3% vs 28.5%). Furthermore, the mature CHD group had higher levels of Lp(a) (33.0 vs 25.3), CRP (1.97 vs 1.43) and Cre (Cre: 57.0 vs 56.0) than the premature CHD group (table 1).

Considerable differences were evident in the TyG index, hypertension, dyslipidaemia, Lp(a) and Cre levels between premature and mature patients with CHD in the multivariate regression models of the whole population. There was a significant higher hypertension prevalence (premature CHD: OR=0.665, 95% CI: 0.505 to 0.877), and higher Lp(a) (premature CHD: OR=0.998, 95% CI: 0.996 to 0.999) and Cre (premature CHD: OR=0.989, 95% CI: 0.979 to 0.998) levels in the female mature CHD group than those in the premature CHD group. The occurrence of premature CHD was significantly higher in female patients with dyslipidaemia (OR=1.412, 95% CI: 1.029 to 1.936) than those without dyslipidaemia. A greater percentage of patients in TyG index quartiles 3 and 4 were found in the male mature CHD group than in the premature group (premature CHD: quartile 3: OR=0.613, 95% CI: 0.392 to 0.958, quartile 4: OR=0.536, 95% CI: 0.338 to 0.850) (table 2).

The indicators associated with the TyG index are shown in the online supplemental tables S2 and S3. The TyG index levels were positively associated with diabetes (female: $\beta=0.606$, $p<0.001$; male: $\beta=0.556$, $p<0.001$), dyslipidaemia (female: $\beta=0.665$, $p<0.001$; male: $\beta=0.703$, $p<0.001$) and Hb (female: $\beta=0.005$, $p<0.001$; male: $\beta=0.004$, $p=0.007$) and negatively correlated with Lp(a) (female: $\beta=-0.001$, $p<0.001$; male: $\beta=-0.001$, $p<0.001$), regardless of sex. Female patients with obesity ($\beta=0.073$, $p=0.028$) had a higher TyG index level. Unlike female patients, the male patients with a higher CRP level ($\beta=0.002$, $p=0.022$) and without OMI ($\beta=-0.119$, $p=0.033$) or a family history of CHD ($\beta=-0.128$, $p=0.003$) had a higher TyG index level.

Risk factors in the onset age of MVD and SVD

The characteristics of the different ages of MVD and SVD onset are presented in the online supplemental tables S4 and S5. When premature SVD was taken as the reference, in the crude model, the occurrence of premature (OR=2.065, 95% CI: 1.426 to 2.991) and mature (OR=1.837, 95% CI: 1.104 to 3.056) MVD was significantly higher in female patients with TyG index quartile 4 than those with TyG index quartile 1. The same trend was found in the crude model of the whole population (premature MVD: OR: 1.567, 95% CI: 1.209 to 2.031, mature MVD: OR: 2.072, 95% CI: 1.446 to 2.969). Among male patients, the patients in TyG quartile 4 had more prevalence of mature MVD than those in quartile 1 (OR=2.272, 95% CI: 1.312 to 3.937) (table 3). The significance of the TyG index was also not shown in the multivariate analyses, regardless of the analysis of the whole population or stratification analysis by sex (table 3 and figure 1). The patients with premature and mature MVD had higher prevalence of hypertension and OMI



Table 1 Baseline characteristics of premature and mature CHD

Variables	Total		Female		Male		P value	
	Premature (n=2161)	Mature (n=685)	Premature (n=1093)	Mature (n=356)	Premature (n=1068)	Mature (n=329)		
	P value	P value	P value	P value	P value	P value		
Age, years	45.3±6.7	50.5±5.0	<0.001	50.7±3.6	55.3±0.5	39.7±4.0	45.3±0.5	<0.001
BMI, kg/m ²	25.9±2.7	25.9±2.6	0.978	25.9±2.6	25.7±2.6	25.8±2.7	26.0±2.6	0.432
Obesity, n (%)	1652 (76.4)	525 (76.6)	0.916	841 (76.9)	269 (75.6)	811 (75.9)	256 (77.8)	0.484
Smoking, n (%)	1015 (47.0)	299 (43.6)	0.129	212 (19.4)	69 (19.4)	803 (75.2)	230 (69.9)	0.057
Hypertension, n (%)	1276 (59.0)	451 (65.8)	0.002	692 (63.3)	254 (71.3)	584 (54.7)	197 (59.9)	0.097
Diabetes, n (%)	544 (25.2)	199 (29.1)	0.044	312 (28.5)	122 (34.3)	232 (21.7)	77 (23.4)	0.521
Dyslipidaemia, n (%)	1549 (75.1)	469 (72.2)	0.135	687 (65.5)	206 (61.1)	862 (85.0)	263 (84.0)	0.672
Missing	98	35	44	19	54	16		
Family history of CHD, n (%)	430 (19.9)	142 (20.7)	0.636	220 (20.1)	73 (20.5)	210 (19.7)	69 (21.0)	0.603
>3 traditional risk factors, n (%)	734 (35.6)	234 (36.0)	0.845	262 (25.0)	94 (27.9)	472 (46.5)	140 (44.7)	0.572
Missing	98	35	44	19	54	16		
Diagnosis, n (%)			0.523					0.746
SA	207 (9.6)	63 (9.2)	110 (10.1)	37 (10.4)	97 (9.1)	26 (7.9)		
UA	1357 (62.8)	450 (65.7)	819 (74.9)	277 (77.8)	538 (50.4)	173 (52.6)		
NSTEMI	148 (6.8)	46 (6.7)	45 (4.1)	11 (3.1)	103 (9.6)	35 (10.6)		
STEMI	449 (20.8)	126 (18.4)	119 (10.9)	31 (8.7)	330 (30.9)	95 (28.9)		
ACS, n (%)	1954 (90.4)	622 (90.8)	0.766	983 (89.9)	319 (89.6)	971 (90.9)	303 (92.1)	0.509
OMI, n (%)	162 (7.5)	48 (7.0)	0.670	41 (3.8)	16 (4.5)	121 (11.3)	32 (9.7)	0.416
MVD, n (%)	1147 (56.6)	369 (57.7)	0.643	530 (52.5)	176 (52.9)	617 (60.7)	193 (62.9)	0.500
Missing	135	45	83	23	52	22		
TyG Index	8.96 (8.56, 9.38)	9.01 (8.61, 9.45)	0.121	8.88 (8.49, 9.30)	8.90 (8.49, 9.31)	9.05 (8.64, 9.45)	9.11 (8.73, 9.54)	0.060
Missing	98	35	44	19	54	16		
TG/HDL ratio	1.73 (1.08, 2.71)	1.77 (1.07, 2.68)	0.884	1.38 (0.89, 2.16)	1.36 (0.89, 2.13)	2.13 (1.40, 3.22)	2.10 (1.41, 3.12)	0.839
Missing	98	35	44	19	54	16		
LVEF, %	60.0 (56.0, 64.0)	60.0 (56.0, 64.0)	0.708	62.0 (58.0, 65.0)	62.0 (58.0, 65.0)	58.0 (52.0, 62.0)	59.0 (54.0, 63.0)	0.187
Missing	90	19	50	13	40	6		
Hb, g/L	139.0 (127.0, 151.0)	138.0 (128.0, 150.0)	0.202	129.0 (121.0, 137.0)	129.0 (121.0, 137.0)	150.0 (142.0, 158.0)	149.0 (141.0, 156.0)	0.121

Continued

Table 1 Continued

Variables	Total			Female			Male		
	Premature (n=2161)	Mature (n=665)	P value	Premature (n=1093)	Mature (n=356)	P value	Premature (n=1068)	Mature (n=329)	P value
Missing	138.8±16.8	138.3±15.9		128.1±13.2	129.0±11.0		149.8±12.5	148.3±14.2	
	28	11		17	5		11	6	
FBG, mmol/L	5.37 (4.83, 6.61)	5.50 (4.88, 7.05)	0.017	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
	6.28±2.58	6.47±2.57		6.43±2.64	6.47±2.62		6.12±2.52	6.47±2.52	
Missing	94	33		43	19		51	14	
TC, mmol/L	4.67 (3.95, 5.39)	4.66 (3.89, 5.56)	0.692	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
	4.75±1.17	4.8±1.24		4.77±1.13	4.85±1.18		4.72±1.20	4.75±1.30	
Missing	98	35		44	19		54	16	
LDL-C, mmol/L	3.06 (2.39, 3.74)	3.06 (2.33, 3.82)	0.702	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±1.03	3.16±1.08		3.12±1.00	3.18±1.03		3.13±1.06	3.13±1.14	
Missing	98	35		44	19		54	16	
HDL-C, mmol/L	1.01 (0.85, 1.21)	1.02 (0.86, 1.22)	0.330	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
	1.05±0.29	1.06±0.29		1.17±0.29	1.17±0.30		0.93±0.22	0.95±0.23	
Missing	98	35		44	19		54	16	
TG, mmol/L	1.72 (1.23, 2.45)	1.75 (1.25, 2.38)	0.729	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
	2.11±1.67	2.14±1.86		1.86±1.31	1.83±1.10		2.37±1.94	2.46±2.38	
Missing	98	35		44	19		54	16	
Lp(a), mg/L	22.0 (8.3, 61.6)	26.0 (8.9, 76.9)	0.061	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
	50.2±68.5	58.8±78.4		57.0±75.5	71.1±91.3		43.1±59.6	45.5±59.0	
Missing	99	35		44	19		55	16	
CRP, mg/L	1.96 (0.75, 5.05)	2.00 (0.78, 4.85)	0.968	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
	7.21±22.11	6.82±19.11		5.05±19.05	5.39±15.04		9.45±24.70	8.36±22.62	
Missing	98	35		44	19		54	16	
Cre, µmol/L	65.0 (55.0, 77.0)	67.0 (56.0, 78.0)	0.094	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
	67.5±17.9	68.7±17.6		57.0±12.4	58.7±12.3		78.4±16.1	79.3±16.1	
Missing	57	20		25	12		32	8	

 Bold values: $P < 0.05$.

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

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

Variables	Total		Female		Male	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Model 1						
TyG index		0.233		0.835		0.141
Quartile 1	1		1		1	
Quartile 2	0.898 (0.696 to 1.158)	0.407	0.984 (0.705 to 1.373)	0.924	0.755 (0.503 to 1.132)	0.174
Quartile 3	0.869 (0.675 to 1.120)	0.279	0.982 (0.697 to 1.383)	0.917	0.709 (0.478 to 1.053)	0.088
Quartile 4	0.770 (0.600 to 0.989)	0.041	0.862 (0.612 to 1.215)	0.396	0.634 (0.430 to 0.934)	0.021
Model 2						
TyG index		0.073		0.793		0.065
Quartile 1	1		1		1	
Quartile 2	0.836 (0.639 to 1.094)	0.192	0.939 (0.659 to 1.337)	0.725	0.708 (0.463 to 1.083)	0.111
Quartile 3	0.735 (0.547 to 0.988)	0.041	0.864 (0.576 to 1.296)	0.480	0.613 (0.392 to 0.958)	0.032
Quartile 4	0.658 (0.478 to 0.905)	0.010	0.793 (0.500 to 1.258)	0.324	0.536 (0.338 to 0.850)	0.008
Obesity	0.978 (0.789 to 1.212)	0.836	1.051 (0.781 to 1.415)	0.742	0.907 (0.663 to 1.241)	0.541
Smoking	1.139 (0.939 to 1.382)	0.185	0.968 (0.705 to 1.329)	0.841	1.317 (0.987 to 1.757)	0.061
Hypertension	0.770 (0.638 to 0.930)	0.007	0.665 (0.505 to 0.877)	0.004	0.874 (0.670 to 1.140)	0.321
Diabetes	0.925 (0.742 to 1.154)	0.491	0.843 (0.620 to 1.145)	0.274	1.028 (0.742 to 1.425)	0.867
Dyslipidaemia	1.451 (1.135 to 1.854)	0.003	1.412 (1.029 to 1.936)	0.033	1.491 (0.990 to 2.244)	0.056
Family history of CHD	0.953 (0.761 to 1.193)	0.676	0.947 (0.694 to 1.293)	0.733	0.923 (0.665 to 1.281)	0.632
Lp(a)	0.998 (0.997 to 1.000)	0.006	0.998 (0.996 to 0.999)	0.005	0.999 (0.997 to 1.001)	0.418
CRP	1.002 (0.997 to 1.006)	0.484	1.001 (0.994 to 1.007)	0.877	1.003 (0.997 to 1.008)	0.398
Cre	0.994 (0.989 to 0.999)	0.021	0.989 (0.979 to 0.998)	0.021	0.997 (0.989 to 1.005)	0.485

Bold values: $P < 0.05$.

CHD, coronary heart disease; Cre, creatinine; CRP, C reactive protein; Lp(a), lipoprotein (a); TyG index, triglyceride–glucose index.

and higher Lp(a) levels than those with premature SVD. In addition, obesity and lower Hb level in male patients and smoking, diabetes and higher CRP level in female patients were common risk factors for premature and mature MVD. Nevertheless, the differences in the characteristics between the patients with premature SVD and those with mature SVD were not significant.

DISCUSSION

We compared the clinical characteristics of the patients and explored the risk factors in premature and mature CHD. Our results showed that female patients in the premature group had higher dyslipidaemia prevalence than those in the mature group, and the TyG index was not a useful marker for premature CHD diagnosis and prevention. When only TyG index was included in the analysis, female patients with MVD and male patients with mature MVD had higher TyG index levels than those with premature SVD. Additionally, a significantly higher prevalence of hypertension, diabetes, OMI, smoking (females), obesity (males) and higher levels of Lp(a) and CRP (females) were observed in patients with MVD, considering traditional risk factors and other clinical indicators.

Notably, the differences in most patient characteristics between premature and mature CHD were not statistically significant. Moreover, among the few statistically significant risk factors, their proportions and levels were higher in mature than in premature CHD. The opposite trend was observed only for dyslipidaemia in female patients. Previous studies have explored the association between risk factors and the age of CHD onset. Our finding is similar to that of Mohammad *et al*, who found that patients with premature CHD had higher hyperlipidaemia prevalence and a family history of CHD than those with mature CHD.¹⁴ However, this is in contradiction to the results of Zhou *et al*, who found that the prevalence of family history of hypertension and diabetes and the levels of BMI, TG, TC and LDL-C were higher in a premature CHD group than those in a mature CHD group.⁶ Both studies found more patients with MVD in the mature CHD group than in the premature CHD group, which was not observed in our study.^{6,14} One explanation for these conflicting results is that the studies enrolled different populations and sample sizes. In addition, our study performed stratified analyses by sex and included new risk factors for CHD, such as TyG index, Lp(a), CRP and Cre for multivariate analysis.

Table 3 Multinomial regression models on the risk factors of the onset age of MVD and SVD in CHD compared with premature SVD of CHD

Variables	Premature MVD of CHD	P value	Mature SVD of CHD	P value	Mature MVD of CHD	P value
Model 1						
Total						
TyG index						
Quartile 1	1		1		1	
Quartile 2	1.016 (0.790 to 1.308)	0.900	1.036 (0.702 to 1.529)	0.860	1.177 (0.815 to 1.699)	0.386
Quartile 3	1.247 (0.969 to 1.604)	0.086	1.146 (0.776 to 1.693)	0.493	1.408 (0.978 to 2.025)	0.066
Quartile 4	1.567 (1.209 to 2.031)	0.001	1.322 (0.886 to 1.972)	0.171	2.072 (1.446 to 2.969)	<0.001
Female						
TyG index						
Quartile 1	1		1		1	
Quartile 2	0.905 (0.643 to 1.275)	0.570	0.956 (0.582 to 1.572)	0.859	0.966 (0.596 to 1.567)	0.889
Quartile 3	1.273 (0.901 to 1.798)	0.171	1.142 (0.688 to 1.895)	0.608	1.156 (0.707 to 1.892)	0.564
Quartile 4	2.065 (1.426 to 2.991)	<0.001	1.670 (0.982 to 2.841)	0.058	1.837 (1.104 to 3.056)	0.019
Male						
TyG index						
Quartile 1	1		1		1	
Quartile 2	1.057 (0.720 to 1.551)	0.778	1.177 (0.624 to 2.222)	0.614	1.492 (0.833 to 2.672)	0.178
Quartile 3	1.104 (0.757 to 1.609)	0.608	1.184 (0.633 to 2.215)	0.597	1.704 (0.967 to 3.003)	0.065
Quartile 4	1.110 (0.762 to 1.619)	0.586	1.107 (0.588 to 2.086)	0.752	2.272 (1.312 to 3.937)	0.003
Model 2						
Total						
TyG index						
Quartile 1	1		1		1	
Quartile 2	0.829 (0.627 to 1.095)	0.187	1.074 (0.710 to 1.623)	0.736	1.044 (0.703 to 1.550)	0.831
Quartile 3	0.823 (0.608 to 1.113)	0.206	1.254 (0.791 to 1.989)	0.336	1.106 (0.722 to 1.697)	0.643
Quartile 4	0.861 (0.616 to 1.204)	0.382	1.376 (0.823 to 2.299)	0.223	1.385 (0.871 to 2.202)	0.169
Obesity	1.274 (1.019 to 1.593)	0.034	1.145 (0.823 to 1.593)	0.422	1.393 (1.910 to 1.016)	0.040
Smoking	1.500 (1.213 to 1.854)	<0.001	0.987 (0.718 to 1.358)	0.938	1.394 (1.861 to 1.044)	0.024
Hypertension	1.628 (1.338 to 1.981)	<0.001	1.308 (0.978 to 1.750)	0.070	2.051 (2.708 to 1.553)	<0.001
Diabetes	1.889 (1.475 to 2.420)	<0.001	1.326 (0.919 to 1.913)	0.132	1.844 (2.544 to 1.337)	<0.001
Dyslipidaemia	1.616 (1.244 to 2.099)	<0.001	0.777 (0.534 to 1.132)	0.189	1.115 (1.597 to 0.779)	0.552
Family history of CHD	1.024 (0.807 to 1.300)	0.845	0.939 (0.656 to 1.345)	0.731	1.036 (1.436 to 0.748)	0.830
ACS	2.331 (1.632 to 3.328)	<0.001	0.778 (0.518 to 1.170)	0.228	2.610 (4.552 to 1.497)	0.001
OMI	3.556 (2.247 to 5.627)	<0.001	1.393 (0.670 to 2.899)	0.375	3.019 (5.292 to 1.723)	<0.001
LVEF	0.995 (0.982 to 1.009)	0.492	1.013 (0.992 to 1.035)	0.223	0.991 (0.973 to 1.008)	0.294
Hb	0.996 (0.990 to 1.003)	0.273	1.001 (0.991 to 1.010)	0.862	0.995 (0.987 to 1.004)	0.266
Lp(a)	1.003 (1.001 to 1.004)	0.001	1.002 (1.000 to 1.004)	0.100	1.004 (1.003 to 1.006)	<0.001
CRP	1.007 (1.001 to 1.012)	0.016	1.004 (0.995 to 1.012)	0.390	1.002 (0.995 to 1.010)	0.553

 Bold values: $P < 0.05$.

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

Increasing age is plausibly responsible for the higher prevalence of hypertension and higher Lp(a), Cre and TyG index levels in mature CHD than those in premature

group.^{431–33} Because of the role of endogenous oestrogen in enhancing vascular relaxation and improving blood lipids and blood coagulation, the onset of CHD in women

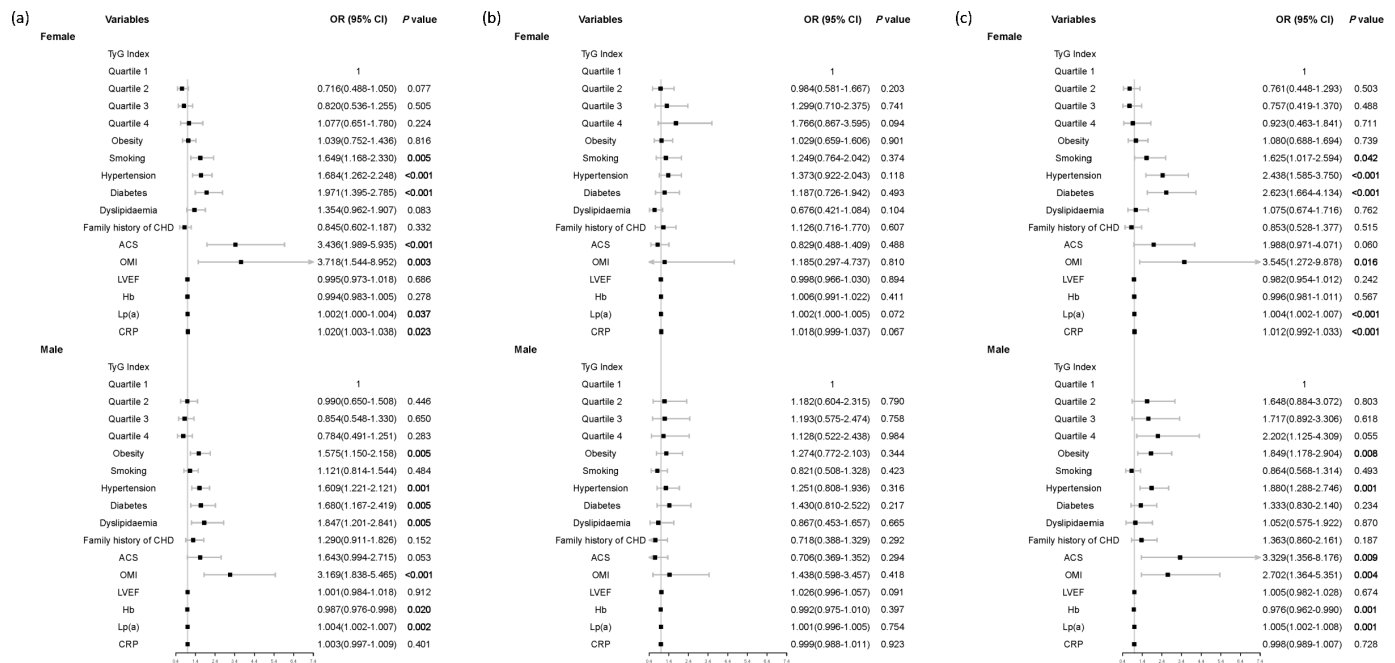


Figure 1 Multivariate analysis on the risk factors of the onset age of MVD and SVD in CHD compared with premature SVD of CHD. (A) Premature MVD of CHD; (B) Mature SVD of CHD; (C) Mature MVD of CHD. ACS, acute coronary syndrome; CHD, coronary heart disease; CRP, C reactive protein; Hb, haemoglobin; Lp(a), lipoprotein (a); LVEF, left ventricle ejection fraction; MVD, multivessel disease; OMI, old myocardial infarction; SVD, single-vessel disease; TyG Index, triglyceride–glucose index.

is 7–10 years later than in men.^{34 35} However, because of this late onset, CHD mortality is higher in women than in men.³⁶ We found a higher incidence of dyslipidaemia in female patients with premature CHD, consistent with the findings of Pineda *et al.*³⁷ 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 be regularly screened for CVDs.

IR is defined as the reduction in insulin sensitivity in insulin-dependent cells.³⁸ It induces an imbalance in glucose metabolism and leads to dyslipidaemia and lipid triad, each of which contributes to development of CVD and atherosclerotic plaque.³⁹ The TyG index proposed by Simental-Mendia *et al* can be useful as a simple and reliable surrogate to measure IR in clinical practice.³⁰ Compared with the traditional index for predicting IR (ie, HOMA-IR), the TyG index is easier to obtain and has higher sensitivity.^{20 23 30} Furthermore, an increased TyG index is associated with an increased risk of CHD.^{20 22 40} 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 TyG index level. Therefore, the TyG index was not superior in predicting premature CHD. Furthermore, the TyG index was positively associated with diabetes, dyslipidaemia, obesity and increased Hb and CRP levels, which is partly consistent with the results of Jin *et al* and Wang *et al.*^{19 21 23} The main explanation for this correlation is that most of these factors are components of metabolic syndrome and IR.²¹

In this study, the TyG index was used as a marker of CHD severity, represented by whether the patients had SVD or MVD. Although MVD is not claimed to be more severe than SVD, a published study identified that patients with MVD were more likely to experience complications such as diabetes, renal insufficiency and a history of myocardial infarction than those with SVD.⁴¹ Park *et al* and Lopes *et al* found that MVD was associated with a worse prognosis than SVD.^{24 42} Therefore, prevention of MVD risk factors and early prediction of the number of diseased vessels can reduce the risk and burden of CHD through appropriate interventions.² Our finding that the highest TyG index was more common in patients with premature and mature MVD than those with premature SVD is consistent with that of Mao *et al.*²¹ 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) were positively associated with vascular disease severity. This may be because the TyG index is associated with cardiometabolic risk factors, which have a stronger effect on vascular disease severity than the TyG index in our models.²¹ This suggests that the TyG index should be added as a risk factor for CHD or CVD screening and can be used as an auxiliary indicator for identifying vascular disease severity.

To our knowledge, this is the first study to fully explore the correlation between risk factors, the onset age of CHD, and vascular disease severity and to include the TyG index as a potential risk factor. Compared with previously published studies, this study had a larger sample size, and all the enrolled patients were younger, reflecting the real

clinical characteristics of patients with premature CHD. Considering that Tianjin is a major city in China, the study results can be generalised to other cities with a similar socioeconomic level. However, this study had several limitations. First, due to the young age of the entire study population, the distribution of characteristics between patients in the premature and mature CHD groups was similar, and the number of patients in the mature group was small. This might have led to a selection bias. Second, this study only collected the baseline data of patients at the time of attendance and did not conduct follow-up; therefore, the correlation of age of disease onset and risk factors of CHD with disease progression and prognosis cannot be explored. In addition, because there are no data on physical activity, which is associated with CHD, in the patient medical records, we did not include it as a variable in the study. Third, the OGTT was performed only in patients with diabetic symptoms, which may lead to missed diagnosis in asymptomatic patients. Fourth, the family history of CHD relied on self-reports from patients, which may lead to information bias.

CONCLUSIONS

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

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Contributors HC and AW conceived and designed the study. HC supervised the research process. AW, JL and LW collected, cleaned and coded the study data. AW, LW and SZ performed the data analysis. AW, JL and SZ drafted and revised the manuscript. HC is responsible for the overall content as guarantor, who accepts full responsibility for the finished work and the conduct of the study, had access to the data, and controlled the decision to publish. All authors contributed to and approved the final version, and agreed to publish the manuscript.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by medical ethics committee of Tianjin Chest Hospital, ID: 2018XKZ23. Participants gave informed consent to participate in the study before taking part.

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Data availability statement Data are available upon reasonable request. The data presented in this study are available on request from the corresponding author.

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Supplementary Files

1. Characteristics of CHD patients by sex

Table S1 Baseline characteristics of CHD patients by sex (N=2846).

Variables	Female (n=1449)	Male (n=1397)	P value
Premature CHD, n (%)	1093 (75.4)	1068 (76.4)	0.525
MVD, n (%)	706 (52.6)	810 (61.2)	<0.001
Age, years	51.8±3.7	41.1±4.2	<0.001
BMI, kg/m ²	25.8±2.6	25.9±2.7	0.718
Obesity, n (%)	1110 (76.6)	1067 (76.4)	0.887
Smoking, n (%)	281 (19.4)	1033 (73.9)	<0.001
Hypertension, n (%)	946 (65.3)	781 (55.9)	<0.001
Diabetes, n (%)	434 (30.0)	309 (22.1)	<0.001
Dyslipidaemia, n (%)	893 (64.4)	1125 (84.8)	<0.001
Family history of CHD, n (%)	293 (20.2)	279 (20.0)	0.868
≥3 traditional risk factors, n (%)	356 (25.7)	612 (46.1)	<0.001
Diagnosis, n (%)			<0.001
SA	147 (10.1)	123 (8.8)	
UA	1096 (75.6)	711 (50.9)	
NSTEMI	56 (3.9)	138 (9.9)	
STEMI	150 (10.4)	425 (30.4)	
ACS, n (%)	1302 (89.9)	1274 (91.2)	0.223
OMI, n (%)	57 (3.9)	153 (11.0)	<0.001
TyG Index	8.89 (8.49, 9.31)	9.06 (8.67, 9.48)	<0.001
	8.95±0.68	9.14±0.70	
TG/HDL Ratio	1.38 (0.89, 2.15)	2.13 (1.40, 3.19)	<0.001
	1.82±1.77	2.88±3.19	
LVEF, %	62.0 (58.0, 65.0)	59.0 (53.0, 62.0)	<0.001
	61.0±6.7	56.6±8.7	
Hb, g/L	129.0 (121.0, 137.0)	150.0 (142.0, 157.0)	<0.001
	128.3±12.7	149.4±12.9	
FBG, mmol/L	5.42 (4.90, 6.89)	5.39 (4.78, 6.56)	0.005
	6.44±2.63	6.20±2.52	
TC, mmol/L	4.70 (3.97, 5.43)	4.60 (3.86, 5.43)	0.032
	4.79±1.14	4.73±1.22	
LDL-C, mmol/L	3.08 (2.40, 3.75)	3.02 (2.36, 3.76)	0.266
	3.13±1.00	3.13±1.08	
HDL-C, mmol/L	1.13 (0.97, 1.34)	0.91 (0.78, 1.05)	<0.001
	1.17±0.29	0.93±0.23	
TG, mmol/L	1.56 (1.12, 2.19)	1.95 (1.37, 2.68)	<0.001
	1.85±1.26	2.39±2.05	
Lp(a), mg/L	27.1 (10.2, 75.4)	18.9 (7.1, 55.3)	<0.001
	60.4±79.8	43.7±59.4	
CRP, mg/L	1.51 (0.64, 3.89)	2.46 (0.93, 6.39)	<0.001
	5.13±18.15	9.19±24.22	
Cre, μmol/L	56.0 (50.0, 63.0)	77.0 (69.0, 85.0)	<0.001
	57.4±12.3	78.6±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, 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.

2. Indicators associated with TyG index

Linear regression analyses were applied to determine the indicators associated with TyG index.

Table S2 Univariate and multivariate liner regression analysis for TyG index in women.

Variables	Univariate			Multivariate		
	β	Standard β	P value	β	Standard β	P value
≥ 55 years old	0.007	0.003	0.906	-0.001	-0.001	0.978
Obesity	0.126	0.079	0.003	0.073	0.046	0.028
Smoking	0.074	0.043	0.111	0.030	0.018	0.389
Hypertension	0.148	0.104	<0.001	0.016	0.011	0.597
Diabetes	0.681	0.460	<0.001	0.606	0.409	<0.001
Dyslipidemia	0.725	0.511	<0.001	0.665	0.472	<0.001
Family history of CHD	-0.023	-0.014	0.610	-0.036	-0.021	0.307
ACS	0.133	0.059	0.027	-0.009	-0.004	0.849
OMI	0.051	0.015	0.582	-0.004	-0.001	0.957
LVEF	-0.010	-0.104	<0.001	-0.003	-0.032	0.150
Hb	0.006	0.121	<0.001	0.005	0.100	<0.001
Lp(a)	-0.001	-0.037	0.166	-0.001	-0.081	<0.001
CRP	0.001	0.037	0.172	0.001	0.027	0.217
Cre	-0.001	-0.025	0.358	<0.001	-0.001	0.947

* ACS: acute coronary syndrome, OMI: old myocardial infarction, LVEF: left ventricle ejection fraction, Hb: haemoglobin, Lp(a): lipoprotein (a), CRP: C-reactive protein, Cre: creatinine.

Table S3 Univariate and multivariate liner regression analysis for TyG index in men.

Variables	Univariate			Multivariate		
	β	Standard β	P value	β	Standard β	P value
≥ 45 years old	-0.029	-0.013	0.649	-0.014	-0.006	0.801
Obesity	0.163	0.098	<0.001	0.070	0.043	0.077
Smoking	0.077	0.048	0.080	0.070	0.043	0.073
Hypertension	0.066	0.047	0.089	0.026	0.019	0.442
Diabetes	0.621	0.369	<0.001	0.556	0.330	<0.001
Dyslipidemia	0.772	0.396	<0.001	0.703	0.363	<0.001
Family history of CHD	-0.089	-0.050	0.067	-0.128	-0.072	0.003
ACS	0.126	0.050	0.067	0.038	0.015	0.528
OMI	-0.115	-0.051	0.063	-0.119	-0.052	0.033
LVEF	-0.004	-0.045	0.109	-0.001	-0.016	0.507
Hb	0.003	0.062	0.024	0.004	0.066	0.007
Lp(a)	-0.001	-0.114	<0.001	-0.001	-0.091	<0.001
CRP	0.001	0.041	0.133	0.002	0.057	0.022
Cre	-0.002	-0.037	0.189	-0.001	-0.021	0.385

* ACS: acute coronary syndrome, OMI: old myocardial infarction, LVEF: left ventricle ejection fraction, Hb: haemoglobin, Lp(a): lipoprotein (a), CRP: C-reactive protein, Cre: creatinine.

2. Characteristics of different onset age of MVD and SVD in CHD

Table S4 Baseline characteristics of different onset age of MVD and SVD in CHD in women.

Variables	Premature SVD of CHD (n=480)	Premature MVD of CHD (n=530)	Mature SVD of CHD (n=157)	Mature MVD of CHD (n=176)	P value
Age, years	50.5±3.4	50.9±3.7	55.3±0.4	55.3±0.5	<0.001
BMI, kg/m ²	25.9±2.7	25.9±2.6	26.0±2.7	25.6±2.4	0.556
Obesity, n (%)	362 (75.4)	411 (77.5)	120 (76.4)	137 (77.8)	0.852
Smoking, n (%)	76 (15.8)	124 (23.4)	30 (19.1)	39 (22.2)	0.022
Hypertension, n (%)	274 (57.1)	380 (71.7)	104 (66.2)	134 (76.1)	<0.001
Diabetes, n (%)	94 (19.6)	201 (37.9)	44 (28.0)	76 (43.2)	<0.001
Dyslipidaemia, n (%)	287 (61.6)	355 (70.6)	88 (58.7)	106 (64.2)	0.008
Family history of CHD, n (%)	103 (21.5)	100 (18.9)	36 (22.9)	32 (18.2)	0.527
≥3 traditional risk factors, n (%)	83 (17.8)	168 (33.4)	38 (25.3)	55 (33.3)	<0.001
ACS, n (%)	409 (85.2)	507 (95.7)	133 (84.7)	165 (93.8)	<0.001
OMI, n (%)	8 (1.7)	29 (5.5)	4 (2.5)	12 (6.8)	0.002
TyG Index	8.81 (8.41,9.18)	8.99 (8.55,9.47)	8.93 (8.49,9.32)	8.96 (8.51,9.35)	<0.001
	8.86±0.63	9.06±0.72	8.98±0.64	8.97±0.69	
TG/HDL Ratio	1.28 (0.83, 1.94)	1.54 (0.95, 2.33)	1.35 (0.92, 2.18)	1.46 (0.86, 2.12)	<0.001
	1.73±2.11	1.96±1.66	1.73±1.28	1.89±1.67	
LVEF, %	63.0 (60.0,65.0)	61.5 (58.0,65.0)	62.0 (60.0,65.0)	62.0 (57.0,65.0)	0.028
	61.6±6.0	60.5±6.8	61.3±6.2	60.2±7.2	
Hb, g/L	129.0 (122.0,137.0)	128.5 (120.0,136.8)	130.0 (123.0,137.0)	128.0 (120.0,137.0)	0.337
	128.5±13.2	127.9±13.5	130.1±10.9	127.9±11.4	
FBG, mmol/L	5.30 (4.85,6.35)	5.65 (5.01,7.97)	5.45 (4.91,7.10)	5.56 (4.90,7.21)	<0.001

	6.06±2.23	6.92±3.01	6.53±2.72	6.57±2.63	
TC, mmol/L	4.67 (4.00,5.33)	4.78 (3.98,5.53)	4.72 (4.00,5.50)	4.68 (3.89,5.64)	0.487
	4.71±1.00	4.85±1.21	4.84±1.12	4.85±1.26	
LDL-C, mmol/L	3.07 (2.35,3.61)	3.14 (2.47,3.89)	3.16 (2.44,3.78)	3.04 (2.31,3.92)	0.229
	3.04±0.88	3.22±1.06	3.16±0.98	3.19±1.11	
HDL-C, mmol/L	1.18 (0.99,1.41)	1.08 (0.94,1.27)	1.14 (0.99,1.35)	1.11 (0.92,1.33)	<0.001
	1.21±0.31	1.12±0.27	1.19±0.30	1.14±0.29	
TG, mmol/L	1.52 (1.08,2.07)	1.64 (1.14,2.31)	1.56 (1.15,2.31)	1.62 (1.08,2.24)	0.059
	1.77±1.32	1.96±1.33	1.82±1.00	1.86±1.20	
Lp(a), mg/L	26.6 (9.8,66.9)	25.3 (10.5,76.2)	29.5 (9.6,91.7)	38.0 (12.3,117.8)	0.041
	52.0±65.1	63.7±85.7	63.2±80.8	82.8±102.7	
CRP, mg/L	1.45 (0.57,3.62)	1.58 (0.70,4.27)	1.44 (0.73,4.25)	2.10 (0.74,4.25)	0.049
	3.15±6.53	7.12±26.37	5.29±13.70	5.00±14.26	
Cre, µmol/L	56.0 (50.0,62.0)	56.0 (50.0,63.0)	58.0 (49.5,64.0)	56.0 (50.0,66.0)	0.134
	56.7±11.2	57.3±13.7	59.1±12.8	58.3±12.0	

* SVD: single-vessel disease, MVD: multivessel disease, BMI: body mass index, ACS: acute coronary syndrome, OMI: old myocardial infarction, 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.

Table S5 Baseline characteristics of different onset age of MVD and SVD in CHD in men.

Variables	Premature SVD of CHD (n=399)	Premature MVD of CHD (n=617)	Mature SVD of CHD (n=114)	Mature MVD of CHD (n=193)	P value
Age, years	39.5±4.4	39.9±3.7	45.3±0.5	45.3±0.5	<0.001
BMI, kg/m ²	25.5±2.8	26.0±2.7	25.8±2.6	26.1±2.5	0.021

Obesity, n (%)	283 (70.9)	486 (78.8)	85 (74.6)	157 (81.3)	0.010
Smoking, n (%)	299 (74.9)	470 (76.2)	78 (68.4)	139 (72.0)	0.284
Hypertension, n (%)	194 (48.6)	364 (59.0)	64 (56.1)	124 (64.2)	0.001
Diabetes, n (%)	65 (16.3)	159 (25.8)	25 (21.9)	50 (25.9)	0.003
Dyslipidaemia	308 (81.5)	514 (87.9)	88 (80.0)	161 (87.0)	0.017
Family history of CHD, n (%)	73 (18.3)	133 (21.6)	17 (14.9)	44 (22.8)	0.222
≥3 traditional risk factors, n (%)	144 (38.1)	313 (53.5)	41 (37.3)	95 (51.4)	<0.001
ACS, n (%)	356 (89.2)	572 (92.7)	98 (86.0)	187 (96.9)	0.001
OMI, n (%)	21 (5.3)	94 (15.2)	8 (7.0)	23 (11.9)	<0.001
TyG Index	9.05 (8.61,9.43)	9.06 (8.67,9.47)	9.02 (8.69,9.48)	9.17 (8.78,9.62)	0.033
	9.09±0.71	9.14±0.69	9.10±0.69	9.27±0.72	
TG/HDL Ratio	2.05 (1.28, 3.10)	2.24 (1.44, 3.28)	1.94 (1.18, 2.74)	2.34 (1.52, 3.28)	0.016
	2.74±3.35	2.96±3.00	2.75±3.27	3.14±3.68	
LVEF, %	59.0 (53.0,62.0)	58.0 (51.0,62.0)	60.0 (55.0,64.0)	58.0 (52.0,62.0)	0.050
	56.9±8.5	56.3±8.5	58.3±8.1	56.5±8.1	
Hb, g/L	151.0 (144.0,158.0)	149.0 (141.0,157.0)	151.0 (142.0,157.0)	148.0 (139.0,156.0)	0.009
	150.9±11.7	148.9±13.0	150.5±12.6	147.0±15.2	
FBG, mmol/L	5.25 (4.72,6.18)	5.44 (4.78,6.48)	5.53 (4.90,6.86)	5.58 (4.85,7.46)	0.009
	5.99±2.43	6.23±2.61	6.26±2.28	6.61±2.71	
TC, mmol/L	4.63 (3.95,5.27)	4.70 (3.90,5.53)	4.50 (3.72,5.46)	4.53 (3.82,5.61)	0.573
	4.68±1.07	4.79±1.29	4.59±1.15	4.87±1.40	
LDL-C, mmol/L	3.02 (2.45,3.67)	3.09 (2.37,3.88)	2.90 (2.19,3.71)	3.01 (2.35,3.89)	0.170
	3.06±0.92	3.21±1.14	2.95±1.01	3.25±1.22	
HDL-C, mmol/L	0.94 (0.80,1.11)	0.88 (0.75,1.02)	0.97 (0.82,1.12)	0.90 (0.77,1.04)	<0.001
	0.97±0.24	0.90±0.20	1.00±0.25	0.91±0.21	
TG, mmol/L	1.95 (1.33,2.77)	1.92 (1.36,2.67)	1.79 (1.33,2.40)	2.00 (1.51,2.86)	0.207

	2.35±2.00	2.39±1.95	2.33±2.08	2.59±2.63	
Lp(a), mg/L	17.1 (6.5,46.2)	20.9 (7.5,63.4)	17.4 (7.3,44.1)	22.1 (7.1,75.7)	0.011
	35.6±51.6	49.1±64.9	35.2±46.3	51.0±62.1	
CRP, mg/L	2.65 (0.98,6.57)	2.72 (1.03,7.04)	1.68 (0.64,4.68)	2.11 (0.90,6.39)	0.032
	8.51±20.16	10.44±27.76	7.28±23.38	8.58±20.47	
Cre, µmol/L	76.0 (70.0,84.0)	77.0 (68.0,86.0)	74.0 (68.0,85.0)	78.0 (70.0,87.5)	0.203
	78.1±15.0	78.8±17.1	77.1±13.9	80.6±16.9	

* SVD: single-vessel disease, MVD: multivessel disease, BMI: body mass index, ACS: acute coronary syndrome, OMI: old myocardial infarction, 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.