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# Clinical Characteristics and Prognosis of Young Patients with Coronary Heart Disease

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**Background:** The objective of this study was to investigate the clinical characteristics and prognosis of coronary heart disease (CHD) in young patients.





**Material/Methods:** We included 972 CHD patients ( $\leq 50$  years old) with coronary artery stenting who were prospectively enrolled and followed for 1 year. Clinical characteristics, risk factors, and predictors of outcomes were evaluated.

**Results:** The prevalence of current smoker, hypertension, diabetes mellitus, dyslipidemia and positive family history of CHD were 18.9%, 34.3%, 14.5%, 4.4%, and 44.2%, respectively. Most of the patients underwent coronary stenting due to stable angina (48.8%) and unstable angina (UA; 48.1%). After 1-year follow-up, 64 patients (6.6%) experienced clinical outcomes and the most common event was UA ( $n=56$ ). Compared to patients without clinical outcomes, those with outcomes were more likely to be male, have higher systolic blood pressure, more likely to have hypertension and diabetes mellitus, and more likely to be presented as unstable angina. Multivariate regression analysis showed only age (hazard ratio [HR]: 1.12 and 95% confidence interval [CI]: 1.07–1.26), smoking (HR: 1.15 and 95% CI: 1.06–1.23), presence of hypertension (HR: 1.19 and 95% CI: 1.13–1.31), and diabetes mellitus (HR: 1.16 and 95% CI: 1.09–1.28), more vessels with stenosis (HR: 1.27 and 95% CI: 1.20–1.48) and presented with acute coronary syndrome (HR: 1.35 and 95% CI: 1.21–1.55) were independently associated with clinical outcomes.

**Conclusions:** Most of the young ( $\leq 50$  years of age) CHD patients had poor management of risk factors and better controlling these risk factors would be helpful for the primary and secondary prevention of premature CHD in Guangdong province.

**MeSH Keywords:** **Coronary Disease • Outcome Assessment (Health Care) • Risk Factors**

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## Background

Coronary heart disease (CHD) is a leading cause of morbidity and mortality in developed and developing countries [1–4]. Hypertension, dyslipidemia, diabetes mellitus and smoking are major risk factors for CHD. Prior randomized clinical trials and prospective cohort studies have consistently demonstrated that controlling these risk factors is beneficial for primary and secondary prevention of CHD in the overall populations [5–7].

A recent report of the China Patient-centered Evaluation Assessment of Cardiac Events (China PEACE) study found that the incidence of ST-segment elevation myocardial infarction (STEMI) in China from 2001 to 2011 was gradually increased [8]. A report from the Chinese Ministry of Health epidemiological survey additionally showed that the prevalence and incidence of CHD among Chinese young populations has also increased [9], which was postulated to be attributed to the pandemic of cigarette smoking, hypertension, diabetes mellitus, and dyslipidemia. These data together support the notion that controlling risk factors would be beneficial to reduce health and economic burdens of CHD in China [10].

A recent retrospective study showed that the overall incidence of cardiac death and major adverse cardiovascular event of the young Chinese CHD patients had increased compared to the past decades [11]. However, this study was compromised by its retrospective design. The aim of current study was to evaluate the clinical characteristics, risk factors associated with CHD severity, and predictors of cardiovascular outcomes in young CHD patients after coronary artery stenting. From a clinical standpoint, this information will not only help better understand the clinical features of premature CHD, but also will provide information about potential therapeutic targets that physicians should focus on in the future.

## Material and Methods

### Studied participants enrollment

This study was approved by the Ethics Committee of Clinical Research of The Third People's Hospital of Huizhou and informed consent was obtained before participants' enrolment. Inclusion criteria were as follows:  $\leq 50$  years old and had angiographical-diagnosis of CHD and had underwent coronary artery stenting for the first time. Exclusion criteria were as follows: had coronary artery stenting before this hospitalization, or had severe complication during percutaneous coronary intervention (PCI) including coronary artery perforation and dissection and pericardial effusion with hemodynamic instability, or had complications during hospitalization such as rupture of ventricular septum or papillary muscle, ventricular arrhythmias

required resuscitation and defibrillation, or severe congestive heart failure required invasive hemodynamic support such as intra-aortic balloon pump.

### Baseline data collection

Baseline data were collected during the indexed hospitalization using a structured questionnaire administered by independent investigators. The questionnaire comprised information of demographics (age and gender), smoking status, prior medical history, risk factors, and comorbidities. Fasting venous blood was used for lipid profile, fasting plasma glucose, and liver and renal function panel assessments. Clinical presentations in terms of stable angina, unstable angina, non-STEMI (NSTEMI) or STEMI were diagnosed based on clinical manifestation, electrocardiography changes, and cardiac biomarkers by 2 independent cardiologists. The number of coronary arteries with stenosis ( $\geq 50\%$  stenosis of coronary artery diameter) were recorded during angiography.

### Clinical outcomes definition and assessment

In this study, clinical outcomes after stent placement were defined as all-cause mortality, cardiovascular death, nonfatal myocardial infarction, nonfatal ischemic stroke, UA, and coronary revascularization. Patient follow-up was at the twelfth month after discharge via telephone call and/or at outpatient department. The clinical outcomes were adjudicated by 2 independent cardiologists who did not participate in current study.

### Statistical analysis

Continuous variables were expressed as mean $\pm$ standard deviation (SD) or median (interquartile ranges) and categorical variables were expressed as number and frequency of cases. Between-group differences were evaluated by the independent Student *t*-test or the Kruskal-Wallis test for continuous variables as appropriate; or were compared by the chi-square analysis or Fisher's exact tests for the categorical variables as appropriate. Cox proportional hazards regression analysis was used to evaluate the potential risk factors for prediction of clinical outcomes prediction. The hazard ratio (HR) and associated 95% confidence interval (CI) represents the risk associated with each 1-SD change of continuous variables or the presence of categorical variables for clinical outcomes. Statistical analysis was conducted in SPSS 23.0 (IBM, USA). All *P* values were 2-sided, and statistical significance was defined as *P* $<0.05$ .

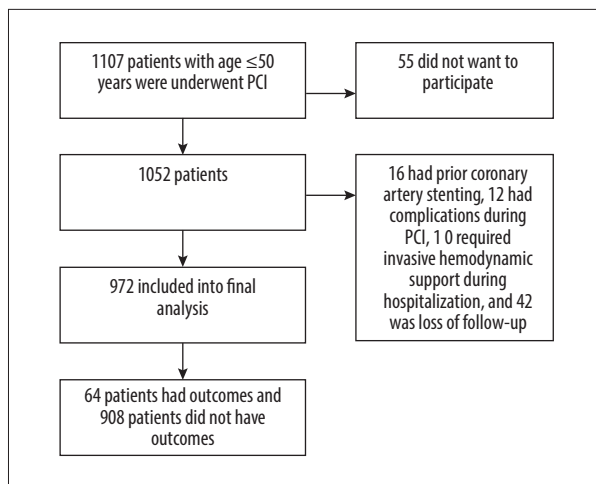


Figure 1. Research schematic.

## Results

### Baseline characteristics

A total of 1107 patients with age  $\leq 50$  years who received PCI in our hospital were enrolled. Among these patients, 55 patients did not want to participate in the study, 16 patients had prior coronary artery stenting, 12 patients had complications during PCI, 10 patients required invasive hemodynamic support during hospitalization, and 42 patients were lost to follow-up (Figure 1). The remaining 972 patients were included in the final analysis, and no significant differences in the baseline characteristics were observed between the 972 patients and the excluded patients.

As presented in Table 1, the median age was 46 years old and male patients accounted for 90.2% of the included participants. The prevalence of patients who were current smokers, had hypertension, diabetes mellitus, dyslipidemia, and positive family history of CHD were 18.9%, 34.3%, 14.5%, 4.4%, and 44.2%, respectively. Before hospitalization, only 16.9%, 8.1%, 13.7%, and 10.9% of patients were treated with anti-hypertensive, anti-diabetic, anti-platelet medications, and statins, respectively.

Most of the patients underwent coronary stenting due to stable angina (48.8%) and UA (48.1%). Most of patients had cardiac function of New York Heart Association (NYHA) class I and II at baseline. Nearly 30.0%, 24.8%, 39.3%, and 5.9% of patients had single, double, triple, and left main plus triple vessel stenosis, respectively. The median number of stent implantation was 1.

### Incidence of clinical outcomes after 1 years' follow-up

After the 1-year follow-up, 64 patients (6.6%) experienced clinical outcomes; the most common event was UA ( $n=56$ )

and a minority of patients had nonfatal myocardial infarction ( $n=2$ ), nonfatal ischemic stroke ( $n=4$ ), and coronary revascularization ( $n=2$ ).

### Comparisons between patients with and without clinical outcomes

Baseline characteristics between patients with and without clinical outcomes were compared. As presented in Table 2, compared to patients without clinical outcomes, those with outcomes were more likely to be male, have higher systolic blood pressure, more likely to have hypertension and diabetes mellitus, and more likely to present as unstable angina.

### Risk factors associated with CHD severity

The severity of CHD was divided into 3 categories with respect to the number of arteries with stenosis, the cardiac function, and the CHD classification. As presented in Table 3, male gender, hypertension, and diabetes mellitus were significantly associated with an increased number of coronary arteries with stenosis. Regarding the cardiac function, no significant risk factors were observed. However, within the category of CHD classification, increased baseline low density lipoprotein cholesterol (LDL-C) level was significantly associated with non-STEMI and STEMI.

### Predictors of clinical outcomes

Cox proportional hazards regression analysis was used to evaluate potential predictors of clinical outcomes. As presented in Table 4, in the univariate regression analysis, age, male gender, smoking, serum LDL-C level, presence of hypertension and diabetes mellitus, more vessels with stenosis, and patient presented as having acute coronary syndrome were all independently associated with incident clinical outcomes. With multivariate regression analysis, only age (HR: 1.12 and 95% CI: 1.07–1.26), smoking (HR: 1.15 and 95% CI: 1.06–1.23), presence of hypertension (HR: 1.19 and 95% CI: 1.13–1.31) and diabetes mellitus (HR: 1.16 and 95% CI: 1.09–1.28), more vessels with stenosis (HR: 1.27 and 95% CI: 1.20–1.48) and presented with acute coronary syndrome (HR: 1.35 and 95% CI: 1.21–1.55) remained independently associated with clinical outcomes.

## Discussion

In the current prospective study, we found that most of young Chinese CHD patients undergoing PCI did so because of stable angina and unstable angina. Notably, approximately 45% of these patients had triple vessel stenosis and triple vessel plus left main stenosis. Nearly 6.6% of these patients 1 year after stent implantation had ischemic events in terms of unstable

**Table 1.** Baseline characteristics (n=972).

Variables	Value
Age <sup>#</sup> , years	46 (43–49)
Male, n (%)	877 (90.2%)
Current smoker, n (%)	184 (18.9%)
Systolic blood pressure, mmHg	126.2±16.9
Diastolic blood pressure, mmHg	77.7±11.7
Heart rate, beats per minute	75.7±11.2
Alanine aminotransferase, U/L	27.9±14.8
Albumin, g/L	39.0±3.1
Total cholesterol, mmol/L	4.74±1.13
Triglyceride <sup>#</sup> , mmol/L	1.51 (1.06-2.19)
High density lipoprotein-cholesterol, mmol/L	0.93±0.18
Low density lipoprotein-cholesterol, mmol/L	2.51±1.06
Glycated hemoglobin A1c,%	5.9±0.8
eGFR, 1.73 m <sup>2</sup> /mL/min	95.0±10.9
Hypertension, n (%)	333 (34.3%)
Diabetes mellitus, n (%)	141 (14.5%)
Dyslipidemia, n (%)	43 (4.4%)
Family history of cardiovascular disease, n (%)	430 (44.2%)
CAD classification	
Stable angina, n (%)	474 (48.8%)
Unstable angina, n (%)	468 (48.1%)
Non-ST elevation myocardial infarction, n (%)	11 (1.1%)
ST-elevation myocardial infarction, n (%)	19 (2.0%)
Cardiac function (NYHA)	
Class I, n (%)	671 (69.1%)
Class II, n (%)	250 (25.7%)
Class III, n (%)	44 (4.5%)
Class IV, n (%)	7 (0.7%)
Number of coronary arteries with stenosis	
Single, n (%)	292 (30.0%)
Double, n (%)	241 (24.8%)
Triple, n (%)	382 (39.3%)
Left main plus triple, n (%)	57 (5.9%)
Left ventricular ejection fraction,%	57.4±8.2
Number of stents implantation <sup>#</sup>	1 (0–2)
Medications	
Anti-hypertensive, n (%)	164 (16.9%)
Anti-diabetic, n (%)	79 (8.1%)
Anti-platelet, n (%)	133 (13.7%)
Statins, n (%)	106 (10.9%)

<sup>#</sup> Presented as median and interquartile range; NYHA=New York Heart Association; eGFR=estimated glomerular filtration rate

**Table 2.** Comparison between patients with and without clinical outcomes.

Variables	With outcomes (n=64)	Without outcomes (n=908)
Age#, years	45 (42–48)	46 (43–49)
Male, n (%)	60 (93.4%)*	817 (90.0%)
Current Smoker, n (%)	12 (19.3%)	172 (18.9%)
Systolic blood pressure, mmHg	129.4±17.5*	123.6±16.1
Diastolic blood pressure, mmHg	76.7±11.3	77.9±12.5
Heart rate, beats per minute	78.4±11.6	73.3±10.6
Alanine aminotransferase, U/L	28.4±13.3	26.1±14.5
Albumin, g/L	39.6±3.5	38.5±3.0
Total cholesterol, mmol/L	4.88±1.15	4.70±1.06
Triglyceride#, mmol/L	1.56 (1.07–2.15)	1.47 (1.02–2.11)
High density lipoprotein-cholesterol, mmol/L	0.92±0.17	0.93±0.17
Low density lipoprotein-cholesterol, mmol/L	2.64±1.09	2.47±1.01
Glycated hemoglobin A1c, %	5.9±0.8	5.9±0.8
eGFR, 1.73 m <sup>2</sup> /mL/min	94.5±10.7	95.3±11.2
Hypertension, n (%)	25 (38.3%)*	308 (33.9%)
Diabetes mellitus, n (%)	11 (16.7%)*	130 (14.3%)
Dyslipidemia, n (%)	3 (4.8%)	40 (4.4%)
Family history of cardiovascular disease, n (%)	29 (45.7%)	401 (44.2%)
CHD classification		
Stable angina, n (%)	30 (47.3%)	444 (48.9%)*
Unstable angina, n (%)	32 (49.5%)*	436 (48.0%)
Non-ST elevation myocardial infarction, n (%)	1 (1.6%)	10 (1.1%)
ST-elevation myocardial infarction, n (%)	1 (1.6%)	18 (2.0%)
Cardiac function (NYHA)		
Class I, n (%)	44 (68.4%)	627 (69.1%)
Class II, n (%)	16 (25.3%)	234 (25.8%)
Class III, n (%)	3 (4.6%)	41 (4.5%)
Class IV, n (%)	1 (1.6%)	6 (0.6%)
Number of coronary arteries with stenosis		
Single, n (%)	19 (29.5%)	273 (30.1%)
Double, n (%)	16 (25.3%)	225 (24.8%)
Triple, n (%)	25 (39.7%)	357 (39.3%)
Left main plus triple, n (%)	4 (6.4%)	53 (5.8%)
Left ventricular ejection fraction,%	55.9±7.3	57.9±8.6
Number of stents implantation#	1 (0–2)	1 (0–2)
Medications		
Anti-hypertensive, n (%)	10 (16.2%)	154 (17.0%)
Anti-diabetic, n (%)	5 (7.8%)	74 (8.1%)
Anti-platelet, n (%)	8 (12.8%)	125 (13.8%)
Statins, n (%)	7 (10.2%)	99 (10.9%)

# Presented as median and interquartile range; \*  $P < 0.05$  versus without outcomes group. CHD – coronary heart disease; NYHA – New York Heart Association; eGFR – estimated glomerular filtration rate.

**Table 3.** Comparisons of risk factors of CHD severity.

	n (%)	n (%)	n (%)	P value
<b>Number of artery stenosis</b>	<b>Single (n=292)</b>	<b>Double (n=241)</b>	<b>Triple/Left main+triple (n=439)</b>	
Age*	46 (42–49)	46 (43–49)	46 (43–49)	0.691
LDL-C	2.49±1.04	2.51±1.07	2.52±1.06	0.860
Male	257 (88.0)	224 (92.9)	414 (94.3)	0.007
Current smoker	58 (20.1)	49 (20.5)	83 (19.0)	0.878
Hypertension	78 (26.8)	85 (35.4)	185 (42.2)	<0.001
Diabetes mellitus	30 (10.3)	37 (15.4)	87 (19.9)	0.002
<b>Cardiac function (NYHA)</b>	<b>Class I (n=671)</b>	<b>Class II (n=250)</b>	<b>Class III–IV (n=51)</b>	
Age*	46 (43–49)	46 (43–49)	46 (42–48)	0.936
LDL-C	2.48±1.05	2.50±1.03	2.51±1.06	0.546
Male	614 (91.6)	234 (93.6)	46 (90.2)	0.545
Current smoker	123 (18.5)	54 (21.7)	13 (25.5)	0.320
Hypertension	218 (32.6)	109 (43.8)	21 (41.2)	0.075
Diabetes mellitus	95 (14.2)	48 (19.4)	10 (19.6)	0.125
<b>CHD classification</b>	<b>Stable (n=474)</b>	<b>Unstable (n=468)</b>	<b>Non-STEMI/STEMI (n=30)</b>	
Age*	46 (42–49)	46 (43–49)	45 (43–48)	0.512
LDL-C	2.45±1.06	2.49±1.04	2.53±1.09	0.010
Male	432 (91.1)	435 (92.9)	28 (93.3)	0.570
Current smoker	71 (15.1)	112 (24.1)	7 (23.3)	0.092
Hypertension	180 (38.1)	161 (34.5)	7 (23.3)	0.174
Diabetes mellitus	73 (15.5)	78 (16.7)	3 (10.0)	0.579

\* Continuous variables were presented as median and interquartile range, tested with Kruskal-Wallis Test; categorical variables are presented as n (%), tested with chi-square tests and linear-by-linear association. CHD – coronary heart disease; LDL-C – low density lipoprotein cholesterol; NYHA – New York Heart Association; STEMI – ST-segment elevation myocardial infarction.

angina. Cox proportional hazards regression analysis indicated that age, smoking, presence of hypertension and diabetes mellitus, the number of vessels with stenosis, and acute coronary syndrome presentation during admission were independently associated with ischemic events.

The prevalence and incidence of hypertension, diabetes mellitus, and dyslipidemia has dramatically increased in the last 3 decades in China due to economic development [12–16]. These comorbidities together contribute to the initiation and progression of CHD. The prevalence and incidence of CHD among young adults has been reported to be similar to the ageing population in China [17,18], which is a big challenge

to the health and economic system due to health-related productivity loss [19].

Coronary artery stenting is an effective and efficient approach for restoring myocardial reperfusion and improving cardiac function. However, a large proportion of patients with coronary artery stenting still experience ischemic events over time [20,21], and the underlying mechanisms might be due to poor risk factor management and/or poor adherence to medications [22].

In this prospective study, we firstly evaluate the clinical characteristics of young CHD patients with coronary artery stenting. We found that premature CHD was more common in male

**Table 4.** Cox proportional hazards regression analysis.

Variables	Studied outcomes	
	Univariate HR (95% CI)	Multivariate HR (95% CI)
Age, years	1.25 (1.16–1.39)	1.12 (1.07–1.26)
Male vs. Female	1.18 (1.06–1.27)	1.05 (0.94–1.11)
Smoker vs. non-smoker	1.27 (1.14–1.40)	1.15 (1.06–1.23)
LDL-C, mmol/L	1.15 (1.06–1.52)	1.09 (0.98–1.07)
HbA1c, %	1.06 (0.97–1.12)	NA
eGFR, 1.73 m <sup>2</sup> /mL/min	1.08 (0.95–1.07)	NA
Hypertension (presence vs. absence)	1.30 (1.18–1.53)	1.19 (1.13–1.31)
Diabetes mellitus (presence vs. absence)	1.28 (1.17–1.50)	1.16 (1.09–1.28)
Cardiac function (III/IV vs. I/II)	1.08 (0.92–1.14)	NA
Number of artery stenosis (triple/left main plus triple vs. single/two)	1.39 (1.26–1.55)	1.27 (1.20–1.48)
CHD classification (acute coronary syndrome vs. stable angina)	1.44 (1.29–1.64)	1.35 (1.21–1.55)

LDL-C – low density lipoprotein cholesterol; eGFR – estimated glomerular filtration rate; CHD – coronary heart disease; NA – non-applicable; HR – hazard ratio; CI – confidence interval. Acute coronary syndrome includes unstable angina, non-STEMI and STEMI.

patients which might be due to more risk factors among males versus females. In addition, estrogen might also play a protective role in the young female patients [23]. We also observed that the treatment for risk factors in the young CHD patients before admission were also low, with only 16.9%, 8.1%, 13.7%, and 10.9% of patients treated with anti-hypertensive, anti-diabetic, anti-platelet medications, and statins, respectively. These data strongly support the notion that risk factor treatment is essential to prevent CHD [24]. Interestingly and importantly, we found that the reason most of young CHD patients underwent coronary artery stenting was not due to myocardial infarction. Rather, nearly 96.8% of these patients underwent coronary artery stenting due to chest pain. We are unsure about the underlying mechanisms. However, these data indicate that in young CHD patients, cardiac stress testing might be helpful to timely identify those who are at risk for cardiovascular events [25].

We secondly evaluate the risk factors of CHD severity in order to identify potential modifiable factors. We divided the severity of CHD into 3 categories in terms of the number of arteries with stenosis, cardiac function, and CHD classification. We found that male gender, hypertension, and diabetes mellitus were all significantly associated with increased number of coronary arteries with stenosis. However, regarding the cardiac function, no significant risk factors were observed. Only increased baseline serum LDL-C level was significantly associated with non-STEMI and STEMI. Once again, these findings

suggest that controlling risk factors in terms of hypertension, dyslipidemia, and diabetes mellitus could help to prevent CHD progression and reduce the severity of CHD.

We lastly evaluate the predictors of cardiovascular outcomes in the young CHD patients after coronary artery stenting. At the 1-year follow-up, among the 972 participants, 64 patients (6.6%) had clinical outcomes and the most common event was unstable angina, while a minority of patients had non-fatal myocardial infarction, nonfatal ischemic stroke, and coronary revascularization, indicating the most common ischemic events of the young CHD study patients after coronary artery stenting were due to chest pain. The underlying mechanisms might be due to anxiety after coronary artery stenting or disease progression. Future studies are warranted to evaluate the anxiety status of these young patients after coronary artery stenting. In addition, cardiac stress testing could also be helpful to identify the progression of disease.

We compared the baseline clinical characteristics between patients with and without clinical outcomes. We found that those with outcomes were more likely to be male, have higher systolic blood pressure, more likely to have hypertension and diabetes mellitus, and more likely to be presented as unstable angina. Cox proportional hazards regression analysis shows that age, smoking, presence of hypertension and diabetes mellitus, more vessels with stenosis and patient presenting with acute coronary syndrome were independently associated with

clinical outcomes. These findings strongly indicated that controlling the modifiable risk factors including smoking, hypertension, and diabetes mellitus would be beneficial to prevent ischemic events after stenting. In addition, in male patients and patients with more vessels with stenosis and those who presented with acute coronary syndrome, close follow-up and optimization of risk factors would also be helpful.

The clinical implications of current study were as follows: 1) young CHD patients had specific clinical characteristics and physicians should better screen and recognize the age-specific characteristics; 2) independent risk factors identified in this study might be used to establish risk predictive model in the future; 3) physicians should better manage the risk factors which might help to improve outcome for young CHD patients. For example, both physicians and social media should advocate and encourage young CHD patients to stop smoking; financial incentive might also help. Regarding hypertension and diabetes mellitus, not only should there be better screening, but also there should be increased utilization of guideline-recommended medications to treat these comorbidities. In addition, young people should be encouraged to live a healthy lifestyle such as stop smoking, eat more vegetables, and do regular exercise, which might reduce systemic inflammation and retard atherosclerosis progress. Finally, multidisciplinary team and holistic approach might provide a comprehensive management of CHD in young patients. In addition, based on our study findings, future research should focus on: 1) whether targeting the age-specific risk factors could result in greater benefits in younger rather than older CHD patients; 2) multi-center clinical studies are needed to establish and validate risk predictive model for young CHD patients.

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There were several limitations to our study. First of all, this was a single center study and the findings from this study should be further corroborated in other areas and medical centers of China. Second, we did not obtain information about the medication usage during follow-up which did not allow us to evaluate the adherence to treatment of these young CHD patients. Moreover, we also did not evaluate the control rate of risk factors during follow-up. Third, most of the ischemic events were unstable angina. As we discussed, some of these symptoms might be due to anxiety or other diseases such as gastric esophagus regurgitation disorder. Long-term follow-up for clinical events such as myocardial infarction, plus cardiac stress testing could be helpful to evaluate the outcomes of these young CHD patients.

## Conclusions

Our current study indicated that most of the young CHD patients underwent coronary artery stenting due to angina, and poor management of risk factors contributed to the development of premature coronary artery stenosis. Physicians should better screen and recognize age-specific characteristics. In addition, better management of these risk factors would be beneficial for improving clinical outcomes for young CHD populations.

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## Conflict of interests

None.



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