Original Article
Analysis of high risk factors and characteristics of coronary artery in premenopausal women with coronary artery disease

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Abstract: Objective: The aim of this study was to explore the high risk factors and coronary lesion features in premenopausal women with coronary artery disease (CAD) and provide guideline for diagnosis and therapy. Methods: 114 premenopausal women and 134 postmenopausal women were conducted coronary angiography in our hospital from September, 2012 to September, 2014. According to the results of coronary angiography, premenopausal and postmenopausal women with coronary artery disease were divided into two groups respectively, including 48 premenopausal women with CAD group, 66 premenopausal women with normal coronary artery group, 76 postmenopausal women with CAD group and 58 postmenopausal women with normal coronary artery group. Clinical characteristics and coronary lesion features were analyzed. Results: Incidence rates of hypertension disease and diabetes were higher in premenopausal women with CAD group than control group. Most of premenopausal women suffered from single vessel lesion and the length of impaired vessel was less than 20 mm, meanwhile, postmenopausal women easily confronted from double vessels or mutivessle lesion and the length of impaired vessel was more than 20 mm. Left anterior descending coronary artery lesion was common for premenopausal women. Conclusion: Hypertension disease and diabetes were the main high risk factors for premenopausal women and high triglyceride was the optimal predictable factor, furthermore, single vessel lesion and short artery lesion were common in premenopausal women, which often happened in the anterior descending coronary artery.

Keywords: CAD, premenopause, coronary angiography, coronary artery feature, risk factor

Introduction

It's a well-known that coronary artery disease (CAD) has become the first killer for health. Heart disease and stroke statistics (2011) from American Heart Association indicated that cardiac death is the first cause of death for women with any age stage, and the prevalence rate of women with CAD was 6.1% and men with CAD was 8.3% [1-4]. CAD risk increased along with an increase of age, interestingly, premenopausal women had much lower incidence of CAD compared with males, just only 1:3-10, but the incidence rate of CAD increased fast in postmenopausal women, and there was a nearly incidence of CAD between males and women with the age of 65 years, women, over 75 years of age, had higher incidence of CAD than men. Additionally, the mortality rates of women with

CAD and incidence rates of heart failure were both higher than men. Some studies suggested that mortality rate one year after myocardial infarction was 38% in women and 25% in men, and the incidence rate of heart failure within 6 years after myocardial infarction was 22% in men and 46% in women [5, 6]. Incidence rate and mortality rate were associated with gender and age, possible related to the estrogen level and its protective effect on heart vessel [7-12].

Presently, more and more premenopausal women had CAD. Traditional opinion considered that men were easily suffered from CAD and young premenopausal women never had CAD, and CAD had typical symptoms of acute coronary syndrome (ACS), which cause many premenopausal women with abnormal chest symptom without adequate concern, especially atyp-

ical angina symptom. Furthermore, they described the chest pain as other emotional words, which delayed the diagnosis of CAD, the frequency of women in hospital due to chest pain was more than men though [13-16]. The atypical symptoms of female patients were possible to the differences of anatomy, pathology and social psychology [17]. This study mainly analyzed the clinical characteristics of premenopausal women with CAD and coronary angiography features.

Materials and methods

Populations and groups

A total of 114 premenopausal women and 134 postmenopausal women who underwent coronary angiography selectively in the affiliated cardiovascular hospital of Henan University of Science and Technology from September, 2012 to September, 2014 were enrolled. According to the results of coronary angiography, 114 premenopausal women were divided into two groups, including 48 CAD women (mean age: 44.1±4.3 years), which had total seventy coronary artery lesions (narrow degree of coronary artery ≥ 50%), and 66 normal women without CAD (mean age: 44.3±3.8 years). 134 postmenopausal women were also divided into two groups, including 76 CAD women (mean age: 58±4.6 years), 58 normal women without CAD (mean age: 56±4.1 years). The clinical data and coronary artery lesion characteristics were compared between the premenopausal and postmenopausal CAD groups. This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of Henan University of Science and Technology. Written informed consent was obtained from all participants.

Exclusion criterion

Angina and MI were excluded caused by other severe heart diseases, such as dissection of aorta, severe aortic stenosis and hypertrophic cardiomyopathy. Patients who had hyperthyroidism, gout, renal inadequacy, immune system diseases, hepatic and cholalic system diseases, malignant tumors, severe hematological system diseases, combined with valvular heart disease or primary myocardiopathy, LVEF < 15% and multiple organs failure were excluded.

Clinical data

All patients were asked medical history in detail, and collected relevant data, including age, diabetes, hypertension, hyperlipemia, early vascular diseases family history, smoking, body mass index (BMI), urine acid and chest discomfort, ect.

Coronary angiography technique and analysis

Coronary angiography was conducted by two interventional cardiologists and used Judkins method to photography through multi-position, and left coronary and right coronary artery were performed angiography. Left major coronary artery (LM), left anterior descending coronary artery (LAD), left circumflex artery (LCX) and right coronary artery (RCA) were undergone segmented analysis. Major branches, such as diagonal artery (D1), obtuse marginal artery (OM) and acute marginal artery (AM), were also analyzed.

1250 mA digital subtraction angiography machine (SHIMADZU Company, Japan) and coronary artery angiography quantitative analysis software (QCA) were used in this study. Meanwhile, vascular diameter, stenosis degree and length were measured at the end diastolic period after vessels adjusted. Measurement data was repeated twice by the same operator and the mean value was the final data. Defined the diameter of normal coronary artery lumen as 100%, and narrow degree ≥ 50% was diagnosed as coronary artery disease. According to injured vascular numbers, lesion conditions were classified as single vessel lesion and multi-vessel lesion that also included two or more coronary artery lesions and left major lesion. Single lesion was defined that the narrow degrees of LAD, LCX, RCA and other major branches were more than 50%. Left major lesion, whatever LAD or LCX coronary artery lesion belonged to double coronary artery lesion, which combined with LAD or LCX defined as triple coronary artery lesion. The length of coronary artery lesion less than 20 mm was defined as short lesion and more than 20 mm was defined as long lesion.

Statistical analysis

Statistical analysis was performed using the SPSS17.0 software and measurement data

Table 1. Clinical characteristics of coronary artery in premenopausal women

Risk factor	Premenopausal CAD women (n=48)	Premenopausalwomen without CAD (n=66)	P
Age	44.1±4.3	42.1±4.8	> 0.05
Hypertension	30 (62.5%)	24 (36.3%)	0.006
Diabetes	33 (68.7%)	19 (28.7%)	< 0.001
Family history	3 (6.3%)	4 (3.3%)	> 0.05
Abnormal lipid	16 (33.3%)	18 (27.2%)	> 0.05
Smoking	2 (4.2%)	5 (7.5%)	> 0.05
BMI	22.4±3.28	22.8±3.58	> 0.05
Urine acid (μmol/L)	264.5±78.0	264±78.0	< 0.05
*Chest discomfort	23 (47.9%)	21 (31.8%)	> 0.05

*Chest discomfort: chest pain, chest distress, palpitation, nerves.

Table 2. Rank-Sum testcomparison of blood lipid components

Blood lipid	Premenopausal CAD women (n=48)	Premenopausal women without CAD (n=66)	P
TC (mmol/L)	4.90±1.13	4.45±0.72	> 0.05
TG (mmol/L)	1.72±0.70	1.13±0.60	0.004
LDL-C (mmol/L)	3.01±0.79	3.64±0.79	> 0.05
HDL-C (mmol/L)	1.09±0.26	1.14±0.31	> 0.05

results were presented as mean ± SD. Student-t test was used to compare two groups. Count data was compared using Chi-square test. $P < 0.05$ was considered statistically significant.

Results

The risk factors of premenopausal CAD women compare with premenopausal women without CAD

The risk factors of premenopausal CAD women and premenopausal women without CAD is summarized in **Table 1**. The prevalence rates of hypertension and diabetes were higher in premenopausal CAD women than in premenopausal women without CAD (62.5% vs. 36.3%, 68.7% vs. 28.7%, respectively, all P < 0.05), but there were no statistical significances of smoking, abnormal blood lipid, BMI and urine acid between two groups (P > 0.05). **Table 2** shows blood lipid components of two groups, TG level was higher in premenopausal CAD women than in premenopausal women without CAD (P < 0.05), there were no statistical significances of LDL-C, TC, HDL-C between two groups (P > 0.05).

The risk factors of postmenopausal CAD women compare with postmenopausal women without CAD

The risk factors of postmenopausal CAD women and postmenopausal women without CAD is summarized in **Table 3**, the prevalence rates of hypertension, diabetes and abnormal blood lipid were higher in postmenopausal CAD women than in postmenopausal women without CAD (78.6% vs. 54.2%, 83.4% vs. 17.1%, 52.4% vs. 31.4%, respectively, all P < 0.05).

The risk factors of premenopausal CAD women compare with postmenopausal CAD women

The risk factors of premenopausal CAD women and postmenopausal CAD women is depicted in **Table 4**. Additionally, the prevalence rates of hypertension, diabetes and abnormal blood lipid were lower in premenopausal CAD women than in postmenopausal women with CAD (78.6% vs. 62.5%, 83.4% vs. 68.7%, 52.4% vs. 33.3%, respectively, all P < 0.05), and there were no significant differences of smoking, BMI and urine acid between premenopausal CAD women and postmenopausal CAD women (P > 0.05).

Chest discomfort of premenopausal CAD women and postmenopausal women

Tables 1 and **4** show chest discomfort of premenopausal CAD women compare with premenopausal women without CAD and postmenopausal women. Moreover, 47.9% premenopausal CAD women and 31.8% premenopausal women without CAD had chest discomfort, which was no statistical significance (P > 0.05), premenopausal CAD women and postmenopausal CAD women was also no statistical significance (P > 0.05). But **Table 3** shows 88.3% postmenopausal CAD women had chest discomfort compared with postmenopausal women without CAD (P < 0.05).

Table 3. Clinical characteristics of coronary artery in postmenopausal women

Risk factor	Postmenopausal CAD women n=48	Postmenopausal women without CAD n=66	P
Age	58±4.6	57±3.8	> 0.05
Hypertension	60 (78.6%)	31 (54.2%)	0.005
Diabetes	64 (83.4%)	10 (17.1%)	< 0.001
Family history	3 (3.9%)	3 (5.1%)	> 0.05
Abnormal lipid	40 (52.4%)	18 (31.4%)	0.032
Smoking	5 (4.8%)	2 (5.7%)	> 0.05
BMI	22.4±3.28	22.8±3.58	> 0.05
Urine acid (μmol/L)	272.6±74.0	258±69.0	> 0.05
Chest discomfort	66 (88.3%)	11 (20%)	0.001

Table 4. Comparison of clinical characteristics between premenopausal CAD women and postmenopausal CAD women

Risk factor	Premenopausal CAD women (n=48)	Postmenopausal CAD women (n=76)	P
Age	44.1±4.3	58±4.6	> 0.05
Hypertension	30 (62.5%)	60 (78.6%)	0.036
Diabetes	33 (68.7%)	64 (83.4%)	0.017
Family history	3 (6.3%)	3 (5.8%)	> 0.05
Abnormal lipid	16 (33.3%)	40 (43.3%)	0.028
Smoking	2 (4.2%)	5 (4.8%)	> 0.05
BMI	22.4±3.28	22.8±3.2	> 0.05
Urine acid (μmol/L)	264.5±78.0	272.6±74.0	> 0.05
Chest discomfort	23 (47.9%)	66 (88.3%)	> 0.05

Table 5. Coronary artery quantity

Coronary artery quantity	Premenopausal CAD women (n=48)	Postmenopausal CAD women (n=76)	P
Single Coronary artery	31 (64.5%)	18 (23.6%)	< 0.001
Double Coronary artery	12 (25%)	39 (52%)	
Multiple Coronary artery	5 (10.5%)	19 (24.4%)	

The coronary artery quantity of premenopausal CAD women

Table 5 shows the coronary artery quantity of premenopausal CAD women and postmenopausal CAD women, of women with CAD and found more frequent involvement of single vessel lesion in premenopausal CAD women (64.5% vs. 23.6%, P < 0.05), and more frequent involvement of double or multi-vessels lesion in postmenopausal CAD women (25% vs 52%, 10.5% vs. 24.4%, respectively, all P < 0.05).

The coronary artery length of premenopausal CAD women

Table 6 shows the coronary artery length of premenopausal CAD women and postmenopausal CAD women, short lesion was more frequent involvement in premenopausal CAD women and long lesion or diffuse lesion was more frequent involvement in postmenopausal CAD women (60% vs 18.3%, P < 0.05), which indicated that the coronary artery lesion was more severe in postmenopausal CAD women, possible related to the high prevalence rates of hypertension, diabetes and abnormal blood lipid in postmenopausal CAD women [18, 19]

The coronary artery length of premenopausal CAD women

Table 7 shows the coronary artery lesion position of premenopausal CAD women and postmenopausal CAD women, Furthermore, we also found that about 70% lesion position was anterior descending coronary artery for premenopausal CAD women.

Discussion

Heart artery disease is a chronic disease caused by many kinds of risk factors. Traditional risk factors such like hypertension, diabetes, abnormal lipid metabolism and smoking, is sill major risk factors. The mechanisms included that vascular endothelial injury, abnormal lipid metabolism, chronic inflammation and immune response. Some studies indicated that hypertension is one of the most important risk factors to cause atherosclerosis in premenopausal women. Framinghan heart research center implied that systolic blood pressure (SBP) ≥ 140 mmHg is much more important risk factor of heart artery disease than diastolic

Table 6. Coronary artery length

Coronary artery length	Premenopausal CAD women	Postmenopausal CAD women	P
	Lesion quantity: 70	Lesion quantity: 152	
< 20 mm	42 (60%)	27 (18.3%)	0.038
≥ 20 mm	28 (40%)	125 (81.7%)	

Table 7. Coronary artery lesion position

Coronary artery lesion position	Premenopausal CAD women	Postmenopausal CAD women	P
	Lesion quantity: 70	Lesion quantity: 152	
LAD	49 (70%)	71 (47.1%)	0.001
LCX	9 (12.8%)	36 (23.5%)	> 0.05
RCA	10 (14.2%)	38 (25%)	> 0.05
LM	2 (3%)	7 (4.4%)	> 0.05

LAD: left anterior descending coronary artery; LCX: left circumflex artery; RCA: right coronary artery; LM: left major coronary artery.

pressure, furthermore, the relationship between blood pressure and risk of CAD events is consistency, independently of other risk factors [20-24]. Metabolism disorder caused by diabetes could promote the formation of atherosclerosis directly, and hyperinsulinemia promotes lipid synthesis and intake of arterial wall but inhibits the clearance of cholesterol and promotes the arterial smooth muscle cell proliferation, which aggravates atherosclerosis and impairs other systems and organs, like eyes, kidneys and nerves. A survey showed that [25, 26]. patients who combined with diabetes and peripheral nervous system lesion had higher incidence rate of cardiovascular events and mortality rate than patients with diabetes [27]. This study improved that prevalence rate of hypertension and diabetes was higher in premenopausal women with CAD group than control group (62.5% vs. 36.3%, 68.7% vs. 28.7%, $P < 0.05$, respectively), but there was no statistically significant differences of smoking, history diseases, urine aid, BMI between these two groups ($P > 0.05$). Lipid metabolism disorder is also the important high risk factor of atherosclerosis. Many studies confirmed that atherosclerosis was a chronic inflammatory response, and LDL might be the early factor to trigger the inflammatory response [28-30]. Goliasch et al. [18] found that LDL and TC were associated with young patients (less than 40 years of age) with atherosclerosis. However, this study found that HDL-C, LDL-C and TC levels were no obvi-

ously statistical significance between CAD group and control group ($P > 0.05$), except obvious increase of TG ($P < 0.05$), which indicated that an increase of TG was possibly associated with the incidence rate of CAD for premenopausal women, and there were no significant differences of TC and LDL levels between CAD group and control group. Dou et al. [19] reported that non-HDLC and TC were the optimal predictable indexes for men with CAD, and TG for women, which was in line with this study, which was related to the high ratio of patients with diabetes (35.4%) in this study, because abnormal blood lipid usually increased lipid protein of TG in patients with diabetes. In a word, hypertension and diabetes were the major risk factors of CAD for premenopausal women, and high TG level was the independent of risk factor in women with CAD.

CAD symptoms of women are different from symptoms of men, and besides angina, women commonly represent indistinct symptoms, such as excessive fatigue, poor scapula and shortness of breath, which couldn't be paid attention. Nearly 50% women with CAD had angina symptom, but 83% men with CAD were diagnosed as CAD through coronary angiography [31, 32]. Our study showed that CAD was diagnosed by coronary angiography in premenopausal women, of which 47.9% women had a complaint of the chest. For patients with acute myocardial infarction, a part of them manifested fatigue, asthenia and shortness of breath, meanwhile, about 31.8% women with normal coronary artery also had chest discomfort ($P > 0.05$). Chest discomfort was a statistical significance between postmenopausal women with CAD group and normal coronary artery group ($P < 0.05$), which indicated that clinical doctors should paid more attention on chest pain and other atypical symptoms in premenopausal women and avoid missed diagnosis and misdiagnosis. For postmenopausal women combined with many high risk factors, if chest pain and distress happened, CAD would be suspected highly.

CAD mostly happened in men with over 45 years old, which was 10-15 years later in women [1, 2]. Therefore, this study chose the postmenopausal CAD women with the age less than 65 years old as control group in order to avoid other complicated factors caused by age. Our results showed that the frequent involvement of one vessel lesion and short vessel lesion was more in premenopausal women (65% vs. 24%, 60% vs. 18.3%, respectively; all $P < 0.05$), and double and multiple vessels lesion and long vessel lesion was more in postmenopausal women (25% vs. 52%, 10% vs. 24%, 40% vs. 81.7%, respectively; all $P < 0.05$). Maybe postmenopausal women with CAD presented more frequently with hypertension, diabetes and hyperlipemia compared with premenopausal women with CAD (78.6% vs. 62.5%, 83.4% vs. 68.7%, 52.4% vs. 33.3%, respectively; all $P < 0.05$). Dou also found more frequent involvement of single vessel in premenopausal CAD and triple vessels in postmenopausal CAD patients, which was similar with our study. Moreover, it was amazing that more frequent involvement of anterior descending artery lesion in premenopausal CAD women was found (70%), and the exact reasons were still not clear. Davidson et al. [33] had the same opinion,and observed that the lesion was found in near end of anterior descending artery for premenopausal CAD women. At present, a great number of studies indicated that the prognosis of lesions with proximal end of anterior descending artery and left main coronary arteries was poorer than non-left main coronary arteries and non-anterior descending artery [34, 35]. Once premenopausal CAD women were miss-diagnosis, it would lead to dangerous outcome.

This study still had some limits, and firstly, this study was a single center, retrospective study which had its defects. Secondly, the samples was too few and the results were not absolute correct. If a large scale study was done, the results would exactly reflect the risk factors and artery lesion features in premenopausal CAD women, thirdly, estrogen level was not detected.

In sum, once female patients who had risk factors like hypertension, diabetes and abnormal blood lipid, felt chest disconfort or other atypi-cal angina symptom, whatever menopause or not, ST-T specific change of ECG or not, they should be diagnosed distinctly. For premenopausal women, once MI was occurred, the sudden death rate and incidence rate of heart failure were both high due to near end of anterior descending coronary artery lesion. Thus, our hygienic management department should enhance publicity of awareness rate, control rate and therapy method of vascular diseases in people. After all, the prevention of vascular diseases is much more important than therapy.

Disclosure of conflict of interest

None.

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