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Factors Associated with Coronary Artery Disease in Young Population (Age ≤ 40): Analysis with 217 Cases

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Key words: young patient; coronary artery disease; relevant factors

Objective To investigate the relevant factors of coronary artery disease (CAD) in young people under 40 years of age.

Methods The study population was 292 young patients accepting coronary angiography in Fuwai Hospital from July to December 2006, including 272 men and 20 women, with the mean age being 36.7 ± 3.7 years. The diagnosis of CAD was made in the cases presenting $\geq 50\%$ stenosis in coronary lumen in coronary angiography. Based on the diagnosis, 217 patients (204 men, 13 women) were assigned to CAD group, and 75 (68 men, 7 women) to non-CAD group. Clinical data and metabolic characteristics of the patients were collected and analyzed using *t*-test, χ^2 test, and multinomial logistic regression with SPSS 8.0 software.

Results Most study subjects were current smokers (209/292, 71.6%), and more than half had body mass index (BMI) > 24 kg/m² (230/292, 78.8%) and usually took high-fat diet (162/292, 55.5%). The proportion of heavy smokers (smoking history ≥ 10 years and ≥ 20 cigarettes per day) were significantly higher in the CAD group than in the non-CAD group [20.7% (45/217) vs. 9.3% (7/75), $P=0.015$]. Heavy smoking [odds ratio (OR), 1.89; 95% confidence interval (CI), 1.74-2.05], hypertension (OR, 1.56; 95% CI, 1.48-1.65), alcohol (OR, 1.37; 95% CI, 1.30-1.46), type 2 diabetes mellitus (OR, 1.37; 95% CI, 1.25-1.50), high-fat diet (OR, 1.35; 95% CI, 1.28-1.43), and BMI > 24 kg/m² (OR, 1.09; 95% CI, 1.03-1.17) were factors related to CAD in the young patients (all $P < 0.05$). Total cholesterol (4.56 ± 1.46 mmol/L vs. 4.09 ± 1.00 mmol/L), low-density lipoprotein cholesterol (2.38 ± 1.11 mmol/L vs. 2.14 ± 0.63 mmol/L), lipoprotein a (134.97 ± 109.70 mg/L vs. 101.58 ± 58.39 mg/L), uric acid (359.89 ± 100.09 μ mol/L vs. 336.75 ± 94.36 μ mol/L), erythrocyte sedimentation rate (9.98 ± 12.19 mm/hour vs. 4.89 ± 4.92 mm/hour), high-sensitivity C-reactive protein (3.42 ± 4.39 mg/L vs. 2.80 ± 3.77 mg/L) and Big endothelin-1 (1.41 ± 1.50 fmol/mL vs. 0.77 ± 1.13 fmol/mL) in plasma were significantly increased in the CAD group compared with the non-CAD group (all $P < 0.05$).

Conclusions Heavy smoking, hypertension, alcohol consumption, type 2 diabetes mellitus, high-fat diet and BMI > 24 kg/m² were significantly related to CAD in patients aged ≤ 40 , with heavy smoking presenting the highest OR. Metabolic syndrome and inflammation were also more common in young CAD patients than in non-CAD patients.

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ACCORDING to the reports on cardiovascular diseases in China 2007 and 2011,^{1,2} the death rate of coronary heart disease in rural male population aged ≤ 40 years was 13.81/100 000 in 2006, which increased to 19.07/100 000 in 2009. The incidence of ischemic heart disease in 2008 in China increased significantly compared to that in 2003 (15.9‰ vs. 4.6‰).² Some reports about young coronary artery disease (CAD) in China published in 2004 also showed an increase in the incidence of CAD in young patients.^{3,4} However, the study samples were small (58 and 161 patients). Moreover, in these reports, few of the metabolic characteristics, especially inflammation information about young CAD were mentioned. In the present study, we retrospectively analyzed the characteristics of coronary angiography in young people (≤ 40 years), compared not only the clinical features but also the metabolic characteristics in the young patients with CAD and those without CAD, aiming to identify the factors related to CAD in young population.

PATIENTS AND METHODS

Sample selection and data collection

From 1st July to 31st December 2006, 292 patients aged ≤ 40 (mean age, 36.7 ± 3.7 years; range, 15-40 years), including 272 men and 20 women, received coronary angiography in Fuwai Hospital. According to the results of coronary angiography, the patients were divided into CAD group ($\geq 50\%$ stenosis in coronary lumen, $n=217$) and non-CAD group ($n=75$). Clinical data were collected from the patients' case records, including body mass index (BMI), high-fat diet consumption, smoking history, hypertension, alcohol consumption and diabetes (type 2). Metabolic characteristics were summarized based on the laboratory reports within 24 hours of admission, including fasting blood glucose (FBG), total cholesterol (TC), total triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), lipoprotein a (LpA), uric acid, erythrocyte sedimentation rate (ESR), high-sensitivity C-reactive protein (hs-CRP), and Big endothelin-1 (Big ET-1).

Statistical analysis

Statistical analysis was performed with SPSS 8.0 software. Categorical variables were expressed as percentages and continuous variables as means $\pm$ SD. Clinical data and metabolic characteristics were analyzed using *t*-test, χ^2 test, and multinomial logistic regression. Multinomial logistic

regression analysis was used to assess variables (BMI > 24 kg/m², heavy smoking, hypertension, type 2 diabetes mellitus, CAD family history, alcohol, hyperlipidaemia and high-fat diet) independently associated with CAD in the young patients ("yes" scored 1, "no" scored 0). $P < 0.05$ was considered statistically significant.

RESULTS

Baseline characteristics

The mean age of the patients was 36.7 ± 3.7 years, 93.2% (272/292) were male. In the CAD group, 69 (31.8%) were diagnosed as acute coronary syndrome (65 cases of acute myocardial infarction and 4 cases of unstable angina), and 148 (68.2%) were stable CAD (91 cases of stable angina and 57 cases of old myocardial infarction). Coronary angiography showed single-vessel disease in 122 cases (56.2%), double-vessel disease in 44 (20.3%), and triple-vessel disease in 51 (23.5%). The total number of lesions was 355, most of which located in left anterior descending coronary artery (171, 48.2%), followed by right coronary artery (90, 25.4%) and left circumflex coronary artery (82, 23.1%), the least were in left main coronary artery (12, 3.4%).

In the non-CAD group, 20 patients had hypertension (26.7%), 19 had hyperlipidaemia (25.3%), 10 had myocarditis (13.3%), 9 had arrhythmia (12.0%), 8 had normal cardiovascular examination results (10.7%), 2 had rheumatic heart disease (2.7%), 2 had congenital heart disease (2.7%), 1 had pulmonary embolism (1.3%), and 4 had other conditions (5.3%).

Relevant factors of CAD

In the total of 292 patients, 78.8% (230/292) had a BMI > 24 kg/m², 71.6% (209/292) were current smokers, 55.5% (162/292) preferred high-fat food, 41.4% (121/292) had hypertension, and 32.5% (95/292) had hyperlipidaemia (Table 1).

Compared with the non-CAD group, the proportion of heavy smokers was significantly higher in the CAD group (20.7% vs. 9.3%, $P=0.015$). Compared with the non-CAD group, the percentages of BMI > 24 kg/m² (81.6% vs. 70.7%), current smokers (73.4% vs. 65.3%), hypertension (44.2% vs. 33.3%), type 2 diabetes mellitus (9.2% vs. 6.7%), CAD family history (19.4% vs. 17.3%), alcohol consumption (30.9% vs. 25.3%), hyperlipidaemia (31.8% vs. 34.7%), and high-fat food consumption (58.1% vs. 48.0%) were higher in the CAD group, but the differences were not statistically significant (Table 1).

Table 1. Baseline characteristics of the study patients and relevant factors of coronary artery disease (CAD)

Groups	Gender [male (%)]	Age ($\bar{x} \pm s$, years)	BMI >24 kg/m ² [n (%)]	Current smo- ker [n (%)]	Heavy smoker [n (%)]	Hypertens- ion [n (%)]	T2DM [n (%)]	CAD family history [n (%)]	Alcohol [n (%)]	Hyper- lipidaemia [n (%)]	High-fat food [n (%)]
non-CAD (n=75)	68(90.7)	36.1±4.6	53(70.7)	49(65.3)	7(9.3)	25(33.3)	5(6.7)	13(17.3)	19(25.3)	26(34.7)	36(48.0)
CAD (n=217)	204(94.0)	36.9±3.4	177(81.6)	160(73.4)	45(20.7)	96(44.2)	20(9.2)	42(19.4)	67(30.9)	69(31.8)	126(58.1)
Total (n=292)	272(93.2)	36.7±3.7	230(78.8)	209(71.6)	52(17.8)	121(41.4)	25(8.6)	55(18.8)	86(29.5)	95(32.5)	162(55.5)
P value	0.278	0.712	0.056	0.120	0.015	0.055	0.384	0.457	0.142	0.324	0.070

BMI: body mass index; T2DM: type 2 diabetes mellitus; heavy smoker: smoking history ≥ 10 years and ≥ 20 cigarettes per day; alcohol: "no" means never takes alcohol.

Table 2. Multiple logistic regression analysis result

Relevant factors	Odds ratio	P value	95% confidence interval
BMI>24 kg/m ²	1.09	0.006	1.03-1.17
Heavy smoking	1.89	0.000	1.74-2.05
Hypertension	1.56	0.000	1.48-1.65
T2DM	1.37	0.000	1.25-1.50
CAD family history	1.07	0.057	1.00-1.14
Alcohol	1.37	0.000	1.30-1.46
Hyperlipidaemia	1.08	0.060	1.02-1.12
High-fat diet	1.35	0.000	1.28-1.43

CAD is dependent variable in the multiple logistic regression analysis, relevant factors are independent variables.

Table 3. Biochemical characteristics of the CAD group and the non-CAD group[§]

Groups	FBG (mmol/L)	TC (mmol/L)	TG (mmol/L)	HDL-C (mmol/L)	LDL-C (mmol/L)
Non-CAD (n=75)	5.17±1.25	4.09±1.00	2.03±1.57	1.01±0.27	2.14±0.63
CAD (n=217)	5.27±1.16	4.56±1.46	2.15±1.84	1.00±0.27	2.38±1.11
P value	0.421	0.012	0.528	0.965	0.038
Groups	LPa (mg/L)	UA (μmol/L)	ESR (mm/hour)	hs-CRP (mg/L)	Big ET-1 (fmol/mL)
Non-CAD (n=75)	101.58± 58.39	336.75± 94.36	4.89± 4.92	2.80±3.77	0.77±1.13
CAD (n=217)	134.97±109.70	359.89±100.09	9.98±12.19	3.42±4.39	1.41±1.50
P value	0.000	0.003	0.008	0.000	0.000

§: Plus-minus values are means±SD.

FBG: fasting blood glucose; TC: total cholesterol; TG: total triglyceride; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; LPa: lipoprotein a; UA: uric acid; ESR: erythrocyte sedimentation rate; hs-CRP: high-sensitivity C-reactive protein; Big ET-1: Big endothelin-1.

As shown by the result of multiple logistic regression analysis, heavy smoking [odds ratio (OR), 1.89; 95% confidence interval (CI), 1.74-2.05], hypertension (OR, 1.56; 95% CI, 1.48-1.65), alcohol (OR, 1.37; 95% CI, 1.30-1.46), diabetes (OR, 1.37; 95% CI, 1.25-1.50), high-fat diet (OR, 1.35; 95% CI, 1.28-1.43), and BMI>24 kg/m² (OR, 1.09; 95% CI, 1.03-1.17) were factors strongly related to CAD in young patients (all $P < 0.01$, Table 2).

Biochemical characteristics

Although the volumes of FBG, TG and HDL-C did not show

significant changes, the levels of TC (4.56±1.46 mmol/L vs. 4.09±1.00 mmol/L, $P=0.012$), LDL-C (2.38±1.11 mmol/L vs. 2.14±0.63 mmol/L, $P=0.038$) and LPa (134.97±109.70 mg/L vs. 101.58±58.39 mg/L, $P=0.000$) were significantly higher in the CAD group than in the non-CAD group (Table 3).

Inflammation-related characteristics, including ESR (9.98±12.19 mm/hour vs. 4.89±4.92 mm/hour, $P=0.008$), hs-CRP (3.42±4.39 mg/L vs. 2.80±3.77 mg/L, $P=0.000$) and Big ET-1 (1.41±1.50 fmol/mL vs. 0.77±1.13 fmol/mL, $P=0.000$) in plasma, were all significantly increased in the

CAD group (Table 3).

DISCUSSION

In this retrospective study in 292 young patients (age ≤ 40) with or without CAD based on coronary stenosis identified by angiography, we found that more than 50% of the study patients had a BMI >24 kg/m², were current smokers, and preferred high-fat diet, and more than 30% of the patients had hypertension and hyperlipidaemia. These results indicate a dangerous prevalence of unhealthy lifestyle among young population in China and the consequent poor health status.

In this study, among all the studied factors, only the proportion of heavy smokers was significantly higher in the CAD group than in the non-CAD group (20.7% vs. 9.3%, $P=0.015$). Multiple logistic regression analysis showed that heavy smoking, hypertension, diabetes, and BMI >24 kg/m² were all factors strongly related to CAD in young patients, consistent with the previously reported and confirmed risk factors of CAD.⁵⁻¹¹

A previous survey suggested exposure to environmental tobacco is likely to be much greater a risk factor for heart disease than for lung cancer.⁶ Shiraishi et al^{9,10} reported that current smoking was associated with a great risk of non-fatal acute myocardial infarction (OR, 2.95; 95% CI, 2.77-3.14; $P<0.0001$), and the risk increased by 5.6% for every additional cigarette smoked. In this study, heavy smoking was found significantly related to CAD in young people. Therefore it is important to educate young people to stop smoking.

It is well known that hypertension is the most important population-attributable and modifiable risk factor for cardiovascular events.¹² Moreover, diabetes mellitus is a CAD risk equivalent, and CAD is more prevalent, more severe, and occurs at younger age in patients with diabetes.¹³ Zarich et al⁵ reported that metabolic syndrome, diabetes, or both were present in nearly 2/3 of young subjects with premature atherosclerosis, as manifested by acute myocardial infarction. Although the present study did not show statistically significant association of CAD family history and hyperlipidaemia with CAD in young patients, they were widely considered as risk factors of CAD, especially in the young population.⁵

The relationship between alcohol and CAD is controversial. Sometimes consumption of a little wine is considered a protective factor of CAD, especially for increasing HDL-C.¹⁴ Fournier et al¹⁵ studied long-term prognosis of young AMI patients (age ≤ 40 years), and found that the mortality rate at 15 years was higher in patients with long-term

excessive alcohol intake ($P=0.035$).¹⁵ In this study, alcohol was related to CAD in young patients. But given the retrospective nature of this study, it did not record daily volume of alcohol intake. Large-size epidemic investigations and more detailed mechanism studies are needed to clarify the relationship between alcohol and prognosis of CAD, especially in young population.

Eating habits might have some influence on incidence of CAD, but that assumption has not been confirmed.¹⁶ In the present study, more than half of the study patients prefer high-fat diet, and the proportion was higher in the CAD group, though the difference was not statistically significant. It was found a relevant factor for young CAD patients in this study.

The levels of TC, LDL-C, and Lp(a) were higher in the CAD group, suggesting the existence of metabolic syndrome. Previous studies have demonstrated that metabolic syndrome is associated with pro-inflammatory and pro-thrombotic cardiovascular risk factors, which results in a 2- to 4-fold increase in cardiovascular events.^{5,17} The presence of metabolic syndrome was defined as having three or more of the following five criteria: BMI >30 kg/m²; hypertension; hyperlipidaemia including increased TC, hypertriglyceridaemia; higher LDL-C and lower HDL-C; and impaired fasting blood sugar.¹⁸ The presence of metabolic syndrome alone in young adults should trigger attention toward patient education and lifestyle modifications.

In this study, the level of uric acid in the CAD group was significantly higher than that in the non-CAD group. Tatli et al¹⁹ also reported that among the patients with acute myocardial infarction and under 35 years old, uric acid concentrations were higher in those with critical CAD than that in those with normal coronary arteries (7.0 ± 1.4 mg/dL vs. 4.9 ± 1.1 mg/dL, $P=0.003$).

Inflammation appears to be integral in the development of atherogenesis and atherothrombosis. It has emerged as a risk factor of CAD that needs to be addressed and modified.²⁰ In this study, the levels of ESR and hs-CRP were significantly higher in the CAD group than those in the non-CAD group. ESR increasing could, to some extent, reflect inflammation status. As a marker of inflammation, hs-CRP is an independent cardiovascular risk factor commonly associated with insulin resistance and metabolic syndrome.⁵ And its value is in its ability to predict cardiovascular risk. JUPITER study found that rosuvastatin-induced hs-CRP decrease could significantly reduce the incidence of cardiovascular events in patients with high hs-CRP baseline level but without hyperlipidaemia.²¹

Big ET-1 is a vascular activator synthesized and released by endothelial cells. It is a contracting factor and a

circulating marker of endothelial function. Endothelial dysfunction is closely related to different risk factors of atherosclerosis.^{22,23} Zhang et al²⁴ reported that the plasma level of Big ET-1 in patients with coronary heart disease was significantly higher than that in healthy controls (2.82 fmol/mL vs. 2.06 fmol/mL, $P < 0.01$). Similar result was reached in this study.

In conclusion, besides the recognized risk factors of CAD, including hypertension, alcohol intake, diabetes mellitus, high-fat diet, and BMI $> 24 \text{ kg/m}^2$, heavy smoking was found as the factor with the most significant association with CAD in young patients aged ≤ 40 years. The prevalence of metabolic syndrome and inflammation were higher in young CAD patients than in non-CAD patients. Therefore, mass education on healthy lifestyle, especially smoking cessation, for Chinese young population is of great urgency.

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