Analyse the risk factors of coronary heart disease in young and middle - aged male patients using multivariate statistical

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ABSTRACT

Objective: To study the correlation between various risk factors and coronary CTA calcification score (CACS) in young and middle-aged male patients with coronary heart disease by multiple linear regression, and to predict plaque properties by Mahalanobis distance discrimination method. This study provides evidence for early clinical evaluation of the extent of coronary artery calcification and the property of plaque in patients having suffered coronary heart disease. **Methods**: choose 98 male patients under 55 years old with coronary heart disease randomly and collecte relevant medical history data and test results while in hospital. Utilizing the theory of multiple linear regression and Mahalanobis distance discriminant to analyse these dates. **Results**: Factors including hypertension classification×years, number of cigarettes smoked(packs / week)×years,and time of diabetes(years) have a positive correlation between CACS respectively. Comparing calcified plaque and vulnerable plaque, mixed plaque and vulnerable plaque,there is a significant differences (p < 0.01) while hs-CRP and IL-6 are as the indicator. Mahalanobis distance discrimination method has a discrimination accuracy of 91.83 % for the group wrih susceptible factors only. **Conclusion**: The model of predicting the extent of coronary artery calcification by multiple linear regression has high reliability. Vulnerable plaques can be distinguished from plaques of other properties efficiently using Mahalanobis distance discrimination method.

Keywords: Multiple linear regression; Mahalanobis distance discrimination; Coronary CTA calcification score; Vulnerable plaques; IL-6

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Introduction

Coronary heart disease (short for coronary atherosclerotic heart disease) refers to the heart disease[1] caused by coronary atherosclerosis blocking the lumen and changes in coronary artery function, resulting in myocardial ischemia and hypoxia.The trend of young and middle-aged male patients with coronary heart disease has been on the rise in [2], with few comprehensive clinical studies to predict the degree and nature of plaques in such patients.Its susceptibility factors, inflammation indicators and CACS were selected as the study parameters, and the feasibility of [4] was explored combined with multiple linear regression model [3] and Mahalanobis distance discrimination model.

Data and Methods

Patients with typical coronary heart disease symptoms in men and coronary CTA younger than 55 years with more than 50% of the coronary artery stenosis between January 2017 and the Second Affiliated Hospital of Xuzhou Medical University and July 2018 were selected.Exclusion indicators: chronic liver disease, chronic inflammatory disease, renal failure, tumor, severe cardiac insufficiency (left ventricular ejection fraction ≤ 3 0%), history of pacemaker placement, severe valvular disease, history of 4 weeks of arteriovenous embolism or infection.In total, 153 patients were collected, 136 patients with CHD confirmed and 98 eligible.

1.1Materials and reagents

Human Interleukin-6 Enzyme Link Immunization Kit (Wuhan Aibotech Biotechnology Co., Ltd.), Cotinin ELISA Kit (Shanghai Jianglai Biotechnology Co., Ltd.)

1.2 Instruments and equipment

GE revolution 256 helix CT (GE, USA), XT-1800i Automatic blood globe (Hison, Japan), ACL TOP 700 coagulation analyzer (Wofen, China), Hitachi 7600-020 Automatic Biochemical Analyzer (Hitachi, Japan), Medical centrifuge LDZ5-2,-80℃ cold refrigerator.

1.3 Method

1.3.1

After admission, the data were collected: [6] of hypertension and hypertension, smoking [7], diabetes [8].Blood blood was measured by cotinine [7,9], total cholesterol, triglyceride [10], low-density lipoprotein [11,12], Hbb [13] and hs-CRP[14], IL-6[15].Blood pressure was measured (the mean was taken 3 times on 1 day).Line coronary CTA (computed tomography angiography), and CACS. was collectedRelated factor testing: after admission, the patient was collected for blood from the elbow vein and measured by hemoglobin, total cholesterol, triglyceride, low density lipoprotein, and hs-CRP. by the laboratory of the Second Affiliated Hospital of Xuzhou Medical UniversitySerum was also isolated by centrifugation at 4 mL, for 20 min (1 000 r / min) and stored in a-80℃ refrigerator.IL-6, cotinine was measured according to the kit method.

1.3.2

The porridge plaque properties and CACS: were scanned with 256 layer spiral CT and 100 ~ 120 ~ 120 mL, via the elbow vein with a scan time of 10 ~ 12s.Raw data obtained from the scan was transmitted to the image workstation and 25% of> coronary stenosis considered plaques.The average CT value [16] was calculated by evenly dividing the patches found in the coronary CT scan images into four random points in the MIP segment face (1 mm) image of each segment, and the CT values were measured and recorded.Image analysis was completed by two deputy chief physicians of the CT Department of the Second Affiliated Hospital of Xuzhou Medical

University.Judgment of plaque nature: According to the plaque value CT, Sehroeder [17]: CT value <60 Hu (Hounsfeild Units) is vulnerable plaque, CT value 60 ~129 Hu is mixed plaque, and CT value> 130 Hu is hard plaque.

1.3.3

Statistical processing: The applied statistical methods include: correlation analysis, multiple linear regression, rank sum test between two non-parameters, Mahalanobis distance discrimination analysis; all using MATLAB2016b.Comparisons between groups were performed with the Mann-Whitney rank-sum test (p=0.01).The Discrimination Act uses the Mahalanobis distance discrimination [18].

2. Result

2.1 Comprehensive statistics of data

Table 1: General information of the selected patients

General information	The average	The scope
Cotinine（ug/l）	80.2000	0.0060-382.9446
Systolic blood pressure（mmHg）	132	101-167
Diastolic blood pressure （mmHg）	87	65-121
Glycosylated hemoglobin(%)	6.6	5.8-9.4
Total cholesterol （mmol/l）	4.89	2.09-8.77
Triglyceride（mmol/l）	1.51	0.26-2.73
Low densith lipoprotein（mmol/l）	80.20	0.14-7.45
Hs-CRP（mg/l）	15.83	2.58-34.00
IL-6(pg/ml)	11.10	1.67-87.16
Calcium integral	343.55	186.00-485.00
Age (years)	50	40~55

Table 2 Statistics of general consultation data

	Hypertension grade 1	Hypertension grade 2	Diabetes	Smoking volume（Package / Week）
Average years (years)	4.04	6.78	4.22	16.41
Number of people	31	9	17	43

2.2 Correlation analysis of susceptible factors and calcification integral and multiple linear regression

Table 3 List of correlations of susceptible factors and calcification integration

	R（correlation coefficient）
Hypertension grade×Fixed number of year	0.3641
Years of diabetes	0.3613
Smoking volume×Fixed number Ser of year	0.2783

Table 4 Multiple regression

	estimated value	standard error	t value	P value
Constant	306.83	8.22	4.22	0.000
Hypertension grade×Fixed number of year	6.79	1.48	4.69	0.000
Years of diabetes	13.50	3.53	3.82	0.000
Smoking volume×Fixed number of year	0.38	0.14	2.63	0.009

Linear regression Y=306.83+6.79X1+13.5X2+0.38X3

X1 stands for Hypertension grade×Fixed number of year, X2 stands for Years of diabetes, X3 stands for Smoking volume×Fixed number of year. The P value of the test (0.000) was less than 0.01. The regression equation can be considered significant.

Table 5 Number of different patch types

	Calcified plaque	Mixed plaques	Vulnerable plaques
Number of people	28	30	40

Table 6 Comparison of inflammatory indicators of different types of plaque

	P value（hs-CRP）	P value（IL-6）
Calcified plaque and mixed plaque	0.354	0.208
Mixed plaque and vulnerable plaque	0.000	0.000
Calcified plaque and vulnerable plaque	0.000	0.000

2.3 Comparison of inflammatory indicators of different types of plaque

Mann-Whitney rank sum test, hs-CRP, IL-6, P (<0.01) in the blood of mixed, calcified and vulnerable plaques.On a large number of study surfaces, h-CRP,IL-6 was statistically different in the blood of different plaques, and Mann-Whitney rank sum test results matched, and hs-CRP, IL-6 was added as a parameter to the Mahalanobis distance discrimination analysis.

Table 7 Mahalanobis distance discrimination analysis

Three classification method				Two classification method			
	Risk factors group	Risk factors and hs-CRP	Risk factors and IL-6		Risk factors group	Risk factors and hs-CRP	Risk factors and IL-6
Accuracy rate	85/98	77/98	83/98	Accuracy rate	90/98	89/98	93/98

Three classification method grouped plaques by hardened patches, mixed patches, and vulnerable patches.Two classification method combines hardened, mixed patches into a category, grouped with vulnerable patches.Easy factors (systolic blood pressure, diastolic blood pressure, hemoglobin glycosyc, total cholesterol, triglycerides, low density lipoprotein, cotinine), hs-CRP, IL-6 as the discrimination indicators, Conduct the Mahalanobis distance discrimination and the misjudgment rate return.Two classification method has higher accuracy than Three classification method and more accurate estimates of vulnerable patches

3. Discussion

1. Selection of population and vulnerable factors: The famous Framinghan[19] heart study showed the incidence of 30-62 CAD with age, for example, 1 in 8 in 40-44,1 in 45-49,1 in 50-55, and 1 in 4 after 55.Although male age> 55 years was included as a risk factor, a higher incidence was found in men <55 years.This CAD at a younger age is called early-onset CAD [20], which occurs before 55 in men and before 65 in women.Early-onset coronary heart disease has unique risk factors and coronary artery characteristics, and its harm is more serious.On the surface of foreign research, early coronary heart disease often has a strong genetic background and the susceptibility basis of lipid metabolism disorders. The main factors mainly include: 1 parents have a history of early coronary heart disease; 2 elevated plasma LDL-C levels and reduced HDL-C levels; 3 smoking; 4 hypertension; 5 diabetes.Because the parental history of coronary heart disease could not be accurately collected, the vulnerable factors group was not included.

2. Selection of statistical method: due to the randomness of the population, the parameter distribution of this study basically does not conform to the normal distribution, and the statistical method uses non-parametric statistical comparison.

3. Selection of parameters: Atherosclerosis is a chronic process, there are many factors causing atherosclerosis, mainly including: age and gender, hyperlipidemia [21], hypertension, smoking, diabetes, obesity, sedentary lifestyle and genetic, drinking, environmental factors, etc.The chronic development of CHD includes lipid deposition, plaque formation, plaque calcification; in which we understand that the factors mentioned, relatively stable parameters including hypertension, smoking, diabetes; and the strength and time, so hypertension × duration, diabetes, and calcification integration are more important to study clinical relevance to guide treatment.Coronary artery CTA can respond well to the degree of atherosclerosis and the nature of the plaque, which is used as an ideal indicator for testing.In the acute phase of coronary heart disease patients, plaque bleeding, plaque rupture, make the lumen stenosis, cause myocardial ischemia, its pathological changes, development process is often rapid, after excluding mental, disease and other factors, the plaque in the internal environment will not change too big, its influence factors mainly including blood flow stress [22] (blood pressure, lumen stenosis), blood sugar (hemoglobin glycosy), lipid oxidation (total cholesterol, triglycerides, low density lipoprotein), nicotine chemistry (cotinin).Due to the difficulty of detecting vascular stenosis, the study can only be ignored, and the genetic factors cannot be included in the category of variable parameters.As acute-phase inflammatory factors, hs-CRP and IL-6 have good predictive effects, and adding them to the analysis is well illustrated.

4. Mahalanobis distance discrimination: when using Mahalanobis distance discrimination, the accuracy of the Three classification method decreases when hs-CRP, IL-6 are added, considering because there is no obvious difference in hs-CRP, IL-6 in hardening patches and mixed patches, but reduces the accuracy when the discrimination.

5. This study strictly followed the principle of sample randomization, but due to the time and patient limitations, the number of samples collected was slightly insufficient and needs to be improved.However, the results well validated the theory of previous research, and the quantitative analysis of the relationship between the main etiology and disease occurrence and development, providing a good data basis for clinical practice.

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