Original Article

IVUS plus multivariate analysis for evaluating the stability of coronary artery plaque in coronary heart disease

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Abstract: Objective: To investigate the effect of intravascular ultrasound (IVUS) plus multivariate analysis in evaluating the stability of coronary artery plaque in coronary heart disease (CHD). Methods: A retrospective analysis was conducted on ninety-five patients with CHD admitted to our hospital from February 2020 to February 2021. Patients with CHD were examined by IVUS and assigned to a stable plaque group (n=60) and an unstable plaque group (n=35) according to their characteristics. Multivariate logistic regression analysis was performed to evaluate the risk factors affecting the stability of coronary artery plaque. Results: Of 95 patients, 35 cases with unstable plaque were determined by IVUS, with a detection rate of 36.84%; notable differences were found in HDL-C, hs-CRP, and homocysteine (Hcy) between the two groups (P<0.05). The eccentricity index and remodeling index of the two groups were statistically different (P<0.05). Moreover, 17 cases were diagnosed by IVUS as mild coronary stenosis, 28 cases as moderate stenosis, and 50 cases as severe stenosis. In addition, compared with the stable plaque group, the unstable plaque group yielded a much higher stenosis rate (P<0.05) and a higher level of plaque thickness and plaque area (P<0.05). Multivariate logistic regression analysis showed eccentricity index, remodeling index, plaque thickness, and plaque area, stenosis rate, HDL-C, Hcy, and hs-CRP were independent risk factors for unstable plaque (P<0.05). Conclusion: IVUS plus multivariate analysis can accurately assess plaque stability.

Keywords: IVUS, coronary heart disease, coronary artery, stable plaque

Introduction

Coronary heart disease (CHD), also known as coronary artery disease, is a common cardiovascular disease. It remains a major cause of morbidity and mortality and takes a considerable toll on patients’ health [1]. World Health Organization (WHO) statistics [2] revealed that deaths from CHD are approximately 7.84 million worldwide annually, and on the rise yearly. It has been reported that the severity of disease, risk, and degree of coronary artery stenosis are closely related to the stability of the plaque [3]. In this regard, an accurate assessment of the stability of the patient’s coronary plaque is crucial for clinical evaluation and prevention of adverse events induced by CHD. Fortunately, intravascular ultrasound (IVUS) can display the cross-sectional area of coronary arteries in real-time, magnifying the chance to accurately assess the severity of lesion stenosis and the size of the lumen, with high spatial resolution and high image quality [4]. In light of this, this study explored the value of IVUS in the assessment of the risk factors in coronary artery plaque stability in CHD patients and analyzed their influence on stability.

Materials and methods

Subjects

A retrospective analysis of 95 patients with CHD admitted to our hospital between February 2020 and February 2021 was conducted, including 59 males and 36 females, aged from 30 to 78 years (mean, 59.16±15.78). Inclusion criteria: (1) Patients met the diagnostic criteria of CHD [5]; (2) Patients had complete clinical data, ultrasound imaging data, and related laboratory indicators; (3) Patients willing to cooperate with the study. Exclusion criteria: (1) Patients with organ dysfunction such as liver
IVUS & multivariate analysis in CHD

Methods

Clinical data and biochemical indicators: Clinical data including gender, age, body mass index (BMI), smoking history, drinking history, history of hypertension, history of diabetes, and blood lipid levels were recorded. 3 mL of fasting blood was extracted in the morning after admission, the serum was isolated, and triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C), uric acid (UA), and homocysteine (Hcy) were detected by Hitachi 7600 automatic biochemical analyzer. The immunoturbidimetric method was used to detect serum high-sensitivity C-reactive protein (hs-CRP).

IVUS inspection: An intravascular ultrasound system (Boston Scientific, USA) was used with a probe of 3.2F and a frequency of 15 MHz. The patient was placed in a supine position, and a thin pillow was placed under the shoulders to fully expose the parts that need to be examined. The inspection was performed from top to bottom, scanned along the long axis of the coronary artery to explore the vascular intima, hierarchical structure, and distal and proximal images of the plaque, and observe the echo and morphologic characteristics of the plaque. The edges of the extima and intima were traced by hand on the short axis. The area included in the extima was the external elastic membrane area (EEM), the intima was the lumen area, the plaque area was the EEM area minus the lumen area, and the plaque load was the plaque area divided by the EEM area. As shown in Figure 1, the plaque burden = (EEM area - lumen area), and the stenosis rate = (EEM area - lumen area)/EEM area × 100%.

Observation indicators

(1) According to the severity of coronary artery wall lesions, the coronary arteriosclerosis is classified as: ① Normal: All coronary arteries have normal diameters, with smooth walls and no thickening; ② Sclerotic plaque: Coronary arteries show uneven diameters, thickening occurs with a thickness of ≥1.5 mm, and plaques have formed. According to the echo characteristics of the plaques, these can be classified into hyperechoic plaques, hypoechoic plaques, and mixed echo plaques. According to the morphology of the plaque, it is classified into ulcer plaque and flat plaque. We defined hyperechoic plaque, soft plaque, ulcer plaque, and flat plaque as unstable plaques. (2) The severity of coronary artery stenosis: ① Mild stenosis: <50%; ② Moderate stenosis: 50%-69%; ③ Severe stenosis: ≥70%. The patient's eccentricity index (EI), remodeling index (RI), and EEM were evaluated by IVUS. The calculation formula is as follows: EI = (thickest plaque-thinnest plaque)/thickest plaque; RI = the area of the blood vessel at the lesion/the average value of the area of the proximal and distal reference blood vessels. RI≥1.05 means positive remodeling; RI<1.05 means no remodeling or negative remodeling.

Statistical analysis

All data analysis in the current study was conducted by SPSS18.0 statistical software package, and the measurement data were expressed as (x ± s) and analyzed by t-test. The count data were expressed as [n (%)] and analyzed by χ² test; the risk factor analysis was performed by binary logistic regression analysis, and the test

Figure 1. A typical image for the calculation of cross-sectional area stenosis.
### Results

**Comparison of baseline data**

Of 95 patients, 35 cases of unstable plaques were detected by IVUS, with a detection rate of 36.84%; no marked difference was observed between the two groups in terms of gender, age, BMI, smoking history, drinking history, hypertension history, diabetes history, TG, TC, LDL-C, and UN (P>0.05); whereas a notable difference was witnessed in HDL-C, hs-CRP, and Hcy (P<0.05). See Table 1.

### Table 1. Comparison of baseline data

<table>
<thead>
<tr>
<th>Group</th>
<th>Stable plaque group (n=60)</th>
<th>Unstable plaque group (n=35)</th>
<th>χ²/t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>32 (62.75)</td>
<td>19 (37.25)</td>
<td>0.008</td>
<td>0.928</td>
</tr>
<tr>
<td>Age (years)</td>
<td>59.50±14.37</td>
<td>58.93±15.21</td>
<td>0.183</td>
<td>0.886</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>22.76±2.87</td>
<td>23.40±2.66</td>
<td>1.077</td>
<td>0.284</td>
</tr>
<tr>
<td>History of smoking</td>
<td>20 (60.61)</td>
<td>13 (39.39)</td>
<td>0.142</td>
<td>0.707</td>
</tr>
<tr>
<td>History of drinking</td>
<td>22 (64.71)</td>
<td>12 (35.29)</td>
<td>0.055</td>
<td>0.815</td>
</tr>
<tr>
<td>History of hypertension</td>
<td>28 (66.52)</td>
<td>15 (34.88)</td>
<td>0.129</td>
<td>0.719</td>
</tr>
<tr>
<td>History of diabetes</td>
<td>30 (71.43)</td>
<td>12 (28.57)</td>
<td>2.213</td>
<td>0.137</td>
</tr>
<tr>
<td>TG (mmol/L)</td>
<td>2.54±0.70</td>
<td>2.62±0.60</td>
<td>0.141</td>
<td>0.888</td>
</tr>
<tr>
<td>TC (mmol/L)</td>
<td>5.25±0.95</td>
<td>5.50±0.97</td>
<td>1.228</td>
<td>0.223</td>
</tr>
<tr>
<td>HDL-C (mmol/L)</td>
<td>1.53±0.45</td>
<td>1.30±0.42</td>
<td>2.462</td>
<td>0.016</td>
</tr>
<tr>
<td>LDL-C (mmol/L)</td>
<td>3.41±1.09</td>
<td>3.12±1.05</td>
<td>1.268</td>
<td>0.208</td>
</tr>
<tr>
<td>hs-CRP (mg/L)</td>
<td>5.20±1.06</td>
<td>7.81±1.43</td>
<td>10.150</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>UN (mmol/L)</td>
<td>515.23±78.13</td>
<td>499.78±68.23</td>
<td>0.973</td>
<td>0.333</td>
</tr>
<tr>
<td>Hcy (µmol/L)</td>
<td>14.84±4.19</td>
<td>17.81±3.76</td>
<td>3.458</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Comparison of eccentricity index and remodeling index

The eccentricity index and remodeling index of the stable plaque group were (0.72±0.16) and (0.65±0.20); those of the unstable plaque group were (0.94±0.17) and (0.86±0.10). The two indexes of the stable plaque group were statistically higher than those of the unstable plaque group (Table 2).

### Table 2. Comparison of eccentricity index and remodeling index between two goups

<table>
<thead>
<tr>
<th>Group</th>
<th>Eccentricity index</th>
<th>Remodeling index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stable plaque group (n=60)</td>
<td>0.72±0.16</td>
<td>0.94±0.17</td>
</tr>
<tr>
<td>Unstable plaque group (n=35)</td>
<td>0.65±0.20</td>
<td>0.86±0.10</td>
</tr>
<tr>
<td>χ²</td>
<td>2.151</td>
<td>2.536</td>
</tr>
<tr>
<td>P</td>
<td>0.034</td>
<td>0.013</td>
</tr>
</tbody>
</table>

**Comparison of coronary stenosis rates**

Ninety-five patients were diagnosed by using IVUS, with 17 cases of mild coronary stenosis, 28 cases of moderate stenosis, and 50 cases of severe stenosis. It was clear that the unstable plaque group yielded a markedly higher stenosis rate of (64.29±10.46)%, in contrast to the rate of (46.07±8.10) in the stable plaque group (P<0.05) (Table 3).

### Table 3. Comparison of coronary stenosis rates between stable and unstable groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Stenosis rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stable plaque group (n=60)</td>
<td>64.29±10.46</td>
</tr>
<tr>
<td>Unstable plaque group (n=35)</td>
<td>46.07±8.10</td>
</tr>
<tr>
<td>t</td>
<td>8.864</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Comparison of IVUS measurement results of coronary artery stenosis lesions**

The extravascular elastic membrane area of the two groups were (14.34±2.30) mm² and (14.45±2.41) mm², respectively, which displayed no great disparity between the two groups (P>0.05). The plaque thickness and plaque area of the stable plaque group were (2.37±0.85) mm and (0.52±0.07) mm², and those of the unstable plaque group were (3.67±1.04) mm² and (0.65±0.11) mm². Higher indicators regarding the plaque thickness and plaque area were observed in the unstable plaque group than the stable plaque group (P<0.05). See Table 4.

**Risk factors affecting the stability of coronary plaque**

The general data, ultrasound characteristics, and laboratory indicators of the two groups of
patients were used as independent variables, and unstable plaques were used as dependent variables. The univariate regression analysis showed that the eccentricity index (<0.5), remodeling index (<0.95), plaque area (<0.5 mm²), and plaque thickness (<3.0 mm) were risk factors of unstable plaque, as shown in Table 5. The multivariate logistic regression analysis showed eccentricity index, remodeling index, plaque thickness, and plaque area, stenosis rate, HDL-C, Hcy, and hs-CRP were independent risk factors for unstable plaque (P<0.05) (See Table 6).

### Discussion

As a public health concern that jeopardizes people’s health, CHD develops progressively and remains a leading cause of high mortality with a somber prognosis [6]. Coronary arteries mainly supply blood to the heart, and heart function is closely related to the ability for cardiovascular blood supply [7]. However, vascular stenosis causes hemodynamic changes if there are plaques in the blood vessels, which will lead to myocardial ischemia and insufficient blood supply to the myocardium, resulting in CHD [8]. Cumulative evidence revealed [9] that the rupture or shedding of unstable plaques can increase the disability and mortality of patients. Therefore, it is of paramount significance to assess the stability of coronary artery plaque for clinical judgment and treatment of CHD.

Coronary angiography has been considered the gold standard of coronary artery morphology, as it can clearly display the two-dimensional image of the vascular lumen and evaluate the degree of stenosis. However, it is susceptible to the reference segment of the blood vessel and the projection angle, which may result in an inaccurate determination of the lesion nature [10]. IVUS, as a biologic examination, has become one of the mainstream techniques of interventional therapy. Depending on the principle of ultrasound reflection imaging to display the thickness of coronary plaques, it can not only intuitively measure the lumen area, and distinguish the shape and size of plaques, but also obtain the blood flow characteristics of the coronary arteries, measure the blood flow velocity, and evaluate the degree of arterial stenosis [11-13]. In addition, IVUS can qualitatively and quantitatively analyze coronary artery wall thickness, lumen inner diameter, plaque area, and plaque load based on different frequency spectra, measure plaque properties, and evaluate plaque stability [14]. The results of this study showed that 35 of 95 patients had unstable plaques detected by IVUS, with a detection rate of 36.84%; a notable difference was witnessed in HDL-C, hs-CRP, and Hcy between the two groups (P<0.05). IVUS is mainly used for vascular cross-sectional imaging, which can accurately present the structural information of the vascular wall, qualitatively and quantitatively analyze the vascular wall, vascular cavity, and atherosclerotic plaque to reflect the phenomenon of vascular remodeling [15]. The comparison of the eccentricity index and reconstruction index between the two groups in this study was significant (P<0.05); 17 of 95 patients in this study were diagnosed by IVUS with mild coronary stenosis.
28 cases with moderate stenosis, and 50 cases with severe stenosis. The stenosis rate, plaque thickness, and plaque area indexes of the unstable plaque group were much higher than those of the stable plaque group.

Plaque instability invariably gives rise to cardiovascular disease, and stable plaques may also develop into unstable plaques with the development of the plaques, leading to bleeding, ulcers or thrombosis, subsequently coronary artery infarction [16]. In addition, in the process of plaque formation, the damaged inner membrane would give rise to unstable plaques, which can cause blood clotting and thrombus formation. The underlying pathogenesis of CHD is currently obscure, in spite of a great body of evidence suggesting that immune mechanisms and inflammatory reactions play an important role in the development of atherosclerosis and thrombosis [17]. IVUS uses an ultrasound probe to obtain cross-sectional images of blood vessels, and performs quantitative and qualitative analysis of coronary artery lumen diameter, wall thickness, plaque area, and plaque load based on different frequency spectra, detects plaque properties, and evaluates plaque vulnerability. Existing studies have shown that most of the ruptured plaques in patients with acute coronary syndromes show obvious eccentricity and positive remodeling characteristics, and unstable plaques often appear as eccentric lipid plaques; the plaque load is significantly greater than that of unstable plaques. The main characteristics of vulnerable plaque are fibrous cap lysis and thinning, larger lipid necrosis nucleus, and plaque load has a greater correlation with vulnerability. Binary logistic regression analysis in this study showed that the eccentricity index, reconstruction index, plaque thickness, plaque area, stenosis rate, HDL-C, Hcy, and hs-CRP were independent risk factors of unstable plaques (P<0.05). HDL-C is mainly secreted and produced in the liver and small intestine, exerting anti-infection, anti-oxidation, repairing vascular endothelial damage, and inhibiting platelet aggregation function, and these functions are closely involved in the occurrence and development of cardiovascular and cerebrovascular diseases triggered by coronary atherosclerosis. The condition of patients with unstable plaque is closely related to the serum hs-CRP level. The existence of serum hs-CRP can lead to the occurrence and development of plaque lesions in patients with unstable plaques, and serum hs-CRP level is closely related to lipid plaques. Scholars have found [18] that the incidence of coronary atherosclerosis is negatively correlated with the level of HDL-C, and that the expression level of HDL-C<1.0 mmol/L is an independent risk factor for patients with CHD. Clinically, HDL-C is also used as a predictor of cardiovascular disease risk [19]. Hcy is a sulfur-containing amino acid, and elevated Hcy is one of the risk factors for CHD [20]. It can damage the function of vascular endothelial cells and promote the development of atherosclerosis by affecting immune response, inflammatory factors, and oxidative stress. The level of hs-CRP can effectively reflect the intensity of the inflammatory response in atherosclerotic plaques. The release of hs-CRP and Hcy can stimulate fibroblasts and smooth muscle cells to migrate to the intima, and boost the formation of new fibrous tissue [21].

Overall, IVUS combined with multivariate analysis is a promising technique to accurately assess plaque stability.

Disclosure of conflict of interest

None.
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