Study on the levels of uric acid and high-sensitivity C-reactive protein in ACS patients and their relationships with the extent of the coronary artery lesion

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Abstract. – OBJECTIVE: We evaluated uric acid (UA) and high-sensitivity C-reactive protein (hs-CRP) levels in different clinical types of acute coronary syndromes (ACS) and in relationship with the severity of coronary artery lesions. Furthermore, we explored its clinical significance.

PATIENTS AND METHODS: From June 2013 to January 2015, we studied patients in their first onset of symptoms and hospitalization for coronary angiography. According to coronary angiography results, we divided patients into two groups: 93 patients with ACS and 30 patients with normal coronary arteries as the control group. ACS patients were divided further into three subgroups: patients with ST-segment elevation myocardial infarction (STEMI) (n=34); patients with non-ST segment elevation myocardial infarction (NSTEMI) (n=29); and patients with unstable angina (n=30). According to their Gensini scores, patients were divided into mild, moderate and severe groups. We compared UA and hs-CRP levels and the relationship with Gensini scores between different groups.

RESULTS: UA and hs-CRP levels in the ACS group were higher than those in the control group (p < 0.05). UA and hs-CRP levels in the STEMI group were higher than those in the NSTEMI unstable angina and control groups (p < 0.05). UA and hs-CRP levels in the NSTEMI patients were higher than those in the unstable angina patients were higher than those in the control group (p < 0.05). UA and hs-CRP levels in the unstable angina patients were higher than those in the control group (p < 0.05). hs-CRP levels in the STEMI patients were higher than the other groups (p < 0.05). hs-CRP levels in the NSTEMI patients were higher than the unstable angina and the control groups (p < 0.05) while hs-CRP levels in the unstable angina patients were higher than the control group (p < 0.05). Additionally, according to the Gensini score group, we discovered that ACS patients in the severe group had higher hs-CRP levels than the other three groups (p < 0.05) while the moderate group had higher levels than the other two groups (p < 0.05). The mild group had higher levels than the control group (p < 0.05). Correlation analysis suggested that UA levels and Gensini scores had a positive correlation (p < 0.05). hs-CRP levels and Gensini scores also showed a positive correlation (p < 0.05). CONCLUSIONS: UA and hs-CRP levels should be considered as factors to use in the risk stratification in ACS patients.

Key Words: Acute coronary syndromes, Uric acid, High sensitivity C-reactive protein, Severity of the coronary artery.

Introduction

Acute coronary syndromes (ACS) refer to a condition with acute myocardial ischemia and necrosis resulting from severe coronary artery stenosis and even occlusion. It is caused by intracoronary plaque rupture, vasospasm and consequent platelet adhesion, aggregation and secondary thrombosis.¹² It poses a serious threat to human life and shows a low aging tendency. The inflammatory response and the stress of the heart itself may participate in the ACS process. In this study, we evaluated and compared the levels
of uric acid (UA) and high-sensitivity C-reactive protein (hs-CRP) in ACS patients. We believe that our results may provide a theoretical basis for the better understanding of prevention and the treatment of ACS.

Patients and Methods

Patients

There were 93 ACS patients who had symptoms for the first time. They were admitted to the hospital and assessed with coronary arteriography in our hospital from June 2013 to January 2015. There were 47 males and 46 females with the mean age of 60.17 ± 15.30 years (45-75 years old). They were divided into three groups according to their clinical diagnosis. There were 34 patients with ST-segment elevation myocardial infarction (STEMI), 29 patients with non ST-segment elevation myocardial infarction (NSTEMI), and 30 patients with unstable angina.

According to the results of a coronary angiogram and the Gensini scores reflecting the severity of coronary artery disease, they were divided into three groups: (i) the mild severity group with scores below 50 (n=29); (ii) the medium severity group with scores between 50 to 100 (n=33); and (iii) the severe group with scores greater than 100 scores (n=31). Additionally, another 30 patients represented the normal coronary control group.

All patients met the ACS diagnostic criteria formulated by the American College of Cardiology/American Heart Association (ACC/AHA) in 2007. Coronary angiography was applied to all patients until the clinical data was complete. Exclusion criteria were as follows: (i) patients with other heart diseases; patients with severe heart failure (cardiac insufficiency grade III-IV) and liver and kidney function deficiency; (ii) patients with acute or chronic concurrent infection, hematologic disease, malignant tumors, rheumatism connective tissues and other immune system diseases; (iii) patients with recent surgery or wounded patients and patients with previous PCI operation history; (iv) patients with diabetes mellitus and other endocrine diseases; (v) patients with cerebrovascular disease; and (vi) patients with peripheral vascular disease.

UA Determination

Fasting vein blood samples (5 ml) were collected from all patients. UA level was determined by single enzyme method using a Hitachi analyzer model 7600 (Hitachi, Tokyo, Japan).

hs-CRP Determination

Vein blood samples (5 ml) were collected in separation gel tube. The supernatant was collected and the hs-CRP in the supernatant was determined by chemiluminescent immunoassay assay using luminol determinator (Stratec, Birkenfeld, Germany).

Coronary Angiogram

Patients took 300 mg of aspirin and 300 to 600 mg of clopidogrel before the operation and after the informed consent was obtained from patients’ family members. Patients were assessed with a coronary angiogram in the catheter room equipped with a full-digital C-arm X-ray cardiovascular angiographic system (Philips, Amsterdam, The Netherlands). Left coronary artery had at least six projected positions. The right coronary artery had at least three projected positions. Other positions were also projected when necessary until each segment of the coronary artery was fully displayed. All operations were completed by experienced cardiologists and assessed by two experienced cardiac intervention physicians. The severity of coronary artery stenosis was determined by the internationally recognized visual estimation method. This was calculated by determining the percentage of diameter decrease at the site of stenosis, inner diameter of a normal coronary at proximal end and a distal end adjacent to the stenotic segments.

Statistical Analysis

SPSS 22.0 software (IBM, Armonk, NY, USA) was used to perform statistical analysis. Measurement data were expressed by mean±standard deviation (x±s).

Comparison between the two groups was tested by t-test. The comparisons among groups were conducted using Fisher’s Least Significant Difference (LSD). The pairwise comparison among groups was tested by SNK-q, and p < 0.05 had statistical significance. The comparison of ratio was tested by chi-square ($\chi^2$). The comparison of diverse sample rate was tested by chi-square of lines×table data, and p < 0.05 had statistical significance. The analysis of correlation among variations was completed by adopting Spearman rank, and p < 0.05 showed statistical significant difference.

Results

Comparison of Baseline Information

There were no significant statistical differences between patients in the ACS group and patients...
in the SA and normal control groups in terms of gender, age, body mass index (BMI), smoking history, drinking history, hypertension history, total cholesterol, triacylglycerol, low density lipoprotein and high-density lipoprotein ($p > 0.05$). There were no statistical differences between patients in each ACS subgroup and patients in the SA and the control groups ($p > 0.05$).

**Comparison of UA and hs-CRP Level in ACS Patients, Including the Subgroups of Different Clinical Types**

We found that the UA and hs-CRP levels in the ACS group were higher than that of the control group. This difference had statistical significance ($p < 0.05$).

The ACS group was divided into three subgroups according to different clinical types: STEMI, NSTEMI and unstable angina. UA level in the STEMI group was higher than that of other two groups ($p < 0.05$) and UA level in the NSTEMI group was higher than that in the unstable angina and the control groups ($p < 0.05$). UA level in the unstable angina group was higher than that of the control group ($p < 0.05$).

hs-CRP level in the STEMI group was higher than that in the other groups ($p < 0.05$). hs-CRP level in the NSTEMI group was higher than that in the unstable angina and the control groups ($p < 0.05$), while the hs-CRP level in the unstable angina group was higher than that in the control group ($p < 0.05$).

**Correlation Between UA and hs-CRP Levels and Gensini Scores**

To verify the correlation between UA and hs-CRP levels and the severity of coronary artery disease, we performed Spearman-related analysis between variations. Our results showed that UA and hs-CRP levels increased along with the rise of Gensini scores. UA levels demonstrated positive correlation with Gensini scores ($r = 0.760; p < 0.05$); and hs-CRP levels had a positive correlation with Gensini scores ($r = 0.801; p < 0.05$).

**Discussion**

In recent years, with changes in living standards and dietary patterns and the increase of atherosclerosis-related risk factors, the occurrence of coronary heart diseases tends to be increasing. The incidence of ACS also shows an increasing tendency, and inflammatory response is an important factor to be considered in this condition. In order to provide some guidance for prevention and hospitalization, a rapid and effective method to assess the ACS risk level is urgently needed.

UA levels often increase with hypertension, lipid metabolism dysfunction and obesity. The increase of UA level may result in cardiovascular disease and can play an important role in the occurrence and development of ACS. UA can pro-

### Table I. Comparison of UA and hs-CRP levels between ACS patients and patients in the SA group and control group.

<table>
<thead>
<tr>
<th>Groups</th>
<th>UA (μmol/L)</th>
<th>hs-CRP (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACS</td>
<td>410.15 ± 100.34</td>
<td>12.84 ± 6.43</td>
</tr>
<tr>
<td>STEMI</td>
<td>435.09 ± 114.68</td>
<td>16.96 ± 7.56</td>
</tr>
<tr>
<td>NSTEMI</td>
<td>394.47 ± 107.51</td>
<td>10.54 ± 5.48</td>
</tr>
<tr>
<td>Unstable angina</td>
<td>379.82 ± 89.27</td>
<td>9.71 ± 4.32</td>
</tr>
<tr>
<td>Control group</td>
<td>296.26 ± 60.09</td>
<td>2.23 ± 1.10</td>
</tr>
</tbody>
</table>

Note: § shows the comparison with the control group ($p < 0.05$).

### Table II. Comparison of UA and hs-CRP level in ACS patients with diversified severity of coronary artery disease.

<table>
<thead>
<tr>
<th>Groups</th>
<th>UA (μmol/L)</th>
<th>hs-CRP (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe group</td>
<td>430.63 ± 109.79</td>
<td>15.90 ± 6.94</td>
</tr>
<tr>
<td>Medium severity group</td>
<td>400.51 ± 104.08</td>
<td>11.82 ± 6.79</td>
</tr>
<tr>
<td>Mild severity group</td>
<td>381.09 ± 90.17</td>
<td>10.75 ± 5.46</td>
</tr>
<tr>
<td>Control group</td>
<td>296.26 ± 60.09</td>
<td>2.23 ± 1.10</td>
</tr>
</tbody>
</table>

Note: * shows the comparison with the control group ($p < 0.0001$); ** shows the comparison with the mild severity group ($p < 0.001$); † shows the comparison with the medium severity group ($p < 0.0001$).
mote low-density lipoprotein cholesterol oxidation and lipid peroxidation, and lead to a rise in oxygen radicals, participating in the inflammatory response and accelerating the formation of atherosclerosis plaque. UA can activate blood platelets and promote platelet adhesion and aggregation. UA crystals can also be deposited in the endarterium with vessel wall injury, which results in a decline in fibrinolytic function and promotes the formation of thrombus. Prior studies showed that the increase in UA level was related to the independent and significant risk factors of coronary heart disease and was an independent predictive factor for the occurrence of cardiovascular events.

Our findings showed that UA level in ACS patients increased significantly, and the UA level in the STEMI group was meaningfully higher than that in the other groups. UA level in the NSTEMI group was obviously higher than that in the control group \( (p < 0.05) \), and the UA level in the unstable angina group was significantly higher than that in the control group.

UA levels increased with the rise in the severity of coronary artery disease and were positively correlated with Gensini scores. These results revealed that the increase in the UA levels in ACS patients contributed to the formation of intracoronary plaques, plaque rupture and the formation of thrombus on the surface of the coronary artery. It also can offer an early detection of the severity of ACS patients.

The CRP level in healthy individuals is generally lower than 3 mg/L. The CRP level in our study was tested by the high-sensitivity test method (lower than 0.3 mg/L). This test measures the high-sensitivity C-reactive protein (hs-CRP) which is a kind of acute phase reaction protein involved in nonspecific immunity. It is produced by the stimulation of liver and epithelial cells by inflammatory lymphoid factors. hs-CRP is known as a sensitive biomarker that can reflect the stability of atherosclerotic plaque. Recent reports showed that hs-CRP is an independent risk factor of ACS, and an independent index that can predict the prognosis of ACS patients.

We discovered that hs-CRP can independently predict the occurrence of future cardiovascular events in ACS patients. Additionally, we observed that hs-CRP had a positive correlation with the complexity of patients’ coronary artery lesions. During the follow-up visits, we have found that the hs-CRP level in the adverse end events group was significantly higher than that in the non-adverse end events group.

Our results demonstrated that the hs-CRP level in the ACS group was significantly higher than that of patients in the healthy control group. Sano et al conducted a study on 90 patients with acute myocardium infarction who were admitted to the hospital within 6 hours from the occurrence of symptoms. Their results showed that the situation of plaque rupture observed in the high hs-CRP group \( (\geq 3 \text{ mg/L}) \) was significantly more severe than that observed in the normal hs-CRP group \( (<3 \text{ mg/L}) \). This suggested that hs-CRP level can reflect the stability of coronary atherosclerotic plaque and as a reliable biomarker can predict the prognosis of AMI patients. According to our research, hs-CRP levels also increased with the rise of the clinical subtypes and coronary artery lesion severity. hs-CRP had a positive correlation with the severity of coronary artery lesions.

These results suggest that hs-CRP can be used as a standard for the instability of coronary atherosclerosis lesions. More specifically, higher hs-CRP levels are associated with wider scope of intracoronary atherosclerotic plaque and the severity of plaque burden. Additionally, stronger local inflammation response and the greater severity of coronary artery disease, were associated with greater myocardial infarction risk and the aggravation of myocardial anoxia and ischemia.

Our results showed that hs-CRP is one of the factors for predicting the risks of acute coronary syndrome and can be used to guide the risk stratification of ACS patients in clinic.

**Conclusions**

UA and hs-CRP levels should be considered as factors targeted for risk stratification in ACS patients. This can enable clinicians to take decisive, timely and effective measures to reduce death rates, prolong the lives of patients and improve their quality of life.

**Conflicts of interest**

The authors declare no conflicts of interest.

**References**

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