Clinical Research

Clinical correlation between myeloperoxidase and acute coronary syndrome

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Objective To study whether myeloperoxidase (MPO) can provide prognostic information in patients with acute coronary syndromes (ACS). Methods The study population consisted of 274 consecutive patients with ACS. All patients underwent coronary angiography which showed significant coronary artery disease and blood samples were collected at admission. Follow-ups were scheduled at 1, 3, and 6 months. The end point included cardiac death, acute myocardial infarction (MI), percutaneous or surgical revascularization. Results Patients with elevated MPO serum levels (MPO ≥72.2 AU/L) were more likely to have diabetics and had a history of coronary events. Kaplan-Meier event rate curves with accumulative incidence of end point at 6-month follow-up in the MPO ≥72.2 AU/L group was significantly higher than in MPO <72.2 AU/L group. Conclusions MPO may be a powerful predictor of adverse outcome in patients with ACS. (J Geriatr Cardiol 2007;4:209-212)

Key Words myeloperoxidase; acute coronary syndromes

Introduction

Levels of cardiac troponins, which are diagnostic biologic markers of myocardial necrosis, are used either alone or in conjunction with levels of C-reactive protein (CRP) as prognostic indicators of myocardial infarction.1,2 Many patients with chest pain have normal levels of troponins at presentation but subsequently have a myocardial infarction, and require revascularization. Additional biochemical measures, ideally based on the pathophysiology of plaque vulnerability, are needed. There is growing evidence that myocardial cell injury is not only related to platelet activation but also preceded by recruitment and activation of polymorphonuclear neutrophils (PMNs)3-4. One of the principal mediators secreted on PMN activation is myeloperoxidase (MPO), a hemoprotein traditionally viewed as a microbicidal enzyme.5 However, there is new evidence that MPO also displays potent proatherogenic properties. For example, MPO levels are elevated in persons with angiographically documented cardiovascular disease6 and within culprit lesions prone to rupture.7 The activation of leukocytes prompts the secretion of MPO and the generation of oxidants in host defense.8 MPO has been linked to the development of lipid-laden soft plaque,9,10 the activation of protease cascades affecting the stability and thrombogenicity of plaque,11,12 the production of cytotoxic and prothrombogenic oxidized lipids,10,13 and the consumption of nitric oxide, leading to vasoconstriction.14,15

In this study, we investigated whether MPO can provide prognostic information in patients with acute coronary syndromes (ACS).

Methods

Study subjects

The study population consisted of 274 consecutive patients with ACS who underwent coronary angiography for suspected or known coronary atherosclerosis at Anzhen Hospital, Capital University of Medical Sciences, Beijing from August 2005 to December 2005. There were 191 men, whose average age was 61.4±10.8 years and 83 women whose average age was 61.4±10.8 years.

The diagnostic criteria for ACS are according to the American College of Cardiology/American Heart Association (ACC/AHA) guideline for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction in 2002, the ACC/AHA guidelines for the management of patients with acute myocardial infarction in 1999, and the ACC/AHA/ACP-ASIM guidelines for the management of patients with chronic stable angina in 1999.16

Patients with pregnancy, acute infection, serious liver or kidney disease, severe heart failure, malignant tumor, rheumatism, cerebral stroke, trauma, or a history of surgery...
during the previous month were excluded.

Measurement of circulating MPO
The blood samples of STEMI (ST elevated myocardial infarction) patients were collected in ethylenediamine tetraacetic acid (EDTA) containing tube within 3 hours of admission; other patients’ blood samples were collected within 8 hours of admission before administration of any anticoagulant. Five milliliter venous blood was collected, centrifuged at 1500r/minute for 15 minutes and then blood serum was stored at –70° C.

Myeloperoxidase IgG Elisa Kit was provided by Zeus Scientific, Inc. (The Netherlands,LO:05030123). Fully automatic enzyme labeling instrument was made by Labsystems Dragon Inc. (Finland, type: Wellscan MK3).

Study protocol
In patients with ACS, according to MPO serum, accumulative incidence of end points (cardiac death, MI, percutaneous or surgical revascularization) was compared between the 2 groups of high MPO level (≥ 72.2 AUU/L) or low MPO level (< 72.3 AUU/L) at 6 month follow-up.

Coronary angiography
Coronary arteries were imaged by the Judkins technique with 5F catheters. The severity of coronary atherosclerosis was defined by the Gensini score system; the Gensini score, a measure of the extent of myocardial ischemia, was computed by assigning the severity score to each coronary lesion, according to the degree of luminal narrowing and its vascular territory importance. Reduction in the diameter of the lumen and the roentgenographic appearance of concentric lesion as well as eccentric plaques were evaluated (reduction of 25%, 50%, 75%, 90%, 99% and complete occlusion values were given Gensini scores of 1, 2, 4, 8, 16 and 32, respectively). According to the functional significance of the myocardial area supplied by this segment, a multiplier was assigned to each principal vascular segment; the left main coronary artery ×5; the proximal segment of the left anterior descending (LAD) ×2.5; the proximal segment of the circumflex artery (LAD) ×2.5; the mid-segment of LAD ×1.5; the right coronary artery, the distal segment of the LAD, the artery, and the obtuse marginal artery, ×1; and others, ×0.5.17

Statistical analysis
Statistical analyses were performed using SPSS 12.0 for Windows. The data were expressed as mean ±SD. According to MPO serum level, Kaplan-Meier event rate curves show accumulative incidence of end point of 6-month follow-up.

Results
Baseline characteristics
There were few significant differences in the baseline characteristics between high MPO level and low MPO level groups. Patients with elevated MPO serum levels (MPO ≥ 72.2 AUU/L) were more likely to have diabetics, a history of coronary events and more severe coronary lesions. (Table 1)

Serum MPO and CRP levels according to baseline TnI status
Serum MPO levels did not differ between patients with serum TnI levels above and below 0.05 ng/ml, whereas C-reactive protein(CRP) levels were significantly higher in

Table 1 Baseline characteristics in patients with ACS (n=274)

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>MPO&lt;72.2 AUU/L (n=137)</th>
<th>MPO≥72.2 AUU/L (n=137)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age(years)</td>
<td>60.4±11.3</td>
<td>62.4±14.3</td>
<td>0.78</td>
</tr>
<tr>
<td>Sex(male/female)</td>
<td>94/43</td>
<td>101/36</td>
<td>0.46</td>
</tr>
<tr>
<td>Risk factors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes (n)</td>
<td>24/137(18)</td>
<td>46/137(34)</td>
<td>0.005</td>
</tr>
<tr>
<td>Hypertension (n)</td>
<td>34/137(25)</td>
<td>40/137(29)</td>
<td>0.55</td>
</tr>
<tr>
<td>Smoking (n)</td>
<td>47/137(34)</td>
<td>43/137(31)</td>
<td>0.32</td>
</tr>
<tr>
<td>MI history (n)</td>
<td>27/137(20)</td>
<td>38/137(28)</td>
<td>0.04</td>
</tr>
<tr>
<td>PTCA history (n)</td>
<td>29/137(21)</td>
<td>42/137(31)</td>
<td>0.01</td>
</tr>
<tr>
<td>TG (mg/dl)</td>
<td>181.1±32.4</td>
<td>184.2±33.1</td>
<td>0.75</td>
</tr>
<tr>
<td>TC (mg/dl)</td>
<td>182.7±43.1</td>
<td>180.8±36.5</td>
<td>0.84</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>35.3±9.6</td>
<td>32.2±9.1</td>
<td>0.45</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>120.3±33.6</td>
<td>129.0±33.7</td>
<td>0.21</td>
</tr>
<tr>
<td>Blood glucose (mg/dl)</td>
<td>91.1±10.2</td>
<td>99.4±12.4</td>
<td>0.03</td>
</tr>
<tr>
<td>Gensini scores</td>
<td>59.2±30.1</td>
<td>62.1±31.2</td>
<td>0.04</td>
</tr>
</tbody>
</table>
patients with TnI levels < 0.05 ng/ml (Table 2). In patients with ACS, according to MPO serum (median 72.2 AUU/L; n=274), accumulative incidence of end point of 6-month follow-up of MPO ≥ 72.2 AUU/L group compared with MPO < 72.2 AUU/L group was shown in Figure 1.

The Kaplan-Meier event rate curves showed that, ac-

Table 2 MPO and CRP serum levels according to baseline TnI status (n=274)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>TnI ≥ 0.05 ng/ml</th>
<th>TnI &lt; 0.05 ng/ml</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MPO (AUU/L)</td>
<td>67.8±22.3</td>
<td>71.8±25.1</td>
<td>0.51</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>3.71±1.8</td>
<td>7.8±3.9</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Fig 1 Kaplan-Meier event rate curves show in patients with ACS, according to MPO serum (median 72.2 AUU/L; n=274), accumulative incidence of end point at 6-month follow-up of MPO ≥ 72.2 AUU/L group compared with MPO < 72.2 AUU/L group.

Discussion

ACS is characterized by increased platelet activation and aggregation within the coronary circulation. Thrombus formation at a ruptured or eroded plaque and distal embolization of platelet aggregates eventually lead to epicardial vessel occlusion and then myocyte necrosis. The occurrence of occlusion at the microvascular level is observed in ACS by measuring the release of troponins, which have emerged as powerful tools for risk assessment and therapeutic management of patients with ACS. There is growing evidence that myocardial cell injury not only is related to platelet activation but also is preceded by recruitment and activation of PMNs. PMNs, despite their apparent insignificance in coronary atherogenesis, have been shown to increasingly undergo degranulation within the coronary circulation in ACS. One of the principal mediators secreted on PMN activation is MPO, a hemoprotein traditionally viewed as a microbicidal enzyme. In addition, there is accumulating evidence that MPO also displays potent proatherogenic properties. For example, MPO can oxidize LDL cholesterol, thereby propagating uptake by macrophages and perpetuating foam cell formation. Furthermore, MPO has been shown to activate metalloproteinases and promote destabilization and rupture of the atherosclerotic plaque.

In this present study, MPO levels were equally distributed among patients with low and high TnI serum levels (Table 2), which indicated at elevated MPO serum levels were not only related to myocardial injury. More importantly, MPO could also identify patients at risk for cardiovascular events who had low baseline TnI serum levels. These data suggested that MPO release actually precede myocardial injury and that MPO elevation identified patients with unstable atherosclerotic plaque formation even before complete microvascular obstruction. So MPO may be a good candidate for risk stratification in patients with ACS and as an independent prognostic determinant of clinical outcome in patients with ACS.

MPO levels did not correlate with C-reactive protein, a systemic marker of inflammation and the most well-characterized index for identifying patients with stable coronary artery disease who are at risk for future cardiovascular events. Because C-reactive protein correlated with TnI levels (Table 2), elevated C-reactive protein serum levels most likely reflect both an inflammatory response and myocardial injury, which suggests that recruitment and degranulation of PMNs be a primary event and be followed by release of other systemic mediators and acute-phase proteins.

In conclusion, plasma MPO levels predict cardiovascular risks independent of the levels of C-reactive protein and other markers on inflammation. An initial plasma MPO level in patients who presented to the emergency department with chest pain provided useful information in determining the risk of myocardial infarction, revascularization, and major adverse cardiac events during the subsequent six months. Perhaps more importantly, even in patients in whom a myocardial infarction was ruled out on the basis of serial measurements of troponin I, an elevated MPO level at presentation was predictive of subsequent major adverse cardiovascular outcomes.

Acknowledgement

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References

2. Sabatine MS, Morrow DA, de Lemos JA, et al. Multimarker


