Diagnostic Use of Serum Deoxyribonuclease I Activity as a Novel Early-Phase Marker in Acute Myocardial Infarction

Yasuaki Kawai, MD; Masahiro Yoshida, MD; Kenichiro Arakawa, MD; Teruhiko Kumamoto, MD; Norihiro Morikawa, MD; Katsuhiko Masamura, MD; Hiroshi Tada, MD; Sachiko Ito, MD; Hiroshi Hoshizaki, MD; Shigeru Oshima, MD; Koichi Taniguchi, MD; Hidekazu Terasawa, MD; Isamu Miyamori, MD; Koichiro Kishi, MD; Toshihiro Yasuda, PhD

Methods and Results—Serum samples were collected from the patients with AMI, unstable angina pectoris, stable angina pectoris, and other diseases. Levels of serum deoxyribonuclease I (DNase I) activity in the patients were determined. An abrupt elevation of serum DNase I activity was observed within approximately 3 hours of the onset of symptoms in patients with AMI, with significantly higher activity levels (21.7 ± 5.10 U/L) in this group compared with the other groups with unstable angina pectoris (10.4 ± 4.41 U/L), angina pectoris (10.8 ± 3.70 U/L), and other diseases (9.22 ± 4.16 U/L). Levels of the DNase I activity in serum then exhibited a marked time-dependent decline within 12 hours and had returned to basal levels within 24 hours.

Conclusions—We suggest that serum DNase I activity could be used as a new diagnostic marker for the early detection of AMI. (Circulation. 2004;109:2398-2400.)

Key Words: myocardial infarction • enzymes • diagnosis
troponin T concentrations were determined using conventional methods. In this study, the cutoff levels for concentration of CK-MB and troponin T were 5.20 and 0.01 μg/L, respectively.

**Statistical Analysis**

Data were expressed as mean±SD. Statistical comparison between patient groups was performed by ANOVA using StatView software. Differences were considered significant at P<0.05.

**Results**

Serum DNase I activity in healthy subjects was determined to be 10.7±3.60 U/L, and the upper limit of the normal range of serum DNase I activity was considered to be 17.9 U/L (mean±2SD). When the serum DNase I activity level was measured periodically in the AMI group, a marked increase in serum DNase I activity was observed immediately after the onset of chest pain, with the maximal level being reached within approximately 3 hours and a gradual decline to basal levels within 24 hours (Figure, A and B). Thus, there was an abrupt and transient elevation in serum DNase I activity in patients with AMI in the early stage soon after the onset of chest pain.

In 18 patients with AMI admitted to our hospitals within 3 hours of the onset of chest pain, the mean serum DNase I activity level was significantly higher than that found in the UAP, AP, or OD group (Table and Figure, C); levels of the activity in the patients with AHF, CHF, CRF, stroke, and trauma were 7.91±3.31, 10.0±4.10, 8.00±3.75, 10.9±3.70, and 7.41±3.50 U/L, respectively. Furthermore, the serum DNase I activity level (8.50±2.80 U/L) in the 9 patients with CPS who were initially considered to have AMI on clinical grounds but found to have no evidence of myocardial infarction on follow-up assessment was within the normal range. Therefore, this elevation in the serum activity level seems to be specific for AMI when compared with other forms of CHD in which onset of acute chest pain is a feature.

When we examined the relationship between serum DNase I activity level in the AMI group and the time delay between symptom onset and hospital admission, the mean serum DNase I activity subsided over time and reached basal levels within 24 hours; the mean value between 0 and 3 hours was 21.7±5.10 U/L (n=18); between 3 and 6 hours was 14.1±2.50 U/L (n=15); between 6 and 12 hours was 10.5±4.20 U/L.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>AMI (n=18)</th>
<th>UAP (n=15)</th>
<th>AP (n=43)</th>
<th>OD (n=75)</th>
<th>Control (n=72)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, male/female, n</td>
<td>12/6</td>
<td>11/4</td>
<td>27/16</td>
<td>42/33</td>
<td>40/32</td>
</tr>
<tr>
<td>Age, y</td>
<td>68.4±9.80</td>
<td>65.0±14.9</td>
<td>70.2±7.50</td>
<td>62.1±17.3</td>
<td>40.1±21.6</td>
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<tr>
<td>Diabetes</td>
<td>47.9</td>
<td>36.4</td>
<td>54.4</td>
<td>25.3</td>
<td>0</td>
</tr>
<tr>
<td>Current smoking</td>
<td>55.1</td>
<td>60.0</td>
<td>54.5</td>
<td>49.3</td>
<td>39.0</td>
</tr>
<tr>
<td>Hypertension</td>
<td>67.8</td>
<td>45.5</td>
<td>58.1</td>
<td>39.4</td>
<td>0</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>64.2</td>
<td>45.5</td>
<td>58.1</td>
<td>21.1</td>
<td>0</td>
</tr>
<tr>
<td>Serum DNase I activity, U/L</td>
<td>21.7±5.10*</td>
<td>10.4±4.41</td>
<td>10.8±3.70</td>
<td>9.22±4.16</td>
<td>10.7±3.60</td>
</tr>
</tbody>
</table>

Values are mean±SD or percentages.

*P<0.0001 vs other groups.
DNase I has been postulated to be responsible for internucleosomal DNA degradation during apoptosis.\textsuperscript{5} Apoptosis is induced by ischemic injuries to myocardium in AMI,\textsuperscript{10,11} and myocyte death attributable to apoptosis in the failing heart has been demonstrated.\textsuperscript{12} Yao et al\textsuperscript{10} reported significant levels of DNase I to be detectable in the human myocardium. Therefore, it is plausible that the ischemic injury may recruit DNase I from the myocardium of patients with AMI. Additional clarification of the mechanism responsible for DNase I elevation and the physiological significance of DNase I in AMI will undoubtedly have important biological and clinical implications.

Serum DNase I activity was significantly elevated within 3 hours of the onset of acute chest pain in the patients with AMI, whereas the serum levels of CK-MB and troponin T were slightly elevated and exceeded the cutoff levels in approximately 45\% of those patients; we were thus able to detect the elevation of the serum DNase I activity earlier than that of CK-MB and troponin T. As an early marker for myocardial necrosis, the serum myoglobin level is a sensitive test but lacks cardiac specificity, because there may be an elevation in the serum levels of myoglobin secondary to musculoskeletal injury.\textsuperscript{13} However, the serum DNase I activity level does not rise after trauma, and surgical trauma has been reported to induce no elevation of the activity,\textsuperscript{14} suggesting that DNase I may be a more specific marker for AMI than myoglobin. Furthermore, there is a slight overlap between the levels of activity in patients with AMI and patients with OD (Figure, C). Because the latter patients do not suffer from chest pain, this overlap would not lower the diagnostic accuracy of serum DNase I activity testing. Thus, the serum DNase I level may be a useful clinical tool in the early diagnosis of AMI within approximately 3 hours of the onset of symptoms.

The results of the present study will facilitate future studies in larger numbers of patients to evaluate the enzyme as a useful biochemical marker with regard to specificity and sensitivity in comparison with the other cardiac markers, such as myoglobin and heart-type fatty-acid binding protein.\textsuperscript{15}

Acknowledgments
This study was supported in part by Grants-in-Aid from Japan Society for the Promotion of Science (14657111 to K. Kishi and 15209023 to T. Yasuda).

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Circulation. 2004;109:2398-2400; originally published online May 17, 2004; doi: 10.1161/01.CIR.0000129232.61483.43

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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