Changes in Creatine Kinase Activity in the Course of Acute Myocardial Infarction
Itzhak Weinberger, Jacob Fuchs, Zvi Rotenberg, Ehud Davidson, Delela Harel, and Jacob Agmon

Peak activity of creatine kinase (CK; EC 2.7.3.2) and its decline were determined in 380 patients with acute myocardial infarction (AMI) whose CK values had peaked after admission to the hospital. During hospitalization, 26 patients either died (14 patients) or experienced nonfatal re-infarction (12 patients). In 22 of these 26 patients CK activity decreased by <50% within 48 h after the peak value was measured. In all patients who did not die or develop re-infarction, CK activity decreased by >50% during the 48 h after the peak. Evidently the rate of decline of CK (i.e., whether more than or less than 50%) from its peak value during the 48 h after AMI may be helpful in assessing which patients are at high risk for developing re-infarction or dying.

Creatine kinase (CK; EC 2.7.3.2) activity is estimated in the course of ischemic heart disease as an aid in diagnosing acute myocardial infarction (AMI) (1, 2), in estimating infarct size (3–5), and in both immediate (6) and late (7, 8) prognostics. Most of these studies dealing with the correlation of CK activity concentrations and estimates of infarct size and prognosis relate the prognosis to the peak enzyme activity in serum, a value subject to influence by spontaneous reperfusion and infarct extension (9–12). Others (6, 7, 13, 14) have reported that measurements of peak enzyme activity alone cannot be used to predict mortality for the individual patient. In this study we investigated the characteristic patterns of CK activity during the course of AMI.

Patients and Methods

The study population consisted of 470 consecutive patients admitted to the Intensive Care Unit and Department of Medicine "A" of Beilinson Medical Center for AMI. The mean age of the subjects was 59 y (range 40–85 y); 385 were men and 85 were women. Blood was sampled for total CK on admission, at 6-h intervals during the first 48 h of hospitalization, and thereafter every 24 h for 10 days. CK was quantified by an optimized standard method (Boehringer, Mannheim, F.R.G.; cat. no. 126357, "CK N-acetyl-cysteine-activated") with a centrifugal analyzer (GRMSABE; Electro-Nucleonics, Inc., Fairfield, NJ). The normal reference intervals for CK in our laboratory by this method are 24–203 U/L for men and 24–175 U/L for women.

Diagnosis of AMI was based on standard criteria, including clinical history, evolutionary electrocardiographic findings, and serial quantification of cardiac enzymes (CK and lactate dehydrogenase, LD, EC 1.1.1.27) in serum indicating an increase of >50% from their normal values. Of 470 patients with AMI, 90 were excluded from the study because the CK activity in serum had peaked at or before admission, so that serial values measured for these patients in the hospital were declining. Results reported in our study are for the 380 patients with AMI whose measured CK activity peaked after they were admitted to the hospital.

We determined peak CK activity in serum and the rate of decline of CK 48 h after this peak, and related this to whether or not re-infarction or death followed admission. Re-infarction was diagnosed on the basis of the re-appearance of chest pain accompanied by electrocardiographic ST-T changes and an increase in cardiac enzymes by >50% over values measured before the episode.

We applied Student's t-test for two variables, comparing peak CK values and age in the groups of patients with and without re-infarction or death. We used the chi-square test to compare effects of sex, previous infarctions, and site of infarction between the two groups. The coronary-risk factors in the same groups were compared by the median test (15).

Results

In all our 380 study patients, peak values for CK occurred within 24 h after admission to the hospital. During the 10-day follow-up period, 26 of these patients (Table 1) either died (14 patients) or experienced nonfatal re-infarction (12 patients). All re-infarctions occurred between the seventh and tenth day of hospitalization. Patients who died did so between the sixth and ninth day of hospitalization. The cause of death in all patients was cardiogenic shock. Post-mortem examination revealed rupture of the myocardium in four of them. There were no statistically significant differences in age, sex, coronary-risk factors, previous infarction, or site of infarction between the group with and those without complications. Also, there was no statistically significant difference (P = 0.56) in mean CK values between the two groups of patients (Table 1).

After analyzing the CK curves, we investigated the decline in CK (from the highest value measured) by >50% in 48 h as a variable to be analyzed in relation to nonfatal re-infarction or death. In 22 of the 26 patients mentioned above (11 patients with nonfatal re-infarction and 11 patients who died), CK activities declined from peak values by <50% in 48 h; in the remaining four patients, CK activity declined by >50% from its peak value in 48 h. In all of the 354 patients with no complications, CK decreased by >50% from its peak value in 48 h (Table 1). Applying Bayesian analysis, we estimated the efficacy of the CK decrease in discriminating between those patients who developed complications and those who did not (Table 2). A decrease of <50% from the peak activity within 48 h was 100% specific and 85% sensitive for development of later complications.

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Table 1: Clinical and Enzymatic Data for AMI Patients with and without Complications

<table>
<thead>
<tr>
<th>Complications</th>
<th>No complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>26</td>
</tr>
<tr>
<td>Age, mean (range), y</td>
<td>68 (58–77)</td>
</tr>
<tr>
<td>Peak CK, mean (and SD), U/L</td>
<td>1126 (1004)</td>
</tr>
<tr>
<td>No. of patients with CK decline &gt;50% of peak value</td>
<td>4</td>
</tr>
</tbody>
</table>

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Table 2. Efficiency of the "CK Decrease" Test In Discriminating between Patients with and without Complications

<table>
<thead>
<tr>
<th>Complications</th>
<th>CK decrease</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;50% (true positive)</td>
</tr>
<tr>
<td>No complications</td>
<td>22</td>
</tr>
<tr>
<td>with complications</td>
<td>0</td>
</tr>
</tbody>
</table>

Sensitivity = 85%, specificity = 100%, efficiency = 99%, predictive value of a positive result = 100%, and predictive value of a negative result = 99%.

Discussion

These results show that patients in whom CK values decline by <50% of their peak value within 48 h after peaking have an increased risk of developing re-infarction or dying. This bad prognosis is not related to sex, previous myocardial infarction, site of infarction, or coronary-risk factors.

Moreover, according to our study, the peak CK value of the group with complications was not different from that of the group without complications (P = 0.8). Thus we hope to discredit the notion that the size of infarct may be estimated clinically from peak CK values.

Previous myocardial infarction and the site of infarction, especially anterior location, have been mentioned (5) as factors affecting short-term prognosis (6) after myocardial infarction. Our study, however, shows no statistically significant differences in infarction size between patients with re-infarction or who die and those without these outcomes.

In previous studies CK activities were measured and, from them, the size of the myocardial infarction was estimated (3, 12, 13, 16). The estimated size of the infarct was then related to left ventricular ejection fraction (17), hemodynamics (13, 18), and arrhythmias (19). Marmor et al. (20) calculated infarct size from CK activities and correlated this with Q-wave or non-Q-wave infarction. They found that patients with Q-wave infarction and higher CK values had a higher risk of mortality than did patients with non-Q-wave infarction. Scheimann and Abbott (21) found no differences in mortality between patients with Q-wave infarction and patients with non-Q-wave infarction and high peak CK values. However, the infarct mass as calculated from peak CK values was not predictive of mortality or development of cardiogenic shock in the individual patient (13). Madsen et al. (6) emphasized the importance of calculating the individual risk for a patient with myocardial infarction rather than categorizing the patient into a high- or low-risk group. Others (22, 23) tried to correlate immediate prognosis in patients after AMI according to clinical or hemodynamic subsets. Failure of CK to decline, as described in the present study, could be a marker for urgent therapeutic intervention to limit infarct size—such as early aortocoronary bypass grafting or percutaneous trans-coronary angioplasty (24). The finding of a single noninvasive clinical variable, as we report, may have an advantage over previous studies (6, 25) that suggested the use of complex multivariate analysis. As to the pathophysiological basis of our observation: theoretically, a slower decline of CK activity during the first 48–72 h after myocardial infarction may reflect a slower washout of CK from infarcted areas through severely narrowed coronary arteries (6).

In conclusion, the rate of decline of CK values may be helpful in determining which patients are at high risk of developing re-infarction or dying. This enzymatic marker may serve to indicate the need for urgent therapeutic intervention to limit infarct size.

References

22. Killip T, Kimbell JT. Treatment of myocardial infarction in a

