THE EFFECTS OF REPERFUSION OF INFARCT-RELATED CORONARY ARTERY ON SERUM CREATINE PHOSPHOKINASE AND LEFT VENTRICULAR FUNCTION

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In 31 patients with transmural myocardial infarction in whom coronary arteriography was performed within 8 hours after the onset of symptoms, we examined (1) the effect of restoration of coronary blood flow on serum CPK time-activity curve and (2) the relationship between cumulative CPKr and the left ventricular function in the chronic phase. We divided 31 patients into 2 groups: Group A consists of 19 patients in whom coronary reperfusion was established. Group B consists of 12 patients whose coronary artery remained occluded. In group A, the time required to reach peak serum CPK activity was significantly shorter than in group B. When comparing CPKr with percent abnormally contracting segment (%ACS) in 2 groups, correlation between CPKr and %ACS was not good, but it revealed linear relation in both group A and B. CPKr divided by %ACS (CPKr/%ACS) was significantly higher in group A than in group B.

We conclude that reperfusion of infarct-related coronary artery changes serum CPK time-activity curve resulting in earlier appearance of peak serum CPK and that infarct size cannot be estimated by serum CPK level alone.

THE spread of coronary care unit decreased the arrhythmic death of patients with acute myocardial infarction (MI) and its prognosis depends on the infarct size more than ever. As one of the indicators of infarct size, cumulative CPK release (CPKr) has been considered useful and precise method.1–8

Recently the coronary angiographic findings in the superacute phase of MI have been reported including those of patients in whom percutaneous transluminal coronary recanalization (PTCR) was performed9–12 but relationships between these coronary angiographic findings and serum CPK activity in the acute phase have not been fully clarified clinically. The experimental studies13,14 indicate that after reperfusion of an occluded coronary artery, serum CPK rises rapidly and reaches the peak significantly earlier and the peak level significantly higher than during a 24 hours occlusion.

The purposes of the present investigation were (1) to elucidate in man how the early restoration of infarct-related coronary arterial circulation effects on serum CPK curve, especially its peak and CPKr and (2) to determine whether the ameriolated coronary circulation changes the correlations between CPKr and left ventricular function in the chronic phase.

Key Words:
Early reperfusion
Serum CPK activity
Left ventricular function
Infarct size

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TABLE 1 SUMMARY OF 31 STUDY PATIENTS

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<th>No.</th>
<th>pts</th>
<th>Age</th>
<th>Sex</th>
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<th>CPKr (iu/l)</th>
<th>Time to peak CPK after start of symptoms &amp; CAG (hours)</th>
<th>EF (%)</th>
<th>% ACS (%)</th>
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|     |     |     |     |              |             | 1.2       | 28.5    | 34.8     | 35.5 | Inf | RCA (1) | 100 |
|     |     |     |     |              |             | 1.2       | 10      | 62.3     | 44.8 | Inf | RCA (2) | 100 |
|     |     |     |     |              |             | 1.2       | 21      | 51.2     | 32.7 | Inf | RCA (2) | 100 |
|     |     |     |     |              |             | 1.2       | 24      | 53.2     | 26.8 | Inf | RCA (1) | 100 |
|     |     |     |     |              |             | 1.2       | 20      | 85.4     | 0    | Inf | RCA (3) | 100 |
|     |     |     |     |              |             | 1.2       | 31      | 52.3     | 31.9 | Inf | RCA (3) | 100 |
|     |     |     |     |              |             | 1.2       | 11      | 48.2     | 30.4 | Inf | RCA (1) | 100 |
|     |     |     |     |              |             | 1.2       | 12      | 35.2     | 26.7 | A-S | LAD (6) | 100 |
|     |     |     |     |              |             | 1.2       | 20      | 61.7     | 26.1 | A-S | LAD (6) | 100 |
|     |     |     |     |              |             | 1.2       | 18.5    | 34.1     | 25.2 | A-S | LAD (6) | 100 |
|     |     |     |     |              |             | 1.2       | 6       | 24.7     | 46.3 | A-S | LAD (6) | 100 |
|     |     |     |     |              |             | 1.2       | 8.5     | 45.2     | 31.8 | A-S | LAD (6) | 100 |

notes: pts = Patients; CPKr = cumulative CPK release; CAG = coronary arteriography; EF = Ejection fraction; % ACS = percent abnormally contracting segment; Inf = inferior infarction; A-S = anteroseptal infarction; RCA = right coronary artery; LAD = left anterior descending artery
* = cases with filling delay; ** = according to AHA criteria.

MATERIALS AND METHODS

Study patients: We studied on 31 patients with transmural infarction (29 males, 2 females, ages ranging from 41 to 73 with mean age of 57.6) who had neither prior MI nor serious complications such as cardiogenic shock, severe congestive heart failure and reinfarction in the

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TABLE II DATA ON SERUM CPK ACTIVITY

<table>
<thead>
<tr>
<th>Group</th>
<th>No of patients</th>
<th>Time between onset of symptoms and start of angiography (hours)</th>
<th>Time to peak CPK after start of symptoms (hours)</th>
<th>Time to peak CPK after start of angiography (hours)</th>
<th>peak CPK (iu)</th>
<th>CPKr (iu/l)</th>
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<tr>
<td>Group A</td>
<td>19</td>
<td>3.7 ± 1.6</td>
<td>12.5 ± 4.8*</td>
<td>8.8 ± 4.4**</td>
<td>2775 ± 1651</td>
<td>3764 ± 2019</td>
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<td>Group B</td>
<td>12</td>
<td>3.6 ± 1.6</td>
<td>20.1 ± 7.4*</td>
<td>16.3 ± 7.4**</td>
<td>2080 ± 668</td>
<td>3086 ± 1011</td>
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<tr>
<td>Total</td>
<td>31</td>
<td>3.7 ± 1.6</td>
<td>15.5 ± 6.9</td>
<td>11.8 ± 6.8</td>
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</table>

*mean ± SD, *p < 0.01 between group A and B, **p < 0.001 between group A and B.

Fig.1. Peak CPK and CPKr in 31 study patients. Peak CPK correlated well with CPKr. The relationships remained linear in both group A and B.

acute phase. Patients with left circumflex arterial lesion were also excluded from the study because it is difficult to assess the left ventricular function in patients with the lesion of this artery by the RAO view left ventriculogram. The patients' age, sex, and data on serum CPK in the acute phase are shown in Table I. According to the coronary arteriographic findings, we divided 31 patients into group A and group B.

Group A consists of nineteen patients with restored circulation of infarct-related coronary artery (Case 1–19). Five of them (Case 1–5) revealed a subtotal occlusion of involved coronary artery at the first injection of contrast medium, whereas 2 of them showed the delayed filling. In fourteen patients, reperfusion in the occluded artery was established during emergency coronary arteriography by the intracoronary administration of isosorbide dinitrate (ISDN 5 mg) (Case 6–7) or the high dose of Urokinase (600,000–1,200,000u) (Case 8–19).

Group B consists of twelve patients with a total occlusion of involved coronary artery (Case 20–31). In seven of them PTCR failed to recanalize the occluded artery.

Emergency Coronary Arteriography

All patients underwent hemodynamic study with Swan-Ganz flow-directed balloon catheter inserted via antecubital or femoral vein on admission to the coronary care unit. Informed consent for emergency coronary angiography including PTCR was obtained from each patient and his
relatives. Coronary angiography and left ventriculography were performed with Judkins' technique according to the protocol previously described. The procedure was started within 8 hours after the onset of symptoms. Coronary arteriographic findings were assessed according to the AHA criteria. No remarkable collateral flow to the ischemic area was recognized during the coronary arteriography in all patients.

**Enzymatic Evaluation of MI**

Blood samples for CPK were obtained through Swan-Ganz catheter or directly from antecubital vein every 4 hours for a period of 72 hours after the admission. Enzymatic activity of CPK was measured by the method of Rosalki. The following values on CPK were evaluated in all patients.

1. Peak CPK value
2. Cumulative CPK release
   Cumulative CPK release (CPKr) was determined using the integrated appearance function curve according to Sobel et al. with the individual disappearance constant (Kd) measured by the method of Norris et al.
3. Time-intervals to peak CPK from the onset of symptoms and from the start of emergency angiography
   If there are continuous 2 peaks of CPK value with less than 5% differences, CPK was regarded to attain the peak at the middle of these 2 peak times.

**Cardiac Catheterization in the Chronic Phase**

During 4–14 weeks (mean 6.4 weeks) after the admission, all patients underwent the single-plane left ventriculography (RAO 30°) before coronary angiography. Nitrates or any other medications that may influence left ventricular performance were not administered before the study. End-diastolic and end-systolic outlines of left ventriculogram for one cardiac cycle were traced on a transparent paper with a sharp pencil. By the area-length method, left ventricular ejection fraction (global EF) was obtained. By the

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Fig.3. CPKr is plotted against global ejection fraction for total patients (a) and 19 patients of group A (b). Linear correlation was observed between CPKr and global EF in group A, but the correlation was not good in total patients.

Fig.4. CPKr is plotted against percent abnormally contracting segment (%ACS) for all study patients (a), 19 patients of group A (b) and 12 patients of group B (c). Correlation between CPKr and %ACS was not good in 31 patients, however, it revealed linear relation in both group A and B. The slope of regression line was significantly (p < 0.01) steeper in group A than in group B.

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method of Feild et al.18 a kinetic and/or dyskinetic segments were determined from the superimposed silhouettes. The percentage of the length of a kinetic and/or dyskinetic segments in the end-diastolic outline to the whole end-diastolic circumference (Percent abnormally contracting segment) was regarded as one of the indicators of left ventricular wall motion in the chronic phase.

Percent abnormally contracting segment (%ACS) = [akinetically and/or dyskinetic length of end-diastolic circumference] / [whole end-diastolic circumference] × 100

Electrocardiographic and coronary arteriographic findings in the acute phase, global EF and %ACS are summarized in Table 1. A computer (NEC PC 8801) program was used for the calculation of data and the statistics. Statistical significance of difference between 2 groups was evaluated by the Student’s t-test and linear regression analysis was employed to estimate the correlation between CPKr and peak CPK, global EF and %ACS.

RESULTS

Table II shows the data on CPK obtained from 31 patients. In group A, patients with restored coronary circulation, serum CPK activity curve reached a peak level (2755 ± 1651 iu) 12.5 ± 4.8 hours after the onset of symptoms. In group B, patients with the occluded infarct-related coronary artery, serum CPK curve was less steep and attained a peak (2082 ± 668 iu) 20.1 ± 7.4 hours after the onset of symptoms. The average time-interval between the beginning of emergency angiography and the time of peak CPK were 8.8 ± 4.4 hours in group A and 16.5 ± 7.4 hours in group B.

Thus, after the onset of acute MI or the start of the emergency coronary angiography, CPK reached a peak significantly earlier in the group A than in group B (p < 0.01). The average CPKr were 3764 ± 2019 iu/L in group A and 3086 ± 1011 iu/L in group B, respectively.

Figure 1 shows the relationships between peak CPK and CPKr in 31 study patients. Peak CPK correlated well with CPKr. The relationships remained linear in each group. As shown in Fig. 2, the linear correlation was also observed between global EF and %ACS.

Figure 3 shows the relationships between CPKr and global EF in the chronic phase and Fig. 4 reveals the relationships between CPKr and %ACS. Open circles represent group A and closed circles group B. Both global EF and %ACS showed non-specific correlations with CPKr in 31 study patients as shown in Figs. 3a and 4a.

However, a linear relationship was observed between %ACS and CPKr when studying each group separately. (Fig. 4b, c) Correlation coefficients were r = 0.77 in group A and r = 0.68 in group B, respectively. A similar relationship was observed between global EF and CPKr in group A, although correlation coefficient was smaller than in case of %ACS and CPKr. (Fig. 3b) In spite of good correlations between %ACS and CPKr in each group, the slope of linear regression was significantly (p < 0.01) steeper in group A than in group B. Thus, the relationship between CPKr and %ACS was different in two groups.

DISCUSSION

Since the introduction of cardiac enzyme for the diagnosis of MI, it has been considered that the prognosis of acute MI is worse in patients with higher levels of serum CPK activity than those with lower serum CPK level. In 1971, Shell et al.19 demonstrated that infarct size calculated from serial serum CPK activities correlated excellently with that measured by myocardial CPK depletion and that observed histologically after 24 hours occlusion coronary artery in conscious dogs and proposed the idea that enzyme levels could be used as an indicator of infarct size. Subsequently, several investigators reported that the infarct size calculated from serum CPK or CK-MB activities correlated closely with infarct size estimated pathologically, angiographically (left ventriculogram) or by radionuclide approach in man.8–8

On the other hand, Roe et al.19 showed that correlations between infarct size calculated from serial serum CPK and that estimated histologically were not good in dogs. Sharpe et al.20 reported that relationships between infarct size estimated from cumulative CPKr and that estimated by radionuclide techniques were not good.

Experimentally, many investigators studied the effect of reperfusion after coronary occlusion on the infarct size.13,14,21–24 and showed that after reperfusion of completely occluded coronary artery in conscious dogs, serum CPK reached the peak significantly earlier and the peak level significantly higher than during a 24 hours occlusion. Vatner et al.14 suggested that this phenomen-
enon might be due to decreased time for local degradation of myocardial CPK because of reperfusion and increased rate of CPK transport into systemic circulation and concluded that infarct size cannot be estimated by serum CPK level alone because the latter is dependent on the presence or absence of reperfusion of occluded coronary artery.

In the present investigation we examined (1) the effect of restoration of coronary blood flow on serum CPK time-activity curve and (2) the relationships between cumulative CPKr and left ventricular performance in the chronic phase in man. In group A in which coronary reperfusion occurred, serum CPK attained the peak earlier than in group B in which coronary occlusion was not relieved during emergency angiography. This may be due to the early CPK washing out of the myocardium as suggested by the animal experiments. In each group CPKr correlated closely with %ACS, though this correlation was not good when comparing in total study patients.

CPKr divided by %ACS (CPKr/%ACS) was significantly higher in group A than in group B. This observation means that left ventricular function is preserved better in group A than in group B when compared at the same level of CPKr.

Thus, the method to determine infarct size from serum CPK activity is influenced by whether the involved coronary artery is patent or not. These results in man are in agreement with those of animal experiment and clearly show that infarct size cannot be estimated by serum CPK level alone. Our study also shows that the short time-interval from the onset of symptoms to peak CPK strongly suggests the possibility of early reperfusion of occluded coronary artery and we consider this phenomenon to be a useful index to know the condition of the coronary circulation involved.

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REFERENCES

15. OMOTE S, YASUE H, TAMAKI A, NAGAO M, HYON H, NISHIDA S, HORIE M: Coronary arteriographic findings during early hours of acute

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