ST-SEGMENT RE-ELEVATION AND LEFT VENTRICULAR EXPANSION SOON AFTER ACUTE ANTERIOR MYOCARDIAL INFARCTION

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The sum of ST-segment elevation (Σ ST on V_{2-4}) was measured to evaluate ST-segment re-elevation during early convalescence in 57 patients with acute myocardial infarction. Following rapid ST-segment elevation resolution during the first 12 h, Σ ST again increased in many patients without signs of reinfarction or pericarditis, reaching a maximum approximately 5 days after onset. The magnitude of this re-elevation ($\Delta \Sigma$ ST) was less than 0.3 mV in 30 patients (group A), and 0.3 mV or more in another 27 (group B). Based upon left ventriculography, the global ejection fraction in group B decreased significantly from $51 \pm 10\%$ at the acute phase to $46 \pm 10\%$ at the chronic phase. No such decreases were seen for group A. Regional ejection fraction in the infarcted portion improved significantly from $28 \pm 13\%$ at the acute phase to $35 \pm 14\%$ at the chronic phase in group A, but did not improve in group B. In addition, the non-infarcted portion in group B showed a significantly reduced regional ejection fraction. These results suggest that myocardial expansion of the infarcted portion may contribute to ST-segment re-elevation, an ominous sign of left ventricular dysfunction soon after acute myocardial infarction.

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CHARACTERISTIC ST-segment elevation at onset of acute myocardial infarction usually returns to the baseline several days after onset^{1,2}. It has been reported by some authors^{3–6} that during the early recovery phase in some patients ST-segment re-elevated without a recurrence of myocardial infarction. There is also some controversy concerning the cause of such ST-segment re-elevation. Some authors have suggested that it is a sign of myocardial ischemia^{7,8} while others have not found any ischemia^{9,10}. It is important therefore to clarify the mechanism

behind ST-segment re-elevation in such patients. In this study, we have attempted to clarify the mechanism and clinical significance of ST-segment re-elevation through acute and chronic phase cine-angiographic data.

SUBJECTS AND METHODS

Fifty seven patients with acute myocardial infarction who had been admitted to the Kinki University Hospital Coronary Care Unit from 1982 to 1988 were studied. There were 50 males and 7 females, all under 75 years old with an average age of 57 ± 10 (mean $\pm$ one standard deviation). Based upon informed written consent, all of the pa-

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Fig.1. Serial electrocardiograms for one patient with anterior infarction from each group. Note that the patient from group B showed a marked re-elevation in ST-segment at the 5th day.

tients underwent coronary angiography within 24 h of the onset of chest pains. Patients with an infarct related to a coronary artery in either segment 6 or 7 of the left anterior descending coronary artery according to the classification of the American Heart Association (AHA)¹¹ were enrolled in the study. Electrocardiogram was recorded until one month after onset in all patients. Patients with signs or symptoms of recurrent myocardial infarction, re-elevation of serum creatine kinase activity (CK), pericardial friction rub, post-infarct pericarditis or intraventricular conduction disturbance during recovery were excluded. Intravenous or intracoronary thrombolysis was performed on 40 of the patients who had been admitted within 6 h of onset.

TABLE I COMPARISON OF CLINICAL AND ANGIOGRAPHIC FINDINGS BETWEEN PATIENTS WITHOUT RE-ELEVATION OF ST-SEGMENT (GROUP A) AND WITH RE-ELEVATION (GROUP B)

	Group A ($\Delta \Sigma ST < 0.3$ mV)	Group B ($\Delta \Sigma ST \geq 0.3$ mV)	p Value (group A vs B)
No. of cases	30	27	
Age (yrs)	56 ± 9	57 ± 10	
Killip class (I/II/III/IV)	26/3/0/1	23/4/0/0	
Peak CK (U/L)	3241 ± 1811	3743 ± 1959	
Thrombolysis (cases)	20	20	
Segment of infarct-related artery (AHA)			
#6	17	12	
#7	13	15	
Number of vessels involved			
One vessel	18	15	
Two vessels	11	10	
Three vessels	1	2	
Global ejection fraction (%)			
Acute phase	54 ± 10	51 ± 10	
Chronic phase	57 ± 9	$46 \pm 10^*$	< 0.001
Regional ejection fraction (%)			
Infarcted portion (Areas 2 and 3)			
Acute phase	28 ± 13	23 ± 15	
Chronic phase	$35 \pm 14^{***}$	24 ± 12	< 0.001
Non-infarcted portion (Areas 1, 4 and 5)			
Acute phase	43 ± 13	43 ± 14	
Chronic phase	42 ± 12	$38 \pm 13^{**}$	< 0.05
Δ EDVI (ml/m ²)	16 ± 20	21 ± 20	
Δ ESVI (ml/m ²)	5 ± 10	16 ± 15	< 0.05
Aneurysm (+/-)	3/21	9/11	< 0.05

Abbreviations: Δ EDVI: difference of end-diastolic volume index between acute and chronic phases, Δ ESVI: difference of end-systolic volume index between acute and chronic phases. Difference between acute and chronic phase: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Fig.2. Σ ST serial changes for groups A and B

Fig.3. Comparison of acute and chronic phase left ventricular volume indices in groups A and B.

Δ ESVI: Difference in left ventricular systolic volumes, acute and chronic phases.
 Δ EDVI: Difference in left ventricular diastolic volumes, acute and chronic phases.

Coronary angiography and left ventriculography: Coronary angiography using 5 to 9 ml of amidotrizoate sodium meglumine was performed from multiple projections by Judkins catheter. Coronary stenosis was evaluated according to AHA classification.¹¹ Delay in contrast material washout downstream from the stenosis was defined as 99%

stenosis with delay. Left ventriculography was taken in the right anterior oblique projection using 40 ml of contrast material at a speed of 15 ml/sec. These studies were performed in acute phase (mean, 7.4 ± 5.4 h after onset; range, 3.4–24 h) and were repeated in chronic phase (mean, 79 ± 53 days after onset; range, 28–150 days).

Left ventricular volume was measured according to the area-length method.¹² The global ejection fraction (EF) was calculated as:

$$\text{global EF} = (\text{EDV} - \text{ESV}) / \text{EDV} \times 100 (\%)$$

wherein end-diastolic volume (EDV) and end-systolic volume (ESV) indicate maximum and minimum volumes during diastole and systole, respectively.

The left ventricular wall on the ventriculography was divided into 5 areas according to Gelberg et al.¹³ Areas 2 (anterolateral) and 3 (apical) correspond to the infarcted portion and areas 1 (anterobasal), 4 (diaphragmatic) and 5 (posterobasal) correspond to the non-infarcted portion in patients with anterior myocardial infarction. Regional ejection fraction was measured as

Fig.4. Changes in acute and chronic phase global and regional ejection fractions.

follows:

$$\text{regional EF} = \frac{(\text{Area EDV} - \text{Area ESV})}{\text{Area EDV} \times 100 (\%)}$$

wherein Area EDV and Area ESV indicate regional areas at end-diastole and end-systole, respectively. To avoid interobserver differences, the left ventricular volume measurements were performed independently by 2 cardiologists. A third measurement was performed whenever the difference between the 2 was greater than 20%. Left ventricular aneurysm was defined whenever, according to left cine-ventriculography at the chronic phase, a part of the ventricular wall protruded outwards through the cardiac cycle!¹⁴

Electrocardiogram: Electrocardiographic ST-segment deviation was measured as a mean of 3 successive beats at 60 msec after the J point of the QRS complex. The sum (Σ ST) of ST-segment deviation on leads V_2 , V_3 and V_4 was measured at admission (Σ STa), at 3, 6, 12, 24 and 48 h, at 4 to 7 and 10 days, at 2 and 3 weeks, and at 1 month. Usually, the highest Σ ST was at admission or at the third hour, then subsequently decreased, normally reaching a minimum value (nadir Σ ST) at between 1 to 7 days. But in approximately half the patients Σ ST rose following the nadir. The highest value of Σ ST elevation following the nadir

was defined as peak Σ ST. The difference between the two was then defined as $\Delta \Sigma$ ST.

The patients were divided into 2 groups according to the magnitude of $\Delta \Sigma$ ST:

Group A: $\Delta \Sigma$ ST < 0.3 mV

Group B: $\Delta \Sigma$ ST $\geq$ 0.3 mV

The arbitrary value of 0.3 mV to divide groups A and B was determined because the change of 0.1 mV in each ST-segment will be unequivocally detected, yielding the sum of 3 leads (V_2 , V_3 , V_4) 0.3 mV.

T wave amplitude was measured as the mean of 3 successive beats on the electrocardiograms.

Statistical analysis: All values were expressed as mean $\pm$ one standard deviation. Statistical significance of difference was evaluated by Student's t test for paired and unpaired data or by using the χ^2 test. A p value of less than 0.05 was considered significant.

RESULTS

Electrocardiogram changes: Thirty (52.7%) of the 57 patients were included in group A and the other 27 (47.3%) assigned to group B. Typical ECG changes for each group are shown in Fig. 1.

There were no significant differences between group A and B in gender, age, infarct-related coronary arteries, clinical severity on

Fig.5. Comparison of coronary angiographic findings in groups A and B. 100, 99, 90 and 75% indicate the grade of coronary artery stenosis based upon AHA classification.

admission or thrombolytic agents used (Table I). Peak serum creatine kinase (CK) activity was slightly higher in group B than in group A, but the difference was not statistically significant.

Fig. 2 shows Σ ST serial changes for groups A and B. For both groups Σ ST was highest at 3 h after onset and then markedly decreased over the next 3 h. In group A, Σ ST continued to decrease until the 5th day but in group B it was again elevated at 12 h and then continued to remain high. As seen in Fig. 2, although there was no significant difference in Σ ST between the groups at 3, 6 or 12 h, the difference became significant at 24 h and continued to be so until one month later. For group B, ST-segment re-elevation was most marked between 4 and 7 days, after which time it began to subside. For both groups, the T wave went from positive to negative sometime between the 24th and the 48th hours. In group A it remained negative but in group B it temporarily returned to positive around the 5th day, on the whole, finally again becoming negative on the 10th day. There was no significant difference in heart rate at the 5th day between

the 2 groups (A: 73 ± 13 vs B: 77 ± 10 beat/min) and so throughout the period of recovery.

Left ventriculogram: The end-diastolic volume index (EDVI) increased between the acute and the chronic phase in both groups. As shown in the right panel of Fig. 3, the difference in EDVI (Δ EDVI) between both phases was 16 ± 20 ml/m² in group A and 21 ± 20 ml/m² in group B. The difference of end-systolic volume index (Δ ESVI) was also significantly ($p < 0.05$) greater in group B than in group A: Δ ESVI was 5 ± 10 ml/m² in group A and 16 ± 15 ml/m² in group B.

In group A, the global ejection fraction did show any significant changes between the acute and the chronic phases. On the contrary, during the chronic phase it markedly decreased in 11 out of the 16 patients in group B and was significantly lower in group B in comparison to group A.

In comparison to the acute phase, the regional ejection fraction of the infarcted portion significantly improved in group A during the chronic phase, but, as shown in Table I and Fig. 4, no improvement was seen for group B. It was also interesting, as shown in the right panel of Fig. 4, that the regional ejection fraction of the non-infarcted portion in group B during the chronic phase was significantly reduced. As shown in Table I, left ventricular aneurysm was more frequent in group B than in group A. These findings indicate that left ventricular function in group B deteriorated during the chronic phase.

Coronary angiography: The 2 groups were compared in regards to the grade of infarct-related coronary artery stenosis and the incidence of collateral supply (Fig. 5). As shown in the upper panel of this figure, there was no significant difference between the 2 groups in the incidence of severity of coronary stenosis preceding thrombolysis. The rate of incidence of complete occlusion of the infarct-related artery after thrombolysis was the same for both groups: 8 (27%) in group A and 7 (26%) in group B. In the former, however, all the patients had good collaterals while in the latter, this was true for only 3 of the 7 cases. At the chronic phase, none of the patients in group A had a complete occlusion but 3 (15%) of those in group B still had an occluded coronary artery.

DISCUSSION

This study has shown that patients with ST-segment re-elevation during the acute recovery phase of anterior myocardial infarction (group B) had distinctive left ventriculograms when compared to patients who do not display such ST-segment re-elevation (group A). Regional ejection fraction did not improve in the infarcted portion for group B patients but, on the other hand, deteriorated in the non-infarcted portion. Also, among group B patients during the chronic phase the global ejection fraction decreased while left ventricular end-systolic volume increased.

ST-segment re-elevation in acute myocardial infarction was first reported by Rosenbaum et al³ in 1945. Since then this phenomenon has been described in a variety of ways. For example, Inoue⁴ termed it "the repeated changes of ST-T" which occurred 5 to 6 days after onset in 9 out of 11 patients with acute myocardial infarction. Solomon et al⁵ reported 7 cases which they described as an "intermediate phase." Maroko et al⁶ and Reid et al⁷ found a high incidence (89%) for ST-segment re-elevation when using precordial mapping, but a low incidence (29%) when using standard 12-lead electrocardiograms. If $\Delta \Sigma ST$ is defined as 0.3 mV or more, the 47% incidence of ST-segment re-elevation reported in this study is equivalent to those of these previous reports.

There may be 2 mechanisms behind ST-segment re-elevation³⁻¹⁰: one being infarct extension and the other being myocardial expansion. Using precordial mapping, Essen et al⁸ found ST-segment re-elevation in half of 24 patients with anterior myocardial infarction. They decided that this finding resulted from infarct extension because most of the patients showed recurrence of chest pain and serum CK elevation. Reid et al⁷, also using precordial mapping found ST-segment re-elevation in 12 of 14 patients and concluded that it was due to infarct extension because of concurrent transient elevations in serum CK.

Mills et al⁹ and Gewirtz et al¹⁰ reported that ST-segment re-elevation was not relieved by sublingual nitroglycerin. Since this was usually observed in patients from 2 to 7 days after onset and persisted for several

days or more, it is likely that this phenomenon reflects a healing process rather than a transient episode of myocardial ischemia. Hutchins and Bulkley¹⁵ pointed to a morphological difference between infarct extension and myocardial expansion of autopsied hearts in 76 patients who died within 30 days after onset. They reported that infarct extension with fresh myocardial necrosis was observed in only 17% of the patients while myocardial expansion, characterized by dilation and thinning of the ventricular wall of the infarcted portion was found in 59% of the cases. Pirolo et al¹⁶ also found expansion in 45% of 204 autopsied hearts. In this study, since cases with infarct extension were excluded by chest pain and serial measurements of serum CK, our results are more closely associated with myocardial expansion than ischemia or infarct extension.

Serial echocardiographic observations of left ventricular wall motion have shown that myocardial expansion took place within 7 days after onset¹⁷. This is consistent with the time frame for ST-segment re-elevation described above. Also, the above-mentioned pathological observations by Hutchins and Bulkley¹⁵ indicate that expansion of infarcted myocardium occurs during this same period.

According to the solid angle theory proposed by Holland et al¹⁸, an ST-segment shift depends upon the solid angle of the infarction border and the difference of electrical potentials between infarcted portion and the normal myocardium. The expansion of the infarcted portion will increase the magnitude of the solid angle so that, in turn, it contributes to ST-segment elevation. On the other hand, as Mills et al⁹ and Gewirtz et al¹⁰ have described, abnormal repolarization, such as hypopolarization within the infarcted portion or peri-infarcted area would also induce ST-segment elevation. Recently, Arita and Nakagawa¹⁹ have reported that over-stretch of the myocardium will induce a hyperpolarization of the myocardial cells. Increased wall tension and expansion of the residual viable muscle in the infarcted area may also contribute to ST-segment re-elevation.

In this study, it is interesting to note that no difference in left ventricular function between the 2 groups was found in the acute phase while those in group B with ST-seg-

ment re-elevation evidenced a significantly deteriorated ventricular function in the chronic phase. Left ventricular end-diastolic volume in group B was also increased in the chronic phase. This increase in ventricular volume was accompanied by a deterioration in regional ejection fraction of the non-infarcted portion, a fact that can be explained by a mathematical model by Klein et al.²⁰ They suggested that normal myocardium next to the infarcted myocardium is forced to dilated whenever the infarcted area exceeds 20% of the entire left ventricle.

Although clinical severity and infarct size at onset were the same for the two groups, the healing process in group B may be considerably hindered. Patients in this group had few collaterals at the acute phase and a high incidence of occluded coronary arteries at the chronic phase. Such differences in coronary blood supplies might be the reason why regional ejection fraction not improved in group B. These observations seen in patients with anterior myocardial infarction were also true in our patients with inferior infarctions, although the re-elevation in these patients was less remarkable than in anterior infarction.

Jugdutt et al.²¹ suggested that myocardial expansion will be modified by medication, but in this study there was no difference in drugs prescribed for either group.

In conclusion, ST-segment re-elevation during early recovery phase of acute myocardial infarction may be an ominous sign of left ventricular dysfunction caused by myocardial expansion to the risk area of infarction in which a very poor blood supply persists.

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