DIFFERENTIATION OF MYOCARDIAL ISCHEMIA AND LEFT VENTRICULAR ANEURYSM IN THE GENESIS OF EXERCISE-INDUCED ST-T CHANGES IN PREVIOUS ANTERIOR MYOCARDIAL INFARCTION

Muneyasu Saito, M.D., Hirohiko Asonuma, M.D., Masaaki Tomita, M.D.
Tetsuya Sumiyoshi, M.D., Kazuo Haze, M.D., Kenichi Fukami, M.D.
Katsuhiro Hiramori, M.D., Toshiha Uehara, M.D.
Kouhei Hayashida, M.D., and Tsuneziko Nishimura, M.D.

We attempted to differentiate between myocardial ischemia and left ventricular asynergy as the underlying mechanisms of exercise-induced ST-segment elevation in patients with previous myocardial infarction (MI). Sixty patients with previous anterior MI, who underwent stress myocardial scintigraphy (SMS) and coronary angiography (CAG), which revealed a single vessel disease of the left anterior descending artery, were entered in this study. SMS and CAG were performed within 3 months of MI onset, and SMS and ECG were quantitatively analyzed. T wave changes to a complete upright position with concomitant ST-segment elevation (T-dominant ST-elevation) was seen in 56% of the patients with post-MI angina pectoris (N = 16) and in 50% of those with significant redistribution in SMS (n = 20). On the other hand, ST-segment elevation without T wave reversion (ST-dominant ST-elevation) was seen in 43% of patients with severe LV asynergy (akinetic and dyskinesis, n = 39) and in 50% of those with severe scintigraphic defect in delayed images (relative thallium uptake < 40%, n = 10). When these findings were combined, T-dominant ST-elevation had sensitivity and specificity of 54% and 78%, respectively, for the diagnosis of myocardial ischemia, while the corresponding values for ST-dominant ST-elevation were 44% and 100%, for the diagnosis of severe ventricular asynergy. We conclude that the two underlying mechanisms, ischemia and asynergy, may produce different changes in ST-T shape in patients with previous myocardial infarction.

Exercise-induced ST-segment elevation in anterior precordial leads associated with abnormal Q-waves is a highly specific but relatively insensitive indicator of severe left ventricular (LV) asynergy or LV aneurysm.1-8 However, it has recently been suggested that myocardial ischemia is also responsible for the exercise-induced ST elevation during stress myocardial scintigraphy (SMS)9-11 or in the analysis of exercise ECG before and after a AC-bypass surgery.12 We previously reported that thallium redistribution to the infarcted area in SMS was related to ischemia of jeopardized viable myocardium in the infarcted area11 and that the factors influencing the extent of ST elevation were LV asynergy, the extent of redistribution.

Key words:
ST-segment elevation
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Department of Internal Medicine and *Radiology, National Cardiovascular Center, Osaka, Japan
Mailing address: Muneyasu Saito, M.D., Department of Internal Medicine, National Cardiovascular Center,
Fujishirodai 5-7-1, Suita, Osaka 565, Japan

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and work load during exercise.\textsuperscript{11}

Accordingly, the present study was undertaken to differentiate by SMS the underlying two possible mechanisms of ST elevation, LV asynergy and myocardial ischemia, in anterior precordial leads in patients with previous anterior myocardial infarction (MI), from the changes in the shape of ST-segment and T-wave.

\textbf{PATIENTS AND METHODS}

\textit{Patient Population}

The study population consisted of 60 patients (54 male and 6 female) with a mean age of 54 years old (range from 29 to 68 years). All patients had previous anterior MI (transmural MI in 55 and non-transmural MI in 5) documented by ECG and enzymatic criteria. They underwent SMS and cardiac catheterization within 3 months of the onset of MI, and were found to have significant stenosis (\textasciitilde 75\%) only in left anterior descending coronary artery (LAD). SMS and cardiac catheterization were performed within 1 month of each other. Patients who did not attain the target heart rate (described in the method section), or did not have progressive chest pain or significant (\textasciitilde 2 mm at J-0.08") ST depression during SMS were excluded from the study. The reasons we selected such patients are as follows; 1) changes in ST-segment and T-wave are more remarkable in anterior than inferior MI, 2) SMS is more easily interpreted in a single vessel disease than a multivessel disease, 3) the extent of ST-segment elevation in patients with previous MI depends on the interval from the onset of MI\textsuperscript{11,13} 4) the extent of ST elevation depends on the work load during stress exercise\textsuperscript{11}

The diagnosis of post-infarction angina pectoris was based on the findings that anginal pain was reproducible by routine exercise test. Patients with exercise-induced ST-segment depression without chest pain were not included in the angina pectoris group. Seventeen patients had post-infarction angina pectoris. Coronary angiogram revealed that 23 patients had complete obstruction of the LAD, while 13 had 99\%, 10 had 90\%, and 14 had 75\% stenosis of the LAD. Left ventriculography (LVG) disclosed 13 patients with anterior dyskinesis, 26 with akinesia, 12 with hypokinesis and 9 with normal contraction.

\textbf{Rest and Exercise ECG}

Resting ECG showed at least one abnormal Q-wave in 55 patients. Negative T-waves were observed in 46 patients while the remaining 14 patients had flat or positive T-waves in anterior chest leads.

Changes in ST-segment and T wave were quantitatively analyzed (Fig. 1). Among the anterior precordial leads, the lead showing the most marked ST-segment elevation (measured at J = 0.08") was selected (16 in V_2, 33 in V_3 and 11 in V_4) and the difference in ST levels between resting and peak exercise ECGs was defined as $\Delta$ST (mm). Similarly, the lead showing the

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greatest changes in the height of T waves was selected (17 in V₂, 39 in V₃ and 4 in V₄) and the difference of the height (peak or nadir) of T wave was defined as ΔT (mm). The interpretation of ECG was done independently and before analysis of myocardial images.

**Ergometry during Stress Scintigraphy**

All patients underwent a symptom-limited multistage exercise test using an electrically-braked bicycle ergometer (Siemens 308B). The initial load depended on their exercise capacity and in most cases started from 50 watts with a 25-watt increment every 3 minutes. At the endpoint described below, 3 mCi of thallium-201 chloride was injected intravenously through a butterfly needle previously inserted, followed by 1 minute of exercise with the same load. The exercise endpoint was: 1) progressive chest pain of mild to moderate degree, 2) horizontal or down-slope ST-segment depression of more than 2 mm at J-0.08", 3) dyspnea and general fatigue, 4) serious arrhythmia, or 5) attaining the target heart rate, which was set at 70% of maximum heart rate in patients with less than 1 month of the onset and 80% in the remaining patients.

ECG was monitored, and blood pressure and standard 12 leads ECG were recorded before and at every one minute during the exercise.

**Analysis of Myocardial Image**

After a short recovery period following exercise, myocardial imagings were obtained with a scintillation camera (Ohio Nuclear Σ410S) with a high resolution collimator, which was fed to an on-line computer system (DEC GAMMA 11). Myocardial images were obtained in 3 views (anterior, LAO 45° and LAO 70°) with pre-set counts of 50 x 10³ per minute. Delayed images were obtained 4 hours after the exercise imaging in the same views with the same pre-set time of the exercise images.

The myocardial images were analyzed by ROI method as shown in Fig. 1. Three ROIs were selected on exercise and delayed images of LAO 45° or 70°: the upper mediasternal area as a background, normal area (inferior or posterior wall) and antero-septal area (infarcted area). The percent defect thallium activity (%D) of the infarcted area was calculated from exercise and delayed images and the difference of %Ds between these two images was defined as %RD, which indicates the extent of redistribution as shown in Fig. 1. Percent RD of more than 10% was considered significant for myocardial ischemia at the infarcted area

**Statistical Procedure**

All data are expressed as mean ± standard
Fig.3. Clinical findings of myocardial ischemia and severe LV asynergy, and ST-T changes during exercise. Patients with clinical angina (closed circle) and those with dyskinesis in LVG (closed triangle) are plotted against ΔST (horizontal axis) and ΔT (vertical axis). Open circle represents those without angina or dyskinesis. No patients belonged to two groups simultaneously.

Fig.4. Scintigraphic findings of myocardial ischemia and severe perfusion defect, and ST-T changes during exercise. Patients with significant redistribution (closed circle) and severe perfusion defect in delayed images (closed triangle) are plotted in the same plane as Fig. 3. Open circle represents those without either significant redistribution or severe defect. No patient was in two groups.

deviation. Paired or un-paired t tests as well as χ² tests were used for the detection of statistical significance. A p-value of less than 0.05 was considered significant.

RESULTS

I. Myocardial Imaging and Clinical Angina Pectoris

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The patients were divided into two groups; those with post-MI angina (n = 17) and those without angina (n = 43). As shown in Fig. 2, patients with angina pectoris were distributed in the upper right quadrant (%D more than 40% and %RD more than 10%) except four cases (two cases are very close to the quadrants), indicating that post-MI angina can occur in patients with less perfusion defects and significant redistribution.

2. ST-T changes, myocardial ischemia and LV asynergy

Figure 3 plots the patients with post-infarction angina pectoris (n = 17), dyskinesis in LVG (n = 13) and those without angina or dyskinesis (n = 30) against the extent of ST segment elevation (ΔST), and T wave changes (ΔT). No patients had both angina pectoris and dyskinesis. Significant correlations were observed for those with post-infarction angina pectoris and those with dyskinesis (r = 0.59 and 0.73, respectively), and the regression equation of the former group was located above the latter, indicating that patients with angina pectoris have more marked T wave changes than those without angina pectoris, and those with dyskinesis have more remarkable ST segment elevation than T wave changes than those without dyskinesis.

Figure 4 shows the same relation as in Fig. 3 among 3 groups of patients classified by scintigraphic image: group 1 with %RD > 10% (n = 20), group 2 with %D ≤ 40% (n = 10) and the remaining patients (group 3, n = 30). No patients with %D ≤ 40% had redistribution more than 10%. Groups 1 and 2 showed significant correlation (r = 0.46 and 0.82, respectively) and the regression equation of the group 1 was located above that of group 2, indicating that patients with significant redistribution in SMS have more marked T wave changes than those with severe perfusion defects. In other words, patients with myocardial ischemia assessed by SMS and those with severe scintigraphic defect have different patterns of exercise-induced ST-elevation; dominant T-wave changes and dominant ST-segment elevation.

![Fig. 5. Three typical cases of ST-T changes during exercise. From the top to bottom, no ST elevation, ST-dominant and T-dominant ST elevation.]

![Fig. 6. Clinical and scintigraphic findings in three groups of patients. (--) no ST elevation, (ST): ST-dominant ST elevation, (T): T-dominant ST elevation.]

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TABLE 1 SENSITIVITY AND SPECIFICITY OF T-DOMINANT AND ST-DOMINANT ST-ELEVATION IN THE DIAGNOSIS OF MYOCARDIAL ISCHEMIA AND SEVERE LV ASYNERGY

<table>
<thead>
<tr>
<th>ST-elevation</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>T-dominant ST-elevation for myocardial ischemia</td>
<td>13/24 = 54%</td>
<td>28/36 = 78%</td>
</tr>
<tr>
<td>ST-dominant ST-elevation for severe LV asynery</td>
<td>17/39 = 44%</td>
<td>21/22 = 100%</td>
</tr>
</tbody>
</table>

3. Type of ST-T Changes and Clinical Characteristics

ST-T changes were classified into 3 groups: group A with no significant ST changes (ΔST < 1 mm), group B with significant ST elevation (ΔST ≥ 1 mm) with a negative terminal portion of T wave, where ST segment was convex from the J point to the terminal portion of T waves (ST-dominant ST-elevation), and group C with significant ST elevation with tall upright T wave, where ST segment was concave from the J point to the peak of T waves (T-dominant ST-elevation). Representative cases are shown in Fig. 5. The clinical characteristics (number of abnormal Q waves, LV ejection fraction, the extent of LV asynery and the presence or absence of post-MI angina pectoris) and scintigraphic findings of ischemia (%RD ≥ 10%) among these 3 groups are shown in Fig. 6. Patients in group B (ST-dominant ST elevation) had a significantly larger number of abnormal Q waves, smaller LV ejection fraction, higher incidence of LV dyskinesis, and lower incidences of angina pectoris and scintigraphic ischemia. On the other hand, patients in group C had the highest incidence of angina pectoris and scintigraphic findings of myocardial ischemia among the 3 groups.

4. Sensitivity and specificity of ST-T changes in the diagnosis of myocardial ischemia and LV asynery

The sensitivity and specificity of T-dominant ST elevation in the diagnosis of myocardial ischemia as well as those of ST-dominant ST elevation in the diagnosis of severe LV asynery are shown in Table I. Here, myocardial ischemia was defined as post-MI angina pectoris and/or scintigraphic myocardial ischemia, while severe LV asynery was defined as LV dyskinesis and/or %D less than 40% in the delayed images. Sensitivity and specificity of T-dominant ST elevation in the diagnosis of myocardial ischemia were 54% and 78%, respectively, while those of ST-dominant ST elevation in the diagnosis of severe LV asynery were 44% and 100%, respectively.

DISCUSSION

There have been many reports on the pathogenesis of exercise induced ST-segment elevation in patients with previous MI and it has been generally receptor that it is a highly specific but relatively insensitive indicator of LV aneurysm or impaired LV function1–8. However, recent studies using SMS revealed that myocardial ischemia is also involved in the genesis of ST-segment elevation in Q-wave leads9–11. Dunn et al9 reported that half of the cases with exercise-induced ST-segment elevation had marked thallium redistribution to the infarcted area in SMS, suggesting the involvement of myocardial ischemia as a possible mechanism of ST-segment elevation. Fox et al10 showed that in 23 patients with previous MI and coronary revascularization, exercise-induced ST-segment elevation in the infarcted area disappeared after surgery, indicating myocardial ischemia as an underlying cause of ST-segment elevation. Using multiple regression analysis we found that that factors influencing the extent of ST elevation during exercise in Q wave leads were LV asynery, myocardial ischemia and the time interval from the onset of MI and work load during SMS11. Even though LV asynery and myocardial ischemia are possible mechanisms of exercise-induced ST-segment elevation, it seems difficult to differentiate these two factors from changes in ST-segment during exercise; moreover, when only the extent of ST elevation is analyzed, the factor of LV asynery conceals that of myocardial ischemia. Gewirtz et al10 examined the role of ischemia in ST-segment elevation in the infarcted area using SMS and found that the thallium defect score positively correlated with the extent of ST elevation and inversely correlated with resting LV ejection fraction. They concluded that although exercise-induced myocardial ischemia occurs as often with as without ST segment elevation, myocardial ischemia is...
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not required for the production of stress-induced ST-segment elevation.

We focused on the changes in the shapes of ST-segment and T-wave, and found these to be related to clinical and scintigraphic findings of ischemia and LV asynergy. The results of the present study can be summarized as follows: 1) patients with significant redistribution in SMS have a higher incidence of post-MI angina pectoris than those without redistribution, suggesting that redistribution in the infarcted area indicates myocardial ischemia sufficient to produce clinical angina pectoris in more than half of the patients, 2) those with myocardial ischemia as judged from clinical and scintigraphic findings have predominant T-wave changes during exercise, while those with severe LV asynergy as judged by LVG and thallium defect in delayed images have convex ST-elevation without complete reversion of T-wave as shown in Fig.5, and 3) sensitivity and specificity of T-dominant ST elevation in the diagnosis of myocardial ischemia were 54\% and 78\%, respectively, while those of ST-dominant ST elevation for the diagnosis of severe LV asynergy were less sensitive (44\%) but highly specific (100\%).

Normalization of negative T-wave in patients with previous MI has long been considered to represent myocardial ischemia. Recently, Noble et al. reported that 38 patients with previous MI had reversion of T-waves to normal, upright position during ischemic attack. Parodi et al. showed that patients with normalization of negative T waves, which occurred during spontaneous anginal attacks as well as exercise-induced angina, had more marked reduction in thallium uptake as compared to those with ST depression. However, they did not refer to the ST elevation concomitant with T-wave changes. Normalization of negative T-waves usually accompanies ST elevation to some extent as shown in Fig.5, therefore, our findings are in accord with those previously reported on T-wave changes.

The definition of myocardial ischemia at the infarcted area is controversial. If ischemic chest pain is a manifestation of myocardial ischemia, only 9 of 21 patients with T-dominant ST elevation had reproducible anginal pain, while 7 of 22 patients with no ST changes also had exercise-induced chest pain. If exercise-induced ST depression is a manifestation of myocardial ischemia, 5 of 21 patients with T-dominant ST elevation had significant ST depression, while 4 of 22 patients with no ST changes also had significant ST depression. These findings indicate that neither ischemic chest pain nor ST depression are specific in the diagnosis of myocardial ischemia. Recently Brunken et al. showed that more than 50\% of the Q wave infarcted area had viable and ischemic myocardium, as assessed by positron-emission CT with \textsuperscript{13}N-ammonia and \textsuperscript{18}F-2-deoxyglucose. Therefore, it is possible that scintigraphic redistribution of thallium is the most sensitive indicator of myocardial ischemia in the infarcted as well as non-infarcted area.

The values of sensitivity and specificity for the diagnosis of myocardial ischemia and asynergy in patients with anterior myocardial infarction were not satisfactory for the differentiation of these two mechanisms. However, this study proved the existence of myocardial ischemia as an underlying mechanism of ST-segment elevation, and these findings may help to interpret stress ECG in the clinical setting.

Further studies are needed to clarify the relation between redistribution of thallium to the infarcted area in SMS and other clinical variables of myocardial ischemia including long-term prognosis (reinfarction and/or mortality) related to the myocardial ischemia in this area.

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