Relationship Between Normalization of Negative T Waves on Exercise ECG and Residual Myocardial Viability in Patients With Previous Myocardial Infarction and no Post-Infarction Angina

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The usefulness of normalization of negative T waves in exercise ECG was investigated as an index of myocardial viability in patients with previous myocardial infarction with no symptoms or ischemic ST-segment change during exercise test. A total of 39 patients, 20 with T-wave normalization (POS group) and 19 without T-wave normalization (NEG group) on exercise ECG, were studied. Myocardial viability was evaluated by thallium-201 single-photon emission computed tomography (SPECT) during exercise or at rest. We also assessed left ventricular ejection fraction (LVEF) by contrast ventriculography before (n=39) and after percutaneous transluminal coronary angioplasty (PTCA) (n=17). SPECT detected myocardial viability in 16 (80%) of the 20 patients in the POS group and in 4 (21%) of the 19 patients in the NEG group (p<0.01). LVEF increased after successful PTCA in the POS group (from 53±13% to 63±8%, p<0.025), but fell in the NEG group (from 57±10% to 51±8%). It is concluded that normalization of negative T waves on exercise ECG is a useful, simple index of myocardial viability in patients with previous myocardial infarction with no symptoms or ischemic ST-segment change during exercise testing. (Jpn Circ J 1998; 62: 153–159)

Key Words: Exercise; Myocardial infarction; Myocardial viability; Negative T waves

The ability to distinguish viable and fibrotic myocardium in patients with previous myocardial infarction is important. There are several clinically useful indicators for identifying viable myocardium, such as thallium-201 (201Tl) redistribution1 or preserved glucose metabolism assessed by positron emission tomography (PET)2. Although these nuclear techniques have excellent diagnostic value, they suffer from the limitations of being complex, expensive, and unavailable to most clinical centers. Therefore, it would be helpful to find a simple electrocardiographic (ECG) variable that is capable of detecting viable myocardium during exercise testing.

Normalization of negative T waves during exercise may be attributed to 1 or more mechanisms, such as secondary to exercise-induced intraventricular conduction disturbance, exacerbation of post-ischemic primary T-wave changes, tachycardia-induced decrease in ventricular gradient, sympathetic stimulation, and subepicardial ischemia.3-5 Salustri et al6 recently suggested that normalization of negative T waves during low-dose dobutamine stress testing may be an indicator of viable myocardium in patients with previous myocardial infarction. However, it has not been established whether normalization of negative T waves during exercise is a sign of myocardial viability in patients with previous myocardial infarction.

We investigated the usefulness of normalization of negative T waves in infarct-related ECG leads during exercise testing as a marker of myocardial viability in patients with previous myocardial infarction who had neither chest pain nor ischemic signs detected by exercise ECG.

Methods

Patients

We studied 55 consecutive patients who experienced a first Q-wave myocardial infarction >2 months before the exercise stress test. Acute myocardial infarction was documented based on the patient’s history and electrocardiographic and enzymatic findings. All subjects demonstrated negative T wave (>0.1 mV) in more than 2 consecutive infarct-related leads on a resting electrocardiogram. Subjects who had experienced spontaneous attacks of chest pain for at least 1 month, chest pain or ST-segment depression (>0.1 mV) induced by a symptom-limited treadmill exercise test were excluded from the present study. Patients with secondary T-wave abnormalities such as left ventricular hypertrophy, Wolff-Parkinson-White (WPW) syndrome, and left or right bundle branch block and those receiving drugs known to affect T waves were also excluded. Informed consent was obtained from all subjects. We studied 39 patients (34 men, 5 women, aged 35-67 years, mean 54±8 years).
Table 1 Clinical and Angiographic Data of the POS Group and the NEG Group

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Age mean (SD)</th>
<th>Location of MI (AII)</th>
<th>No of diseased vessel (1/2)</th>
<th>Diseased vessel (LAD/LCX/RCA)</th>
<th>Severity of stenosis (≥90%/&lt;90%)</th>
<th>Collateral vessel (+/-)</th>
</tr>
</thead>
<tbody>
<tr>
<td>POS group</td>
<td>20</td>
<td>53 (8)</td>
<td>14/6</td>
<td>18/2</td>
<td>15/2/5</td>
<td>2/14</td>
<td>12/8</td>
</tr>
<tr>
<td>NEG group</td>
<td>19</td>
<td>54 (9)</td>
<td>9/10</td>
<td>16/3</td>
<td>8/4/10</td>
<td>2/02</td>
<td>9/10</td>
</tr>
</tbody>
</table>

A, anterior; I, inferior; LAD, left anterior descending branch; LCX, left circumflex branch; MI, myocardial infarction; RCA, right coronary artery.

Table 2 Left Ventricular Function Before and After PTCA in the POS Group and the NEG Group

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>LVEF%</th>
<th>Regional wall motion score (location, severity)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td>POS group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>58</td>
<td>63 (A0, 2, Ap2, S2)</td>
</tr>
<tr>
<td>2</td>
<td>51</td>
<td>60 (A2, 3, Ap2, S2)</td>
</tr>
<tr>
<td>3</td>
<td>67</td>
<td>69 (A0, 1, Ap1, S2)</td>
</tr>
<tr>
<td>4</td>
<td>63</td>
<td>59 (A0, 1, Ap1, S2)</td>
</tr>
<tr>
<td>5</td>
<td>64</td>
<td>77 (A0, 1, Ap1)</td>
</tr>
<tr>
<td>6</td>
<td>55</td>
<td>68 (A0, 1, Ap1, S2)</td>
</tr>
<tr>
<td>7</td>
<td>67</td>
<td>62 (A0, 1, Ap1, S2)</td>
</tr>
<tr>
<td>8</td>
<td>45</td>
<td>63 (A0, 1, Ap1, S2)</td>
</tr>
<tr>
<td>9</td>
<td>48</td>
<td>66 (A0, 2, Ap2, S3)</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>53 (12)</td>
<td>63 (8.3)</td>
</tr>
<tr>
<td>NEG group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>67</td>
<td>54 (A0, 1, S1)</td>
</tr>
<tr>
<td>26</td>
<td>59</td>
<td>60 (A0, 1, Ap1, S2)</td>
</tr>
<tr>
<td>27</td>
<td>69</td>
<td>54 (A0, 1, Ap1, S2)</td>
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<td>64</td>
<td>52 (A0, 1, Ap1, S2)</td>
</tr>
<tr>
<td>36</td>
<td>53</td>
<td>55 (A0, 1, Ap1, S2)</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>57 (10)</td>
<td>51 (8)</td>
</tr>
</tbody>
</table>

A, anterior (Segment 1 and 2); Ap, apex (Segment 3); I, inferior (Segment 4 and 5); LVEF, left ventricular ejection fraction; P, posterior (Segment 7); S, septum (Segment 6).

1)P<0.01, 2)P<0.025 before PTCA compared with after PTCA.

Exercise ECG Testing

Subjects underwent an exercise test seated on a cycle ergometer (Lode model Corival 400, Groningen, The Netherlands) at an initial workload of 30 W/min for 3 min. The workload was increased by 30 W every 3 min until the target heart rate (85% of the predicted maximum heart rate) was achieved or severe leg fatigue occurred. No patient experienced chest pain or ST-segment depression (>0.1 mV at 0.08 sec after the J point) during the exercise test. One electrocardiographic lead was monitored continuously and a standard 12-lead ECG was recorded before exercise and at 1-min intervals during exercise. Blood pressure was measured by the cuff method at 1-min intervals.

Negative T waves that became positive during exercise and achieved an amplitude of at least 0.15 mV in at least 2 adjacent infarct-related leads were defined as normalized T-waves. The amplitude of the T wave was analyzed by measuring the peak of the T wave from the baseline, and was expressed as positive or negative millimeters. The change in the T-wave amplitude (ΔT amp) was calculated by subtracting the amplitude before exercise from the amplitude at peak exercise. Positive exercise-induced ST-segment elevation was defined as the presence of new ST-segment elevations or an increase of 0.1 mV in ST-segment elevations (measured 0.04 sec after the J point) during exercise. Exercise-induced ST-segment elevation in infarct-related leads was not in itself considered a reason for termination of the exercise test. Before entering the study, 29 (74%) of the 39 patients were taking antianginal medications, including nitrates (59%), calcium-channel blockers (54%), or beta blockers (10%). Beta-blockers were discontinued 72 h before initiation of the study, but the other drugs were continued.

Exercise Thallium-201 Imaging

Exercise 201TI imaging was performed within 1 week of the exercise ECG testing using the same protocol of exercise loading. No patients experienced chest pain or ST-segment depression (>0.1 mV) during the exercise test. A dose of 74 MBq of 201TI was injected intravenously 1 min before the exercise was stopped. Images were obtained with a rotating gamma camera (Hitachi RC-150DT) equipped with a high-resolution parallel-hole collimator 10 min (early images) and again 4 h after injection of thallium (delayed images). When an irreversible defect was present, rest images were obtained on a subsequent day. Thirty-two projections were acquired over a 180° arc from the 30° right anterior oblique view to the 60° left posterior oblique view. Short-axial,
T-Wave Normalization and Viability

Fig 1. Exercise ECG (a) and exercise SPECT (b) in a patient in the POS group with an anterior myocardial infarction and a stenotic lesion in the LAD. Normalization of negative T waves was observed in leads V3 and V4. Redistribution involving the anterior wall was detected on short-axis SPECT images. After PTCA, wall motion improved in the anterior wall. REST, before exercise; EX, at peak exercise; EARLY, 10 min after exercise; DELAY, 4 h after exercise.

Fig 2. Exercise ECG (a) and exercise SPECT (b) in a patient in the NEG group with an inferior myocardial infarction and a stenotic lesion in the RCA. No normalization of negative T waves occurred and no redistribution was detected on short-axis SPECT images. Akinesis was still present in the inferior wall after PTCA. Q waves were masked by the use of of the Mason – Likar leads in this patient.

vertical-axial and horizontal-axial single-photon emission computed tomographic images (SPECT) were reconstructed at 6.1-mm intervals using an on-line computer analysis system (Hitachi Harp-2). Transient perfusion defects (redistribution) were determined visually from the early and delayed images by 2 physicians experienced in nuclear medicine who were unaware of the patient's characteristics. When the 2 physicians disagreed, a third physician reviewed the images and consensus was reached. Fill-in phenomenon was considered to have occurred when filling in of the defects on the resting images compared with the delayed images was observed.

Coronary Angiography and Left Ventriculography

Selective coronary angiography was performed by the Judkins technique within 2 weeks of the exercise testing. Images of the left and right coronary arteries were obtained from multiple views, including the craniocaudal projection. Significant coronary artery stenosis was defined as a > 75% narrowing of the lumen diameter. The presence of collateral circulation was also assessed. Bi-plane left ventriculography was performed in the 30° right anterior and 60° left anterior oblique projections. The left ventricular silhouette was divided into 7 segments and the regional wall motion in those segments was graded according to the recommendations of the American Heart Association® using the following scale: 0 = normal; 1 = hypokinesis; 2 = akinesis; and 3 = dyskinesis. Regional wall motion abnormalities were assessed by the regional wall motion score, which was defined as the sum of the score of each segment. The left ventricular ejection fraction (LVEF) was calculated by the standard method. Studies were evaluated by the observers in a blinded manner.

Percutaneous Transluminal Coronary Angioplasty (PTCA)

PTCA was performed within 2 weeks of the diagnostic coronary angiographic studies in 29 patients who accepted the therapy and had technically feasible lesions on coronary angiograms [15 patients with anterior infarction and left anterior descending branch (LAD) lesions, 13 patients with inferior infarction and right coronary artery (RCA) lesions, and 1 patient with inferior infarction and left circumflex branch (LCX) lesions]. In all patients who underwent PTCA, the culprit lesion associated with myocardial infarction was dilated. PTCA of other stenotic vessels was attempted in patients with multivessel disease if technically feasible. The final evaluation was performed 3—6 months after PTCA. Successful PTCA, which was defined as the complete revascularization of 1 or more vessels resulting in no remaining lesion with a stenosis diameter greater than 50% at a repeat angiography, was confirmed in 19 patients (11 patients with LAD lesions, 7 patients with RCA lesions, and 1 patient with LCX). Left ventriculography was performed to
evaluate global and regional left ventricular function in 17 of the 19 patients with successful PTCA. An improvement in regional left ventricular function was considered to be present if the regional wall motion score in the infarcted area decreased by more than 1 point. Electrocardiograms were also recorded.

Definition of Myocardial Viability
Myocardial viability was identified by the presence of a reversible perfusion defect on redistribution images or fill-in on resting images. In the 17 patients with successful PTCA, the improvement in the regional wall motion score in the infarcted area was considered to be another sign of myocardial viability.

Statistical Analysis
Data are presented as the means±SD. The variables were analyzed by the paired Student’s t test and by Wilcoxon’s signed rank-sum test and Fisher’s exact test if appropriate. A p value <0.05 was considered significant.

Results
Negative T waves normalized during exercise in 20 patients (19 men, 1 woman; POS group, Fig 1a). In the remaining 19 patients (15 men, 4 women), T-wave polarity did not change during exercise (NEG group, Fig 2a).

Clinical Characteristics
There was no difference in age between groups (53±8 years vs 54±9 years, Table 1). In the POS group, 14 patients (70%) had anterior infarctions and 6 patients (30%) had inferior infarctions. In the NEG group, 9 patients (47%) had anterior infarctions and 10 patients (53%) had inferior infarctions. There was no significant difference in the incidence of 1- and 2-vessel disease, the LVEF
with anterior infarction and 83%, 80%, 71%, and 89%, respectively, in those with inferior infarction. The heart rate at which negative T waves became positive (HR-POS) was significantly (p<0.05) lower in the 16 patients who showed viability in the POS group (110±13) compared with the 4 patients without viability (126±7). Viability was detected in all patients who exhibited T-wave normalization and HR-POS less than 110 beats/min. Figs 1b and 2b are representative examples of 201TI SPECT images in the POS and NEG groups.

Follow-Up Data

The regional wall motion score decreased after PTCA in 9 (90%) of the 10 patients in the POS group but in only 1 (14%) of the 7 patients in the NEG group (p<0.01, Table 2, Fig 3). Thus, the sensitivity, specificity, and positive and negative predictive values of normalization of negative T waves during exercise for detection of residual viability were 90%, 86%, 90%, and 86%, respectively. The LVEF increased significantly (from 53±12% to 63±8%, p<0.025) after PTCA in the 10 patients in the POS group who underwent follow-up ventriculography (Table 2, Fig 3). There was no significant improvement in LVEF (from 57±10% to 51±8%) in the 7 patients in the NEG group who underwent follow-up examinations (Table 2, Fig 3). Negative T waves in infarct-related leads of resting ECGs were converted to positive T waves after PTCA in 9 (90%) of the 10 patients in the POS group, but only 1 (14%) of the 7 patients in the NEG group (p<0.01).

Discussion

Normalization of negative T waves in infarct-related leads during exercise indicated the presence of residual viable myocardium within the infarcted area. In particular, it was highly specific when it occurred at a heart rate <110 beats/min (Table 3). It may be attributable to non-ischemic causes in some patients when it occurs at a heart rate >110 beats/min because negative T waves became positive in the POS patients without myocardial viability at a significantly greater heart rate than that of POS patients with myocardial viability. The normalization of negative T waves during exercise as a sign of myocardial ischemia is controversial.10–20 Marin et al.11 reported that it was highly specific for the presence of coronary artery disease in patients with a high prevalence for coronary artery disease. However, they did not study its significance as a sign of myocardial viability. Salustri et al.10 recently suggested that normalization of negative T waves during low-dose dobutamine stress testing may be an indicator of viable myocardium in patients with previous myocardial infarction. The present study showed that normalization of negative T waves in infarct-related leads during exercise occurred as a result of myocardial ischemia in 80% of cases. Chronic reversible dysfunctioning viable myocardium is called hibernating myocardium.21 In the present study, none of the patients with hibernating myocardium had clinical signs of myocardial ischemia such as post-infarction angina or significant ST-segment depression during exercise testing in spite of the presence of severe coronary narrowing. Although the exact mechanisms that explain lack of those signs of myocardial ischemia were unclear, one possibility is that hibernating myocardium is tolerant of stress (owing to down-regula-
tion of β-receptors, etc) and another one is that myocardial ischemia is asymptomatic or electrocardiographically masked owing to myocardial infarction.

A change in the polarity of negative T waves during exercise supposedly depends on the intensity of the exercise load. In the present study, there were no significant differences in the peak double product between groups. Furthermore, the peak heart rate in the NEG group was greater than the heart rate at which negative T waves became positive in the POS group. Therefore, the difference in T-wave kinetics during exercise between groups was not explained by a difference in the intensity of the exercise load.

Although more than half of the POS patients had exercise-induced ST-segment elevation, its sensitivity and specificity were apparently less than those of normalization of negative T waves. Although stress-induced ST-segment elevations in infarct-related leads may be a useful sign for detection of residual viability within the infarct area, it may also result from left ventricular wall motion abnormalities or a left ventricular aneurysm. Saito et al. showed that the redistribution on SPECT images occurred in only 10% of patients with an anterior infarction who had exercise-induced ST elevation without T-wave reversion.

Study Limitations

Most subjects had received antianginal drugs that could have influenced the results of both exercise ECG and SPECT before entering the study. However, there was no difference in the types of medication between groups. The T-wave axis in inferior leads may be affected by the position of the electrode. However, the results of the present study were consistent when analysis was limited to data obtained in patients with anterior myocardial infarctions. Although none of the clinical indicators of myocardial ischemia were present in subjects in the present study, the presence of stress-induced myocardial ischemia was not excluded in the patients with reversible perfusion defects (redistribution) on SPECT images. Although Tamaki et al. have suggested that redistribution on 201Tl SPECT may underestimate viability in the infarct area, it was unlikely in the present study because the fill-in phenomenon on resting SPECT imaging was included as a viability criterion. 201Tl scintigraphy performed in the resting state is thought to be the most clinically useful approach for detecting viable myocardium in patients with chronic ischemic heart disease.

The present study had relatively low negative predictive value (79%). The reasons may be (1) insufficient exercise intensity in some subjects and (2) greater negative T-wave amplitude (less than −0.5 mV) before exercise in other subjects. The optimal standard for determining myocardial viability is recovery of function in dysfunctional myocardium after revascularization. In the present study, this standard could be applied only to a small number of patients. However, the positive and negative predictive values were excellent in those patients.

Conclusions

Normalization of negative T waves in infarct-related leads during exercise was a reliable indicator of the presence of residual viable myocardium within the infarct area. Thus, those patients may be good candidates for revascularization procedures, even when there are no other electrocardiographic signs of myocardial ischemia.

Acknowledgment

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References


