Exercise versus dobutamine-induced ST elevation in the infarct-related electrocardiographic leads: Clinical significance and correlation with functional recovery

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Background The clinical significance of stress-induced ST elevation early after acute myocardial infarction and its relation to functional recovery remain controversial. The aims of this study were (1) to determine the incidence of ST elevation during dobutamine and exercise tests and (2) to assess the relative accuracy of exercise and dobutamine ST elevation for predicting functional recovery after acute myocardial infarction.

Methods and Results We investigated 52 patients who underwent supine exercise (from 25 W to maximal charge) and dobutamine (from 5 to 40 µg/kg per minute and up to 1 mg atropine) stress electrocardiography in the same position. ST elevation was defined as new or worsening at >1 mm, 80 ms after J point. Echocardiography and quantitative angiography were available in all patients before hospital discharge. The follow-up resting echocardiogram was recorded 30 ± 6 days after the acute event. ST elevation developed during 30 (58%) dobutamine and 24 (46%) exercise tests. The sum of ST elevation was higher during dobutamine testing (7.7 ± 3.8 mm) than during exercise (5.5 ± 2.5 mm) (P = .03). A low peak creatine kinase level was the single independent predictor of dobutamine-induced ST elevation. Functional improvement occurred in 35 patients. Two independent predictors of functional recovery were selected from multivariate analysis: dobutamine ST elevation (χ² = 9.1; P = .0026) and low peak creatine kinase level (χ² = 5.1; P = .025). When dobutamine ST elevation was not included in multivariate analysis, exercise-induced ST elevation emerged as an independent predictor of functional recovery (χ² = 5.0; P = .023). Significant linear correlation was found between the sum of ST elevation at peak dobutamine stress and the extent of functional recovery (r = 0.87; P < .0001). In contrast, no correlation was observed with exercise ST elevation (r = 0.06; P = not significant).

Conclusions Stress-induced ST elevation is an ancillary sign of viable myocardium that can recover. The sum of ST elevation at peak dobutamine stress correlates with the extent of functional recovery. (Am Heart J 2001;141:772-9.)
on electrocardiography was anterior in 21 patients, lateral in 5, and inferior in 26. Peak serum CK and CK-MB were 1998 ± 1252 and 254 ± 190 IU/L, respectively. Thirty-two (62%) patients were treated with thrombolytic therapy and 5 patients underwent primary angioplasty of the infarct-related vessel. Stress tests and resting echocardiograms were performed 6 ± 2 days after admission. All but the 5 patients treated with primary angioplasty were submitted to coronary angiography 12 ± 3 days after infarction. Mean global left ventricular ejection fraction was 52% ± 14%. Quantitative measurements of coronary stenoses were performed with the use of the CMS system. Mean residual stenosis of the infarct-related artery was 75% ± 19%. Persistent occlusion of the infarct-related artery was observed in 12 patients. Elective angioplasty of the infarct-related artery was performed, always after stress tests, in 37 (72%) patients who had a significant (>50%) residual stenosis. The results of stress testing were not used for the decision to perform the procedure. A follow-up resting echocardiogram was recorded 1 month later. The study was approved by the research ethics committee of our institution; informed consent was obtained in all patients.

Stress test
β-Adrenergic–blocking agents were withdrawn 24 hours before the stress tests. Nitrates and calcium antagonists were not given the day of the test. Each test was performed with the patient lying in the same decubitus position. A 12-lead electrocardiogram was monitored continuously and recorded every minute. Blood pressure was measured at each stage by arm-cuff sphygmomanometer. Stress tests were stopped in the presence of one of the following end points: target heart rate (≥ 230/120 mm Hg), or hypotension (decrease in systolic blood pressure >30 mm Hg). The exercise test was performed with the patient in the supine position on an exercise table. After a single load of 25 W maintained for 3 minutes, the work load was progressively increased every 2 minutes by 25 W. Dobutamine was administered in the same position, at doses of 5 and 10 µg/kg per minute for 3 minutes each, followed by increments of 10 µg/kg per minute every 2 minutes up to a maximal dose of 40 µg/kg per minute. Atropine (0.25 mg to a maximum of 1 mg) was added if the target heart rate was not reached with dobutamine alone.

Electrocardiographic analysis
ST-T segment characteristics were analyzed in the infarct-related electrocardiographic leads, as previously described. During stress testing, ST elevation was defined as new or worsening at ≥1 mm, 80 ms after J point, in ≥2 contiguous infarct-related leads. Initial change of ST segment was related to dobutamine dosage, work load, and rate-pressure product. The sum of ST elevation was calculated at rest and at peak stress. The mean of ST elevation was determined by dividing the sum of ST elevation and the number of infarct-related leads with ST elevation. If ST segment elevation was present at rest, only the difference between peak and rest ST elevation was considered. T-wave normalization was defined as present when inverted T waves at rest became upright during stress in ≥2 infarct-related leads.

Echocardiographic imaging
Two-dimensional echocardiography was performed with a General Electric VingMed System Five with a 2.5-MHz transducer, with images acquired in parasternal long- and short-axis and apical long-axis, 4- and 2-chamber views. Left ventricular wall motion and thickening were evaluated with a 16-segment, 4-grade scale model, in which 1 = normal wall thickening; 2 = hypokinesis; 3 = akinesis; and 4 = dyskinesis. For each segment, reversible dysfunction was defined as improved wall thickening of ≥1 grade at follow-up. A change from dyskinesis to akinesis was not considered as improved function. All patients had an abnormal rest echocardiogram in the infarct zone. Functional recovery was considered to be present in a patient when improvement in wall thickening concerned at least 2 contiguous segments of the affected area. A wall motion score index defined as the sum of the individual segment scores divided by the number of segments was calculated for baseline and follow-up echocardiograms. The change in score index from baseline to follow-up was calculated.

Statistical analysis
Data are expressed as mean ± 1 SD. Sensitivity, specificity, positive and negative predictive values, and accuracy were calculated by standard formulas. To test differences between 2 groups, independent 2-sample t tests were used. Linear regression analysis was applied to study relations between different parameters. Statistical significance was defined as P ≤ .05. Two binary outcome variables were analyzed separately: ST elevation versus no ST elevation and functional recovery versus no functional recovery. For these two outcomes, findings were first examined by univariate analysis for differences between groups. Stepwise logistic discriminant analysis was used to identify the independent variables that best distinguished groups.

Results
Dobutamine and exercise stress electrocardiography
On resting electrocardiography, 35 patients had pathologic Q waves, 32 had negative T waves, and 14 had baseline ST elevation. A significant linear correlation was found in these 14 patients between baseline ST elevation and baseline wall motion score index (r = 0.83; P = .0002) (Figure 1). The peak rate-pressure product was not significantly higher with exercise than with dobutamine (19,880 ± 3488 vs 18,868 ± 3971). Significant ST elevation in the infarct-related leads developed in 30 (58%) patients during dobutamine testing and in 24 (46%) during exercise. ST elevation developed in 21 patients during both tests, and the agreement was significant (κ = 0.41; P = .0001). Worsening of baseline ST-segment elevation occurred in 8 patients during the 2 tests. ST-segment depression was observed in 12 patients during both tests. T-wave
normalization and ST elevation occurred at a lower rate-pressure product than did ST-segment depression during either dobutamine testing (11,697 ± 2835 vs 13,434 ± 2823 vs 19,250 ± 2896, respectively) (P < .02 and P < .0001) or exercise testing (16,141 ± 3117 vs 16,786 ± 2823 vs 20,990 ± 3659, respectively) (P = .0006). At the time of ST elevation, diastolic blood pressure was lower during dobutamine (61 ± 11 mm Hg) than during exercise testing (79 ± 13 mm Hg) (P < .0001). No difference was found between rate-pressure product at the time of ST depression during the two tests. T-wave normalization, ST elevation, and ST depression occurred at different dobutamine doses (16 ± 8, 25 ± 7, and 34 ± 7, respectively) (P < .0001). The mean of the sum of ST elevation was lower during exercise testing (5.5 ± 2.5 mm) than during dobutamine administration (7.7 ± 3.8 mm) (P = .03).

Distinction between patients with and those without ST elevation

The clinical characteristics of the patients with and those without stress-induced ST elevation are depicted in Table I. There were no significant differences in age, sex, site of AMI, proportion of Q-wave infarction, proportion of Q-wave infarction, peak CK, peak CK-MB, baseline score index, follow-up score index, or residual stenosis of IRA between these two groups. However, patients with ST elevation had a lower residual stenosis of IRA and a higher T-wave normalization rate than those without ST elevation. T-wave normalization, ST elevation, and ST depression occurred at different dobutamine doses (16 ± 8, 25 ± 7, and 34 ± 7, respectively) (P < .0001). The mean of the sum of ST elevation was lower during exercise testing (5.5 ± 2.5 mm) than during dobutamine administration (7.7 ± 3.8 mm) (P = .03).

Table I. Comparison between patients with and those without stress-induced ST elevation

<table>
<thead>
<tr>
<th>Data</th>
<th>Dobutamine test</th>
<th>Exercise test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ST elevation (n = 30)</td>
<td>No ST elevation (n = 22)</td>
</tr>
<tr>
<td>Age (y)</td>
<td>59 ± 11</td>
<td>58 ± 13</td>
</tr>
<tr>
<td>Sex (% men)</td>
<td>90</td>
<td>86</td>
</tr>
<tr>
<td>Site of infarction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>12 (40%)</td>
<td>9 (41%)</td>
</tr>
<tr>
<td>Inferior</td>
<td>16 (53%)</td>
<td>10 (45%)</td>
</tr>
<tr>
<td>Lateral</td>
<td>2 (7%)</td>
<td>3 (14%)</td>
</tr>
<tr>
<td>Thrombolytic therapy</td>
<td>16 (53%)</td>
<td>1 (73%)</td>
</tr>
<tr>
<td>Q wave</td>
<td>21 (70%)</td>
<td>14 (64%)</td>
</tr>
<tr>
<td>Peak CK (IU/L)</td>
<td>1797 ± 1304</td>
<td>2272 ± 1149</td>
</tr>
<tr>
<td>Peak CK-MB (IU/L)</td>
<td>193 ± 170</td>
<td>337 ± 187*</td>
</tr>
<tr>
<td>Baseline score index</td>
<td>1.37 ± 0.21</td>
<td>1.38 ± 0.24</td>
</tr>
<tr>
<td>Follow-up score index</td>
<td>1.12 ± 0.14</td>
<td>1.34 ± 0.26</td>
</tr>
<tr>
<td>T-wave normalization</td>
<td>15 (50%)</td>
<td>7 (32%)</td>
</tr>
<tr>
<td>Residual stenosis of IRA (%)</td>
<td>76 ± 21</td>
<td>74 ± 19</td>
</tr>
</tbody>
</table>

IRA, Infarct-related artery.

*P = .007.
Predictors of functional recovery

Functional recovery was observed in 35 (67%) patients. Among the 14 patients with persistent rest ST-segment elevation in the infarct-related leads, all 5 with a mean ST elevation >1.6 mm (sum of ST elevation at rest divided by the number of infarct-related leads with ST elevation) did not have functional recovery at follow-up. In contrast, the 9 remaining patients with a mean ST elevation <1.6 mm recovered at follow-up (Figure 1). Contractile improvement was significant in patients with stress-induced ST elevation. Score index improved from 1.43 ± 0.22 at baseline to 1.17 ± 0.19 at follow-up in patients who had ST elevation during exercise and from 1.37 ± 0.21 to 1.12 ± 0.14 mm in those who had ST elevation during dobutamine (P <.0001).

No significant improvement of wall thickening was observed in patients without ST elevation during either exercise (1.32 ± 0.21 vs 1.24 ± 0.25) or dobutamine (1.38 ± 0.24 vs 1.34 ± 0.26). Clinical, echocardiographic, and angiographic characteristics of patients with and without functional recovery are listed in Table II. There were no significant differences in age, sex, site of infarction, proportion of Q-wave infarction, number of pathologic Q waves, thrombolytic therapy, and residual stenosis of the infarct-related artery. Peak levels of CK and CK-MB were lower in patients who recovered (1679 ± 1112 vs 2654 ± 1299 IU/L; P = .013 and 214 ± 176 vs 337 ± 195 IU/L; P = .037). Elective coronary angioplasty was more frequently performed in patients with functional recovery (28 of 35 vs 9 of 17; χ² = 5.0; P = .024). There was a significant association between the occurrence of dobutamine- or exercise-induced ST elevation and contractile recovery (χ² = 10.5; P = .0012 and χ² = 4.8; P = .028, respectively). In multivariate analysis, 2 independent variables were selected stepwise: dobutamine ST elevation (χ² = 9.1; P = .0026) and a low peak CK level (χ² = 5.1; P = .025). When dobutamine ST elevation was not included in multivariate analysis, exercise-induced ST elevation emerged as an independent predictor of functional recovery (χ² = 5.0; P = .023). Sensitivity of ST elevation for predicting functional recovery tended to be higher but not significantly higher with dobutamine than with exercise (74% vs 57%). Specificity was similar (76%). Positive and negative predictive values were 87% vs 83% and 59% vs 46% for dobutamine and exercise ST elevation, respectively (Figure 2). A high correlation was found between the sum of ST elevation occurring during dobutamine testing and the extent of functional recovery (r = 0.87; P <.0001) (Figure 3). In contrast, no correlation was found between the sum of ST elevation during exercise and the extent of recovery (r = 0.06; P = not significant [NS]).

Discussion

The main findings of this study can be summarized as follows: (1) ST elevation at rest correlates with severe regional dysfunction, (2) the incidence of stress-induced ST elevation is not significantly different during the two tests, (3) ST elevation is higher during dobutamine than during exercise testing, (4) stress-induced ST elevation is a strong predictor of functional recovery, and (5) the degree of dobutamine-induced ST elevation but not that of exercise-induced ST elevation correlates with the extent of recovery.
ST elevation at rest

After healing of AMI, ST elevation persists in more patients with anterior infarction compared with inferior necrosis. Persistent ST elevation on Q leads was observed in 14 of our patients: 12 in the anterior leads and only 2 in inferior leads. In the prethrombolytic era, ST elevation at rest was considered to reflect the extent of ventricular damage or the presence of a left ventricular aneurysm.6,7 This study demonstrates that soon after AMI, ST elevation at rest in Q leads is associated with more severe regional dyssynergy. A high positive correlation was found between the mean degree of ST elevation at rest and the severity of regional dysfunction as evaluated by echocardiographic score index. Recently, Bodi et al8 showed that the presence of ST-segment elevation correlated with worse wall motion abnormalities, lower ejection fraction, and a greater likelihood of an occluded vessel but not with an increase in left ventricular volumes 6 months after AMI. This suggests that residual ST elevation at rest should not rule out the persistence of some subepicardial viable tissue, which could prevent ventricular remodeling. All 5 patients with mean ST elevation >1.6 mm did not show recovery at follow-up. Because left ventricular volumes were not measured in this study, we cannot ascertain whether persistent akinesis was accompanied by adverse remodeling in these patients.

Stress-induced ST-segment elevation

The incidence of stress-induced ST elevation was slightly lower with exercise (46%) than during dobutamine testing (58%). The incidence of ST elevation during exercise or dobutamine testing reported in previous studies was highly variable; this reflects important differences in patient populations and in intervals between AMI and stress testing. ST elevation was first considered to indicate transmural necrosis.7 However, the exact mechanism underlying the development of stress ST elevation in the infarct-related leads remains unclear. Some studies have suggested that myocardial stretching of a dyskinetic ventricle may alter transmembrane potential, causing ST elevation.9 In the present era of acute intervention by thrombolysis or immediate angioplasty, the incidence of transmural infarction and left ventricular aneurysm has largely decreased. Most patients have an incomplete infarction, with an admixture of subendocardial necrosis and salvaged subepicardium that can become ischemic. Several studies have recently found an association between stress-induced ST elevation and evidence of viability, residual ischemia, or both.2-4,10,11 A recent experimental study suggests that stress ST elevation could also be related to ischemia adjacent to transmural infarction.12 A recent transmural infarction is indeed a low resistance medium that allows a good transmission of ST-segment potential changes generated by contiguous peri-infarction ischemia. In the current study, a low peak CK-MB level was the single predictor of dobutamine ST elevation, suggesting a smaller infarct size and a higher proportion of salvaged myocardium. Persistent controversy on the significance of stress-induced ST elevation after AMI may be related more to moderate sensitivity and specificity of the imaging techniques assessing peri-infarction ischemia rather than to poor accuracy of electrocardiographic changes.

Figure 2

Sensitivity (Sens), specificity (Spec), positive (+) and negative (−) predictive values (PV), and accuracy (Accur) of stress-induced ST elevation for prediction of functional recovery. White bar, Dobutamine; black bar, exercise.
Dobutamine-induced versus exercise-induced ST elevation

An unexpected and intriguing finding of this study is a higher ST elevation induced by dobutamine infusion than by exercise despite a slightly lower peak rate-pressure product during the former test. In patients with coronary artery disease but no previous AMI, the incidence and severity of ischemia are less during dobutamine than during exercise echocardiography. However, when ischemia is induced by both stress tests, it occurs at lower levels of external cardiac work during dobutamine than during exercise. This may be caused by the oxygen-wasting effect of dobutamine, by a blunted increase or a paradoxical decrease in myocardial oxygen supply during dobutamine infusion in regions fed by stenotic vessels, or both. Another potential mechanism to explain the greater ST elevation with dobutamine than with exercise could be a higher incidence of dobutamine-induced than exercise-induced coronary vasoconstriction or spasm. Both stress tests may indeed provoke coronary spasm in patients with active coronary artery disease. Dobutamine stimulates β-1, β-2, and α-1 receptors: The β-2-mediated vasodilatory activity is usually offset by the α-1-mediated vasoconstrictor effect. Whereas severity of coronary artery stenosis is the single determinant of a positive exercise echocardiogram, the complexity of the atherosclerotic plaque plays an independent role on the positivity of a dobutamine stress echocardiogram. A lower increase at peak dobutamine-atropine stress in diastolic blood pressure with dobutamine than during exercise may also play a role in our

Figure 3

Linear correlation between sum of ST elevation at peak stress and change in wall motion score index. A, Dobutamine test; B, exercise test.
patients. Both tests were performed in the same supine position, but venous return was strikingly different during the two tests, probably resulting in smaller cardiac volumes and lower diastolic and systolic pressures during the dobutamine test.22

Stress-induced ST elevation and functional recovery

Few studies have assessed the usefulness of stress-induced ST elevation for predicting improvement of function after AMI. Recently, we3 and others4 have found that recovery in regional function was more frequent in patients with than in patients without dobutamine-induced ST elevation. This study confirms and extends these results by demonstrating that both exercise and dobutamine ST elevation are predictors of recovery. The accuracy of dobutamine ST elevation (75%) is similar to that observed by Elhendy et al5 (80%) and in our previous investigation3 (74%) and slightly but not significantly higher than the accuracy of ST elevation during exercise (63%). Stepwise multivariate analysis selected dobutamine-induced ST-segment elevation as the best predictor of functional recovery. It should be emphasized that elective angioplasty of the infarct-related artery was performed in most (72%) of our study patients, but the results of stress testing were not used in this decision. This setting corresponds to our current practice and has probably permitted recovery of hibernating myocardium. Indeed, the need for revascularization of the culprit lesion to achieve functional recovery of viable myocardium at jeopardy after AMI has been previously demonstrated by Barilla et al.23 Exercise-induced ST elevation has also been found to predict improvement in left ventricular ejection fraction as measured by angiography by Schneider et al,10 but exercise was performed after healing in their study, with a mean infarct age of 11 months, ranging from 4 to 49.

In this study, no correlation was found between the sum of ST elevation during exercise and the extent of functional recovery as determined by the reduction in score index from early to follow-up echocardiogram. In contrast, a high correlation (r = 0.87) was observed between this parameter and the sum of dobutamine-induced ST elevation. This is of clinical importance because a significant recovery of function is a major objective of revascularization in this clinical setting.

Limitations

Left ventricular volumes and ejection fraction were not measured. Regional function was assessed by semi-quantitative evaluation and calculation of a score index, but this method is widely validated and accepted for serial evaluation after AMI and revascularization procedures. Coronary angiography was not repeated at follow-up. Thus restenosis or reocclusion cannot be excluded: This could have resulted in lack of recovery in some patients. However, repeated catheterization is not indicated in asymptomatic patients. Our study group consisted of patients with uncomplicated AMI. No patient had echocardiographic or angiographic evidence of large dyskinetic areas or aneurysm. Our results are not necessarily applicable to patients with severe ventricular dysfunction or heart failure or to clinical settings other than AMI.

Clinical implications

In patients with uncomplicated AMI, predischarge stress testing is mandatory.24,25 Exercise or pharmacologic stress tests are usually performed. Although the requirement of an imaging technique coupled to dobutamine stress testing has frequently been emphasized, our study shows that careful observation of ST-segment changes during testing provides an accurate and cost-effective strategy for predicting the extent of recovery in regional function after AMI. This indicates that dobutamine testing could also be applicable to patients with low echogenicity in this clinical setting.

References