The Significance of Stress-Induced ST Segment Depression in Patients With Inferior Q Wave Myocardial Infarction
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OBJECTIVES
This study was conducted to evaluate the relationship between ST segment depression (STD) during dobutamine stress tests in different electrocardiogram (ECG) leads and myocardial ischemia assessed by simultaneous single photon emission computed tomography (SPECT) imaging in patients with inferior Q wave myocardial infarction.

BACKGROUND
STD is a standard electrocardiographic sign of myocardial ischemia. Although STD may represent reciprocal changes in patients with previous myocardial infarction, studies of reciprocal changes during stress tests are scarce.

METHODS
Dobutamine (up to 40 μg/kg/min) stress and rest myocardial perfusion scintigraphy using technetium SPECT imaging was performed in 125 patients >3 months after Q wave inferior myocardial infarction. The location of STD at the ECG was defined as anterior (V1–4), high lateral (I, aVL) and lateral (V5,6). Ischemia was defined as reversible perfusion abnormalities.

RESULTS
STD occurred in the high lateral leads in 20 patients, in the anterior leads in 12 patients and in the lateral leads in 2 patients. ST segment elevation occurred in 25 patients in the inferior leads. High lateral STD was associated with inferior ST elevation in 16 patients (80%). There was a significant inverse linear correlation between the magnitude of ST segment shift from rest to peak stress in the inferior and the high lateral leads (r = −0.8, p < 0.0005), whereas no significant correlation was found between ST segment shift in the inferior and the anterior leads (r = −0.1, p = NS) or between the inferior and the lateral leads (r = 0.15, p = NS). Ischemia was detected in 45% of patients with and in 42% of patients without high lateral STD (p = NS). Patients with high lateral STD had a higher prevalence of fixed perfusion defects in the inferior wall (100% vs. 70%) and in the posterolateral wall (55% vs. 29%) compared with other patients (both p < 0.05). Ischemia was more prevalent in patients with anterior STD than without (75% vs. 39%, p < 0.05).

CONCLUSIONS
In patients with inferior Q wave myocardial infarction, stress-induced STD in high lateral leads should be recognized as a reciprocal change for ST elevation in the inferior leads, and therefore, should be interpreted with the consideration of the significance of ST elevation if present, rather than being indicative of myocardial ischemia on its own. The STD found in the anterior leads appears to be a sign of myocardial ischemia. These findings should be considered in the definition of a positive ECG stress test and in establishing the criteria for the termination of stress test. (J Am Coll Cardiol 1999;33:1909–15) © 1999 by the American College of Cardiology

ST segment depression (STD) is an established electrocardiographic sign of myocardial ischemia during stress testing (1–3). However, STD may represent reciprocal changes corresponding to elevation of ST signal reflecting the opposite electrocardiographic leads rather than myocardial ischemia (4). Previous studies that evaluated the phenomena of reciprocal changes on the electrocardiogram (ECG) were mostly dealing with spontaneous changes after acute myocardial infarction (4–7). Studies of reciprocal changes during stress testing are scarce and are often performed without tomographic evaluation of myocardial ischemia by an independent technique (8). Despite the reported data regarding reciprocal STD after myocardial infarction, STD is still considered a sign of myocardial ischemia regardless of its location (1,2,9,10). The differentiation between reciprocal changes and true ischemia is important for improving the accuracy of stress ECG after myocardial infarction. In addition, the use of STD as an end point for the stress test...
is not appropriate if STD merely represents reciprocal changes. Termination of the test prematurely due to nonischemic ECG changes may reduce the sensitivity of the imaging technique used in conjunction with the stress test.

Myocardial perfusion scintigraphy in conjunction with stress testing is a clinically useful method for the detection of myocardial ischemia and for the diagnosis of significant coronary artery disease (11). Single photon emission computed tomographic (SPECT) imaging improves the localization of myocardial ischemia. Pharmacologic stress testing with dobutamine is a feasible alternative to exercise in patients with limited exercise capacity (12–16). This study evaluates the relationship between STD during dobutamine stress tests in different ECG leads and myocardial ischemia assessed by simultaneous SPECT imaging in patients with inferior Q wave myocardial infarction.

METHODS

Patient population. The study population consisted of patients with inferior Q wave myocardial infarction and limited exercise capacity who were referred to our imaging laboratory for evaluation of myocardial ischemia by dobutamine stress myocardial perfusion scintigraphy >3 months (mean 4.2 ± 4.0 years) after infarction. Patients were not included if they had a history or ECG signs of a previous anterior myocardial infarction, left or right bundle branch block, ST segment depression or elevation at rest or ECG signs of ventricular hypertrophy or pre-excitation. Contraindications for the test were severe heart failure, significant valvular heart disease, severe hypertension (blood pressure ≥180/110 mm Hg), hypotension (blood pressure <90/60 mm Hg) and unstable chest pain. One hundred twenty-five patients fulfilled the selection criteria. There were 94 men and 31 women; mean age was 62 ± 10 years. All patients gave a verbal informed consent to undergo the study. The Hospital Ethical Committee approved the use of dobutamine stress myocardial perfusion scintigraphy.

Dobutamine stress test. Dobutamine was infused through an antecubital vein starting at a dose of 5 μg/kg/min followed by 10 μg/kg/min (3-min stages), increasing by 10 μg/kg/min every 3 min to a maximum of 40 μg/kg/min. Atropine (up to 1 mg) was given to patients not achieving 85% of age-predicted maximal heart rate, and dobutamine infusion was continued. A three-lead ECG was continuously monitored. A 12-lead ECG was printed at rest and every minute during stress and in the recovery period. Cuff blood pressure was measured at rest, every 3 min during stress and at maximal stress. The test was interrupted if severe chest pain, significant ventricular or supraventricular arrhythmia, hypertension (blood pressure ≥240/120 mm Hg), systolic blood pressure fall >40 mm Hg or any intolerable side effect regarded as being due to dobutamine occurred during the test. Metoprolol (1–5 mg) was available and was used intravenously to reverse the effects of dobutamine if they did not revert quickly.

Electrocardiographic evaluation. The level of the ST segment was calculated, after signal averaging by a computer-assisted system (Cardiovet CSG/12; Schiller, Baar, Switzerland). The ECGs were reviewed by two cardiologists unaware of clinical or SPECT data. The ST segment elevation was defined as new or additional ≥0.1 mV elevation of the J point with a horizontal or upsloping ST segment lasting 80 ms during stress in at least two leads regarding the PQ segment as the isoelectric line (17). The STD was defined as ≥0.1 mV horizontal or downsloping depression 80 ms after the J point, below baseline level in at least two leads. The ECG leads were divided into anterior (V1–4), inferior (II, III, aVF), lateral (V5,6) and high lateral (I, aVL) (8).

SPECT imaging. Approximately 1 min before the termination of the stress test, an intravenous dose of 370 MBq of 99mtechnetium sestamibi (80 patients) or tetrofosmin (45 patients) was administered. The acquisition of stress SPECT imaging was started 1 h after the test. Resting studies were performed 24 h after the stress study, 1 h after injection of 370 MBq of sestamibi or tetrofosmin. The same isotope administered during stress was used for rest studies. Image acquisition and interpretation were performed according to the previously described protocols (15). For each study six oblique (short-axis) slices from the apex to the base and three sagittal (vertical long-axis) slices from the septum to the lateral wall were defined. Each of the six short-axis slices was divided into eight equal segments. The interpretation of the scan was performed by visual analysis assisted by the circumferential profiles analysis. All tomographic views were reviewed in a side-by-side pair (stress and rest) by an experienced observer who was unaware of the patients’ clinical or ECG data. A reversible perfusion defect was defined as a perfusion defect on stress images that partially or completely resolved at rest images in two or more contiguous segments or slices. This was considered diagnostic of ischemia. A fixed perfusion defect was defined as a perfusion defect on stress images in two or more contiguous segments or slices that persists on rest images. Six major myocardial segments were identified: anterior, inferior, sep-
tal anterior, septal posterior, posterolateral and apical. To assess the severity of perfusion abnormalities, each of the six major left ventricular segments was scored using a four-grade score method (0 = normal, 1 = slightly reduced, 2 = moderately reduced, 3 = severely reduced or absent uptake). Perfusion score was derived by the summation of the score of the six myocardial segments for rest and stress images. Ischemic score was obtained by subtracting rest from stress score. Rest (fixed perfusion defect) score was considered as infarction score.

Statistical analysis. Unless specified, data are presented as mean values ± SD. The chi-square test was used to compare differences between proportions. The Student t test was used for analysis of continuous data. Differences were considered significant if the null hypothesis could be rejected at the 0.05 probability level.

RESULTS

Symptoms and hemodynamic response. Heart rate and systolic blood pressure increased significantly from rest to peak stress (71 ± 16 vs. 133 ± 18 beats/min, p < 0.00001, and 134 ± 21 vs. 141 ± 27 mm Hg, p < 0.001, respectively). Angina occurred in 45 patients (36%). Mean maximal dobutamine dose was 37 ± 5 μg/kg/min. Atropine was administered in 62 patients (50%). Arrhythmias during the test were nonsustained ventricular tachycardia in eight patients (6%) and supraventricular tachycardia in four patients (3%). Symptomatic hypotension occurred in three patients (2%). Reasons for the termination of the test were the attainment of the target heart rate in 96 patients (77%), administration of maximal dobutamine-atropine dose in 10 patients (8%), hypotension in 3 patients (2%), angina in 12 patients (10%), chills, headache and anxiety in 3 patients (2%) and arrhythmias in 1 patient (1%).

Myocardial perfusion scintigraphy. The SPECT results were normal in four patients (3%). A fixed perfusion defect was detected in 68 patients (54%). Fifty-three patients (42%) had a partial or a completely reversible perfusion defect.

Electrocardiographic changes. The STD in one or more locations occurred in 28 patients (22%). The location of STD was anterior in 12 patients, high lateral in 20 patients and lateral in 2 patients. Six patients had STD in both the anterior and the high lateral leads. ST segment elevation in inferior leads occurred in 25 patients (20%). There was a significant inverse linear correlation between the magnitude of ST segment shift from rest to peak stress in the inferior and the high lateral leads (r = −0.8, p < 0.0005), whereas no significant correlation was found between ST segment shift in the inferior and the anterior leads (r = −0.1, p = NS) or between the inferior and the lateral leads (r = 0.15, p = NS). In patients with ST segment elevation, concomitant ST segment depression was detected in the anterior leads in 5 patients (20%) and in the high lateral leads in 16 patients (64%).

Relation between electrocardiographic changes and perfusion abnormalities. PATIENTS WITH ST SEGMENT ELEVATION. Reversible perfusion defects were detected in 9 of 25 patients (36%) with and in 44 of 100 patients (44%) without ST segment elevation (p = NS; Fig. 1). Patients with ST elevation had a higher prevalence of resting perfusion abnormalities in the inferior wall (25/25 [100%] vs. 69/100 [69%], p < 0.01).

PATIENTS WITH HIGH LATERAL STD. All patients with high lateral STD had perfusion abnormalities on rest images (fixed or partially reversible defects). Reversible perfusion defects were detected in 9 of the 20 patients (45%) with and
Figure 3 demonstrates the quantitative infarction developed lateral ST depression (V5,6). Reversible perfusion in two patients, anterior in one patient and both anterior and posterolateral in one patient. The distribution of these defects was posterolateral wall (11/20 [55%] vs. 30/105 [29%], p < 0.05) compared with patients without high lateral STD, respectively. The ECG and myocardial perfusion images of a patient with ST elevation in the inferior leads and high lateral STD are shown in Figure 2.

Among the nine patients with high lateral STD and reversible perfusion defects, five had STD in the anterior leads as well. Thus, among the 14 patients with STD in the high lateral leads and no concomitant STD in the anterior leads, reversible perfusion defects were detected in 4 patients (29%). The distribution of these defects was posterolateral in one patient, anterior and septal in two patients and both anterior and posterolateral in one patient. Only four patients had high lateral STD in absence of concomitant ST elevation (two of them had anterior STD as well). Reversible perfusion defects were detected in all of these four patients. The distribution of these defects was posterolateral in two patients, anterior in one patient and both anterior and inferior in one patient.

PATIENTS WITH LATERAL ST DEPRESSION. Two patients developed lateral ST depression (V5,6). Reversible perfusion defects were detected in both of them. These defects were detected in the inferior wall in one patient and in the anterior wall in the other.

PATIENTS WITH ANTERIOR STD. Reversible perfusion defects occurred in 9 of 12 patients with (75%) and in 44 of 113 patients (39%) without anterior STD (p < 0.05; Fig. 1). The three patients who had anterior STD without reversible perfusion abnormalities had fixed perfusion defect in the inferior wall. Reversible perfusion defects in patients with anterior STD occurred in the infero-posterolateral segments in four patients, anterior, septal or apical segments in three patients and in both regions in two patients.

Quantitative perfusion abnormalities. INFARCTION SCORE. Figure 3 demonstrates the quantitative infarction (fixed defect) score in the presence and absence of various ECG patterns. Patients with ST elevation had a larger infarction score than patients without ST elevation. Similarly, the infarction score was larger in patients with than those without high lateral STD. No significant difference was found between patients with and those without anterior STD.

ISCHEMIC SCORE. Figure 4 demonstrates the quantitative ischemic (reversible defect) scores. Among the different ECG patterns, only anterior STD was associated with a higher ischemic score.

DISCUSSION

Our study shows that dobutamine-induced STD in patients with inferior Q wave myocardial infarction occurs most frequently in the high lateral leads. The following findings suggest that high lateral STD during pharmacologic stress testing represents reciprocal changes for ST segment elevation in the inferior leads: 1) 80% of patients with high lateral STD had ST elevation in the inferior leads as well; 2) There was a significant inverse linear correlation between dobutamine-induced ST segment shift in the inferior and the high lateral leads; 3) There was no significant difference between patients with and those without high lateral STD with regard to the prevalence of ischemia as assessed by reversible perfusion defects on SPECT imaging, and 4) Patients with high lateral STD had a higher prevalence of resting perfusion abnormalities and a larger fixed perfusion defect score compared with other patients, which is a finding similar to that encountered with ST segment elevation in this study and in previous reports (18,19). Four patients had high lateral STD without concomitant ST elevation, and all of them had reversible perfusion defects. However, this number is too small to make a conclusion regarding the isolated high lateral STD.

In contrast with the poor association between high lateral STD and ischemia, anterior STD was associated with a significantly higher prevalence of ischemia compared with other patients. Patients with anterior STD had a higher ischemic score and a similar infarction score compared with patients without anterior STD.

The severity of perfusion abnormalities. The occurrence of STD in the high lateral leads or ST elevation in the inferior leads was associated with a larger infarct size as assessed by the fixed perfusion defect score. High lateral STD was associated more frequently with the extension of the infarct to the posterolateral wall. Although high lateral STD was not related to myocardial ischemia in most patients, the association between this pattern and a larger infarct size may have prognostic implications in these patients.

Comparison with previous studies. To our knowledge, this is the first study that evaluated the relationship between stress-induced STD in different ECG leads and functional abnormalities by an independent technique in patients with previous Q wave inferior myocardial infarction. Most previous studies evaluated spontaneous changes in the acute phase or early after acute myocardial infarction (4–7). Anterior STD in patients with inferior myocardial infarction has been attributed to left anterior descending coronary artery disease, low ejection fraction and poor prognosis (5,6). However, other authors concluded that it is a benign reciprocal phenomenon without prognostic implications (4,7). Extension of the infarction to the posterior wall was also reported as an underlying mechanism of anterior STD (4,5). In this case, anterior STD was considered as a reciprocal change of a presumed ST elevation in the posterior leads (4). In our study, patients with ST elevation or high lateral STD, but not those with anterior STD, had a higher prevalence of infarct extension to the posterolateral...
Figure 2. A, 12-lead ECG at rest and at dobutamine stress (30 μg/kg/min) of a 57-year-old male patient studied 14 months after Q wave inferior myocardial infarction. The patient developed ST segment elevation in the inferior Q leads (II, III, aVF) and concomitant ST segment depression in the high lateral leads (I, aVL) during stress. B, Stress and rest tetrofosmin SPECT myocardial perfusion images from the short-axis (SA), vertical long-axis (VLA) and horizontal long-axis (HLA) views of the same patient, demonstrating a fixed perfusion defect in the postero-inferior wall (arrows) without reversibility (no scintigraphic evidence of ischemia).
There was no significant correlation between the ST segment level in the inferior and the anterior leads. Anterior STD was associated with reversible perfusion abnormalities in most patients (75%), and the infarction score was similar in patients with and without anterior STD.

Coma-Canella et al. (8) studied 32 patients with inferior myocardial infarction by dobutamine stress ECG. There was a strong inverse linear correlation of ST segment shift between the inferior and high lateral leads. The authors concluded that ST depression is a benign mirror image of opposite ST elevation. The number of patients with inferior infarction in that study was small, and patients with resting STD and elevation were included, which complicates interpretation of data. In addition, no imaging technique was applied for independent evaluation of ischemia. Nevertheless, the findings of Coma-Canella et al. are in line with the conclusions of our study, which confirmed these conclusions by tomographic evaluation of perfusion abnormalities related to ECG changes.

**Limitations of the study.** The functional significance of high lateral STD in the absence of ST elevation could not be adequately studied because this pattern occurred only in four patients. The same applies to lateral STD, which occurred only in two patients. Further studies of a larger number of patients are required to solidify the significance of such changes. This study evaluated the significance of ECG changes during dobutamine stress tests in patients with limited exercise capacity. Although it could be assumed that the findings of this study apply to other forms of stress tests, general extrapolation of these conclusions to other forms of stress testing requires further studies. Finally, we

![Image](image1.png)

**Figure 3.** Fixed perfusion defect (infarction) score as assessed by rest SPECT imaging in the presence and in absence of electrocardiographic changes during dobutamine stress test. **Filled bars,** yes; **open bars,** no.

![Image](image2.png)

**Figure 4.** Reversible perfusion defect (ischemic) score as assessed by stress and rest SPECT imaging in the presence and in absence of electrocardiographic changes during dobutamine stress test. **Filled bars,** yes; **open bars,** no.
did not evaluate the relation between ECG changes and coronary angiography because the latter was not performed in all patients. However, myocardial perfusion scintigraphy is an acceptable method for the functional evaluation of patients referred for stress testing. The presence of perfusion abnormalities provides information that cannot be obtained by the simple angiographic delineation of coronary arterial lumen (11).

**Clinical implications.** In patients with inferior Q wave myocardial infarction, stress-induced STD in high lateral leads should be recognized as a reciprocal change for ST elevation in the inferior leads, and therefore, should be interpreted with the consideration of the significance of ST elevation if present, rather than being indicative of myocardial ischemia on its own. The STD in the anterior leads seems to be a sign of myocardial ischemia, despite the fact that it cannot localize ischemia. These findings should be considered in the definition of a positive ECG stress test and in establishing the criteria for the termination of stress test.

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**REFERENCES**


