Exercise-induced ST-segment Elevation in Leads V_1 or aV_L

A Predictor of Anterior Myocardial Ischemia and Left Anterior Descending Coronary Artery Disease

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SUMMARY  Exercise-induced ST-segment elevation in leads V_1 and/or aV_L in the absence of anterior Q waves occurred in 46 of 190 patients (24%) who underwent 12-lead exercise electrocardiography with thallium-201 myocardial perfusion imaging and coronary arteriography. Significant left anterior descending coronary artery (LAD) disease was present in 38 of 46 patients (83%) with V_1/aV_L ST elevation and in 72 of 144 patients (50%) without V_1/aV_L ST elevation (p < 0.0005). Anterior myocardial ischemia, indicated by reversible anterior perfusion defects on thallium scanning, was present in 40 of 46 patients (87%) with V_1/aV_L ST elevation and in 25 of 144 patients (17%) without V_1/aV_L ST elevation (p < 0.0005). Exercise ST elevation in V_1/aV_L was detected in 38 of 110 of the patients (35%) with LAD disease, for a specificity of 90%, and in 40 of 65 of the patients (62%) with anterior myocardial ischemia, for a specificity of 95%.

We conclude that during 12-lead exercise electrocardiography, ST-segment elevation in V_1 and/or aV_L in the absence of anterior Q waves predicts anterior myocardial ischemia and LAD disease.

ST-SEGMENT ELEVATION during exercise electrocardiography in patients without resting Q waves is uncommon,1-3 but when present, it indicates a region of severe myocardial ischemia.1,4 The site of ST-segment elevation during exercise, in contrast to the site of ST-segment depression,4 appears to predict the site of myocardial ischemia and associated coronary artery obstruction.1,2,4,6 In a previous study in patients with one-vessel disease and no resting Q waves, we found that although ST-segment elevation during exercise was infrequent in most leads, 52% of the patients with LAD disease showed ST elevation in leads V_1 and/or aV_L.4 The purpose of this study was to determine the significance of ST-segment elevation during exercise in leads V_1 or aV_L in the total population of patients undergoing 12-lead exercise electrocardiography, exercise thallium-201 myocardial perfusion scanning and coronary arteriography to assess coronary artery disease.

Methods

Patients

Over a 2-year period, 334 consecutive patients underwent combined exercise electrocardiography and exercise thallium-201 myocardial perfusion scanning to assess coronary artery disease. Forty-nine patients had previous coronary artery bypass surgery or uninterpretable ECGs, including left bundle branch block, left ventricular hypertrophy, preexcitation syndrome and ventricular pacemaker rhythm. Of the remaining 285 patients, 238 underwent coronary arteriography and form the study population.

Exercise-induced ST-segment elevation in V_1 and/or aV_L in the absence of ECG evidence of previous anterior myocardial infarction (defined by Q waves in leads V_1-V_3) was found in 46 patients (44 men and two women); these patients form the study group. Of the remaining 192 patients, 144 (126 men and 18 women) had no ECG evidence of previous anterior myocardial infarction and form the comparison group.

Exercise Electrocardiography

The patients were exercised maximally on an upright bicycle ergometer using a graded multistage continuous protocol until they experienced chest pain, breathlessness or fatigue. Leads were placed in the standard location recommended by Mason et al.8 and a 12-lead ECG was recorded before and during each minute of exercise and recovery using an Avionics three-channel Exerstress 400 unit.

The ECGs were interpreted by two independent observers according to the criteria of the American Heart Association.9 During and after exercise, each lead of the ECG was analyzed for ischemic ST-segment changes: 1 mm or greater horizontal or downsloping ST-segment depression below the baseline, lasting 0.08 second and present in three consecutive beats; and 1 mm or greater horizontal or upsloping ST-segment elevation above baseline, lasting 0.08 second and present in three consecutive beats in any lead without a Q wave other than V_1 or aV_L.

Patients without exercise-induced ischemic ST-
segment changes who reached less than 85% of the predicted maximal heart rate were included in the study only if exercise was limited by angina or if they were taking β-blocking medications and had exercised for 10 minutes on the bicycle.

Myocardial Perfusion Scanning

At peak exercise, 1.5–2.0 mCi of thallium-201 were injected intravenously, and the patients continued exercising for 1 minute longer to allow blood clearance and myocardial uptake of the thallium during conditions of stress. Scanning was begun in the exercise laboratory 5 minutes after the administration of thallium-201 (exercise scan). Four views were taken: anterior, 40° left anterior oblique (LAO), 60° LAO and left lateral using an Ohio Nuclear Sigma 420 camera and a high-resolution parallel-hole collimator. In the first view, 220 thousand counts were collected in an average time of 400 seconds. Counts in the other three views were also taken for 400 seconds. The four scans were completed within 40 minutes of exercise. Scans were repeated 4 hours later in the same four views without additional thallium (4-hour redistribution scan).

The scans were interpreted from the original Polaroid scintigraphic photos without computer enhancement or background subtraction by three experienced observers who had no knowledge of the patient data. Exercise and 4-hour redistribution scans were analyzed for the presence or absence of a thallium defect. A thallium defect was considered to be present if there was a discrete reduction of tracer activity involving at least 15% of the left ventricular circumference. Defects were considered reversible if there was a decrease in either size or intensity of the defect on the 4-hour redistribution scan. Each of the three observers was asked to make a judgment. The interconsensus variability for this technique was 7%.

Thallium defects were localized to three specific vascular areas, anterior, inferior and lateral (fig. 1), as previously described. Defects in each of these specific vascular areas usually extended into the apical vascular area, which was defined as nonspecific.

Coronary Arteriography

Selective coronary arteriography was performed in multiple projections using the Judkins or Sones technique. Each study was reviewed by two independent observers. Coronary artery obstructions of 70% or greater of the luminal diameter were considered significant. Patients with right coronary artery (RCA) obstruction or left circumflex coronary artery (LCX) obstruction were considered as one group (RCA/LCX) because the inferoposterior part of the left ventricle can be supplied by either of these arteries.

Documentation of Coronary Artery Spasm

In four patients, coronary artery spasm was suspected after significant coronary artery obstruction was excluded at coronary arteriography. To provoke spasm, these patients were given incremental doses of i.v. ergonovine. Coronary artery spasm was documented either at coronary arteriography (three patients) or was suggested by reversible ischemic changes on both ECG and thallium scan (one patient).

No complications resulted from any of the procedures.

Data Analysis

Data were analyzed using the Yates-corrected chi-square test or the exact test of Fisher, Irwin and Yates for the 2 × 2 contingency table. Sensitivity was defined as the ratio of true positives to the sum of true positives and false negatives. Specificity was the ratio of true negatives to true negatives and false positives. Predictive value of a positive test was the ratio of true positives to true positives and false positives.

Results

Coronary artery disease was present in 207 of the 238 patients (prevalence 87%) who had 12-lead exercise electrocardiography, exercise thallium-201 myocardial perfusion scanning and coronary arteriography.
ST-segment elevation in V₁ and/or aV₁ during exercise occurred in 46 of the 190 patients without anterior Q waves on rest ECG (24% incidence). ST elevation was present in V₁ alone in 30 patients, in aV₁ alone in five, and in both V₁ and aV₁ in 11. In three of the 46 patients ST-segment elevation in V₁/aV₁ occurred without other ischemic ECG changes, in 14 it was associated with ST elevation in V₂, V₃ or V₄, with or without ST depression in other leads, and in 35 it was associated with ST depression in other leads (the lateral leads V₅₋₆ and/or the inferior leads 2, 3 and aVF). The ECGs and thallium scans of two patients with exercise-induced ST elevation in V₁/aV₁ are shown in figures 2, 3 and 4.

In the 46 patients with ST-segment elevation in V₁/aV₁ during exercise, LAD disease was more frequent than RCA/LCX disease (table 1). Thirty-eight patients (83%) had significant LAD obstruction. In 22
TABLE 1. Results of Coronary Arteriography and Exercise Thallium Scanning in Patients Without Anterior Q Waves: Comparison of Groups with and Without ST-segment Elevation in $V_1/aV_L$ on Exercise Electrocardiogram

<table>
<thead>
<tr>
<th></th>
<th>$V_1/aV_L$</th>
<th>No $V_1/aV_L$</th>
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<tr>
<td></td>
<td>ST elevation</td>
<td>ST elevation</td>
<td></td>
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<tr>
<td>LAD disease</td>
<td>38 (83%)</td>
<td>72 (50%)</td>
<td>$&lt; 0.0005$</td>
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<tr>
<td>RCA/LCX disease</td>
<td>25 (54%)</td>
<td>95 (66%)</td>
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<tr>
<td>Reversible</td>
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<td>anterior</td>
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<td>thallium defects</td>
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<tr>
<td>Reversible</td>
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<tr>
<td>inferior</td>
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<tr>
<td>thallium defects</td>
<td>13 (28%)</td>
<td>41 (28%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

*None of these patients had left main coronary artery disease.
†Five of these patients had left main coronary artery disease, and in three this occurred without significant LAD obstruction.

Abbreviations: LAD = left anterior descending coronary artery; RCA/LCX = right coronary artery and/or left circumflex coronary artery.

the obstruction was proximal to the first septal perforator and in 25, it was 90% or greater. Twenty-five of 46 patients (54%) had significant RCA/LCX obstruction, but it was associated with LAD obstruction in 22. Eight of the 46 patients with ST elevation in $V_1/aV_L$ had no LAD obstruction. Three of these eight had RCA/LCX obstruction, and five had no significant coronary artery obstruction; one patient had normal coronary arteries and four had minor (50% or less) coronary artery obstructions and documented coronary artery spasm. In these four, the LAD was thought to develop spasm during exercise (transient LAD obstruction). All four had exercise-induced anterior myocardial ischemia (inferred from reversible anterior thallium defects in three and from anteroseptal ST-segment elevation associated with a reversible apical thallium defect in one). In one of the four patients, coronary arteriography revealed spasm of the LAD during exercise.3

In the 46 patients with ST-segment elevation in $V_1/aV_L$, reversible thallium defects were more frequent in the anterior vascular area than in the inferior vascular area (table 1). Forty patients (87%) had
EXERCISE ST ELEVATION IN V1/aVL/Dunn et al.

The exercise ECG shows ST-elevation in lead aVL (arrows) and ST depression in leads 2, 3, aVF, and V5. The exercise thallium scan in the 60° left anterior oblique view (left) shows an anteroseptal defect that is represented on the diagram on the middle panel, and which improves on the 4-hour redistribution scan. At coronary arteriography, the left anterior descending coronary artery had a 95% proximal obstruction and the right coronary and left circumflex arteries were normal.

To determine if exercise-induced ST elevation in V1/aVL correlated with the presence of LAD obstruction and with reversible anterior thallium defects, we compared the incidence of each of these findings in the 46 patients with V1/aVL ST elevation, with the incidence in 144 patients without V1/aVL ST elevation during exercise and without resting anterior Q waves (table 1). LAD obstruction and reversible anterior thallium defects were significantly more frequent in the 46 patients with V1/aVL ST elevation than in the 144 patients with V1/aVL ST elevation (p < 0.0005). In patients with LAD obstruction, the LAD obstruction was more frequently severe (90% or greater) in patients with V1/aVL ST elevation (25 of 38; 66%) than in those without V1/aVL ST elevation (30 of 72; 42%; p < 0.05). RCA/LCX obstruction and reversible inferior thallium defects occurred with the same frequency in both groups. The results were similar in men and women, although few women were studied, so the comparison did not reach statistical significance. The 144 patients without V1/aVL ST elevation included patients with and without ischemic ECG changes, so the incidence of LAD obstruction and reversible anterior thallium defects in the 46 patients with V1/aVL ST elevation was also compared with the incidence in 82 of the 144 patients who had an ischemic exercise ECG, defined by ST-segment depression criteria. The correlations remained unchanged (table 2).

The sensitivity, specificity, and predictive value of V1/aVL ST-segment elevation for detecting LAD obstruction and for detecting anterior myocardial ischemia are shown in tables 3 and 4. Exercise-induced ST-segment elevation in V1/aVL was highly specific for and predictive of both LAD obstruction and anterior myocardial ischemia. ST elevation in V1/aVL identified 35% of the patients with LAD obstruction and 62% of the patients with anterior myocardial ischemia.

Discussion

The results of this study indicate that ST-segment elevation in leads V1 and/or aVL during exercise predicts anterior myocardial ischemia and LAD obstruction and is not influenced by obstruction in other arteries. In the 46 patients with ST-segment

<table>
<thead>
<tr>
<th>Table 2. Comparison of Patients with V1/aVL ST-segment Elevation and Patients Without V1/aVL ST-segment Elevation But with an Ischemic Exercise Electrocardiogram</th>
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</thead>
<tbody>
<tr>
<td>V1/aVL ST elevation</td>
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<tr>
<td>(n = 46)</td>
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<tr>
<td>LAD disease</td>
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<tr>
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<tr>
<td>RCA/LCX</td>
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<tr>
<td>40 (87%)</td>
</tr>
<tr>
<td>Reversible inferior thallium defects</td>
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<tr>
<td>13 (28%)</td>
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Abbreviations: LAD = left anterior descending coronary artery; RCA/LCX = right coronary artery and/or left circumflex coronary artery.
Elevation in leads $V_1/aV_L$ during exercise, reversible anterior thallium defects and LAD obstruction were more common than reversible inferior thallium defects and RCA/LCX obstruction. Statistical analysis of these associations would be biased, so a second group of 144 patients without ST elevation in $V_1/aV_L$ was studied. When the two groups were compared, reversible anterior thallium defects and LAD obstruction were found to be significantly more common in the 46 patients with ST-segment elevation in $V_1/aV_L$ during exercise, whereas the frequency of reversible inferior thallium defects and RCA/LCX obstruction were similar in both groups. This confirms that $V_1/aV_L$ ST-segment elevation predicts anterior wall ischemia and LAD obstruction.

These observations differ from the conclusions of Castellanet et al.,\textsuperscript{14} that ST elevation in $V_1$ during exercise represents posterior wall myocardial ischemia. In that study, only patients with prior myocardial infarction, including those with anteroseptal Q waves, were studied, and posterior ischemia was inferred from arteriography rather than located by thallium scanning. We excluded patients with anteroseptal Q waves, and found that posterior or inferior ischemia, as detected by reversible inferior wall thallium defects, occurred with the same frequency in patients with and without $V_1/aV_L$ ST elevation. In contrast, ST elevation in $V_1/aV_L$ was significantly associated with anterior myocardial ischemia on the thallium scan.

Exercise-induced ST-segment elevation in $V_1/aV_L$ associated with ST-segment elevation in other anterior chest leads (as in 14 of our patients) probably represents severe anterior transmural myocardial ischemia.\textsuperscript{1, 2, 4} Exercise-induced ST-segment elevation in $V_1/aV_L$ without associated anterior ST elevation may also represent severe anterior transmural myocardial ischemia, as there was a significantly higher incidence of severe (90% or greater) LAD obstruction and reversible anterior thallium defects in the patients with $V_1/aV_L$ ST elevation during exercise than in those without $V_1/aV_L$ ST elevation. Alternatively, the lead placement used may explain this phenomenon. In Mason's modified 12-lead system, arm electrodes are placed in the infraclavicular fossae and leg electrodes midway between the rib margin and iliac spine.\textsuperscript{4} During exercise, $V_1$ and $aV_L$, like $aV_R$, may face the interior of the left ventricle and manifest ST-segment elevation by directly recording subendocardial ischemia.\textsuperscript{15}

In this study, ST-segment elevation in $V_1/aV_L$ during exercise had a predictive value of 83% for detecting significant LAD obstruction (38 of 46 patients). In eight patients, ST elevation in $V_1/aV_L$ was not associated with significant LAD obstruction, but in four of the eight it was associated with anterior myocardial ischemia. These four patients had variant angina, documented coronary artery spasm and no significant coronary artery disease. The cause of the $V_1/aV_L$ ST-segment elevation and anterior myocardial ischemia during exercise in these patients was thought to be LAD spasm, and in one patient coronary arteriography revealed LAD spasm provoked by exercise.\textsuperscript{13} If the four patients with transient LAD obstruction are included with the 38 who had fixed LAD obstruction, the predictive value of $V_1/aV_L$ ST elevation for detecting LAD disease (fixed obstruction or spasm) is 91%.

In four of our patients, ST-segment elevation in $V_1/aV_L$ during exercise was not predictive of either anterior myocardial ischemia or LAD obstruction. One of these patients had normal coronary arteries and three had significant RCA/LCX obstruction. Exercise-induced ST-segment elevation has been reported by Bruce et al.\textsuperscript{16} in 0.5% of asymptomatic patients with presumably normal arteries, and could explain ST elevation in one of our patients.

During exercise, ST-segment elevation in leads other than $V_1/aV_L$ without resting Q waves is specific for the presence and site of severe myocardial ischemia,\textsuperscript{1, 2, 3, 6} but as only 1–2% of patients\textsuperscript{1, 2} show this on exercise testing, the clinical value is limited. Our study suggests that ST elevation in $V_1/aV_L$ during exercise may be of greater diagnostic value clinically because it occurred in over 20% of our patients who had an 87% prevalence of coronary artery disease, and because it was highly specific for LAD obstruction and anterior myocardial ischemia. The relatively low sensitivity (35%) of ST elevation in $V_1/aV_L$ for detecting LAD obstruction may be related...
to several factors. In some patients, obstruction of the right and/or circumflex coronary arteries was more severe than that of the LAD coronary artery, and exercise induced ischemia of the inferior wall before the anterior wall. In other patients, the LAD obstruction was either not severe enough to produce ST-segment elevation on exercise or, when the obstruction was severe, collateral blood flow may have prevented the severe anterior myocardial ischemia associated with $V_1/aV_L$ ST elevation.

Detection of ST-segment elevation in $V_1/aV_L$ requires 12-lead exercise electrocardiography and careful examination of leads not often used in the past to identify ischemia. From the results of this study, we recommend the routine use of 12-lead exercise electrocardiography in patients with suspected coronary artery disease, as $V_1/aV_L$ ST-segment elevation suggests the presence of anterior myocardial ischemia with severe LAD obstruction and may be an indication for further investigation.

Acknowledgment

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Exercise-induced ST-segment elevation in leads V1 or aVL. A predictor of anterior myocardial ischemia and left anterior descending coronary artery disease.
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