Exercise-induced ST Elevation in Patients Without Myocardial Infarction

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SUMMARY A review of 6040 consecutive exercise tests yielded 106 patients without previous myocardial infarction (MI) who had exercise-induced ST elevation (≥ 0.5 mm in a 15-lead ECG system). In 46, ST elevation was correlated with left ventriculography and coronary angiography. Coronary artery disease (CAD) (≥ 70% narrowing) was detected in 40 of 46 patients: 12 patients had one-vessel disease, 13 had two-vessel disease, and 15 had three-vessel disease. Resting ventriculograms were normal in 36 of 40 patients. Of 21 patients with anterior (V1-V3) ST elevation, 86% had a left anterior descending (LAD) obstruction and 78% had obstruction proximal to the first diagonal branch. LAD disease occurred significantly more frequently than right and circumflex CAD. There was no anatomic correlation of three persons with lateral (leads V4 or aV4) or 27 patients with inferior-posterior (leads II, III, aVr, Y or Z) exercise-induced ST elevation. Therefore, exercise-induced ST elevation is strongly correlated with CAD but not resting wall motion abnormalities. Further, anterior exercise-induced ST elevation in patients without a previous MI often predicts a significant proximal LAD obstruction.

EXERCISE-INDUCED ST displacement away from a recording electrode (i.e., ST depression) is the common manifestation of ischemia. Although Herman et al.1 reported a close anatomic correlation with ST depression and the location of the coronary artery disease, others have been unable to confirm these findings.2, 3 At rest, ST displacement toward the recording electrode, or ST elevation, appears to correlate closely with localized spasm in vessels that contain significant coronary artery obstructions.4 6 Exercise-related ST elevation localizes wall motion abnormalities over an area of old infarction.7 10 A few studies have identified a smaller group of patients with coronary artery disease but no infarction who have exercise-induced ST elevation spatially related to the site of obstruction. To examine this group of patients in more detail, we conducted a retrospective study of a large number of patients who underwent exercise stress testing and subsequent cardiac catheterization. The purpose was to identify the clinical characteristics of this patient group and to critically analyze the spatial relation of ST elevation to the anatomic location of disease.

Methods

Patient Selection

We reviewed 6040 consecutive exercise stress tests, done at St. Paul Hospital in Dallas between 1970–1977, for patients with exercise-induced ST elevation, and examined their medical history, available hospital records and resting ECGs for evidence of a myocardial infarction. The resting ECG was examined for minor, nonspecific ST-segment and T-wave changes that we defined as ST elevation or depression or T-wave flattening ≥ 0.05 mm. An ECG was judged to be abnormal if there was ST elevation or depression ≥ 0.5 mm at rest. The Estes scoring system (≥ 4 points) was used for the diagnosis of left ventricular hypertrophy (LVH).11 A transmural infarction was diagnosed mainly by the appearance of new Q waves ≥ 40 msec in serial ECGs. In addition, at least one of the following criteria was required to substantiate the diagnosis of infarction: a history of chest pain typical for myocardial ischemia lasting at least 15 minutes or serial serum enzyme elevations (creatine kinase, lactic dehydrogenase and glutamic oxaloacetic transaminase). All patients who did not fulfill the above criteria (i.e., those in whom an infarction was uncertain) were rejected from the study; patients who either fulfilled or had none of these criteria were included in the study.

Of the 6040 patients tested, 399 (6.6%) had exercise-induced ST elevation and a myocardial infarction. The majority (95%) of the 399 patients had ST elevation over the area of infarction. One hundred six patients (1.7% of the total population) developed ST elevation and had no evidence of a myocardial infarction, LVH or bundle branch block and were not taking digitalis. Forty-six patients in this latter group had undergone diagnostic cardiac catheterization. Another 21 patients with LVH and 12 patients taking digitalis also had exercise-related ST elevation. Six patients with LVH, one of whom was also taking digitalis, were catheterized.

Exercise Testing

The stress tests were carried out according to either the multistaged Bruce or Balke protocols.12 13 Each patient’s blood pressure was monitored by indirect sphygmomanometry. Also, all patients were questioned during and after the exercise test about the development of symptoms. Angina pectoris was recorded if a patient developed exertional or postexer-
tional chest discomfort that was relieved with rest, nitrates or carotid sinus pressure. The duration and severity of each patient’s chest pain was also recorded. In addition, the relation of ST elevation and chest pain to the termination of exercise, the minutes before and the minutes afterward were noted. For the Bruce protocol we estimated the maximal oxygen consumption (VO₂) by regression analysis for sedentary persons, taking into account the exercise duration, the age and sex of the patient. For the Balke protocol we estimated maximal VO₂ from the regression equation that incorporates the treadmill speed and the angle achieved at the termination of exercise. The percent predicted VO₂ was subsequently calculated for each patient by the formula: (estimated VO₂/predicted VO₂) × 100, where the predicted VO₂ was calculated by the regression equation incorporating age, sex, weight and physical status. In addition, the heart rate and ST-T-wave changes were monitored by a combined 12-lead conventional and three-lead orthogonal (Frank) ECG system, as previously described. In all leads of each ECG, ST elevation or depression during exercise was measured as the additional shift in ST segment from the resting pre-exercise isoelectric PR segment at a point 80 msec after the R wave. Measurements of the ST segment were estimated to the nearest 0.01 mV (0.1 mm). A significant spatial change in the ST segment was defined as upsloping or flat elevation ≥ 0.05 mV (0.5 mm). Measurements of the ST elevation were done by at least two persons who were not aware of the results of coronary angiography.

Catheterization Studies

All patients were studied by cardiac catheterization using either the Sones or Judkins techniques. Resting left ventriculograms were done and the contraction pattern was analyzed either during beats that were not premature ventricular depolarizations (PVDs) or during the third or fourth beat after a PVD. Estimation of left ventricular volumes for calculating the ejection fraction was done by the single-plane method of Greene. Abnormal contraction areas were described qualitatively as hypokinetic when systolic movement was less than normal, dyskinetic when paradoxical systolic movement was seen, and akinetic when there was no inward systolic movement. Selective left and right coronary angiography was done in multiple axial and hemiaxial projections. Significant coronary artery obstructions were defined as at least 70% reduction in luminal diameter. Obstructions were localized in the proximal, middle or distal third of the coronary artery. The proximal third of the left anterior descending coronary artery corresponded in most cases to that segment of the vessel up to and including the first diagonal branch. Measurements of the coronary artery obstructions were taken by at least two persons who were not aware of the exercising electrocardiographic changes.

For each group of patients, the anatomic relationship of ST elevation to coronary artery disease was assessed with a 2 × 3 contingency table by the chi-square method (2 degrees of freedom). The null hypothesis was rejected (i.e., a relationship was felt to exist) at p < 0.05.

Results

Patient Selection

Tables 1–4 list the clinical characteristics, the resting and exercise blood pressure, heart rate, electrocardiographic and maximal VO₂ data, symptoms of angina and the cardiac catheterization results for each patient. Each table reports a group of patients who were separated either according to the spatial orientation of their exercise-induced ST elevation or electrocardiographic LVH and digitalis therapy. No patient’s data were listed more than once. The patients in table 1 had only anterior ST elevation. Table 2 lists the patients with combined anterior, inferior-posterior and lateral ST displacement. Table 3 contains the data from patients with only inferior-posterior ST elevation. Table 4 contains the data from patients with LVH and patients on digitalis.

Clinical Characteristics of Patients Without LVH, Digitalis or Myocardial Infarction (tables 1–3)

The mean age of the 46 patients studied was 52 years. The ratio of men to women was approximately 4:1. One-third of the patients had a history of hypertension. Thirty-nine were referred with a history considered typical for angina pectoris. Only one patient had a history of angina at rest. Two patients had a history of atypical chest pain and five were seen as part of a screening physical examination.

Resting Electrocardiographic and Exercise Data of Patients without LVH, Digitalis or Myocardial Infarction (tables 1–3)

Of the 46 patients studied, 22 had normal and five had abnormal resting ECGs, while 19 had minor non-specific ST-segment and T-wave changes. Eighteen patients had a single resting pre-exercise blood pressure > 140/90 mm Hg. The average blood pressure increased from a resting value of 132/84 to 172/76 mm Hg during peak exercise. Thirteen of the patients elevated their systolic pressures above 200 mm Hg. Eight of the 46 patients elevated their diastolic pressures more than 10 mm Hg above the resting value. Five patients developed angina and dropped their systolic blood pressures during exertion, which ended their test immediately. Three of the five patients with exercise-induced hypotension developed ST elevation ≥ 3 mm. The heart rate for the 46 patients increased to an average of 153 beats/min (range 101–190 beats/min). Thirty-three of 46 (72%) patients achieved 85% of their maximum predicted heart rate. The end point of the exercise test in 31 was angina, in 13 fatigue, in two arrhythmias (one ventricular tachycardia, one multifocal PVD), and in five both angina and arrhythmias. ST elevation was noted.
either at the end of exercise or within 10 seconds in all of the 46 patients, including the 31 who stopped with angina. Eighteen of 46 patients (39%) achieved 85% of their predicted maximal VO₂. The mean estimated VO₂ was 27 ml/min/kg for all the patients, which was 79% of the predicted maximum.

Angina occurred slightly before or with the ST elevation in 22 of the 31 patients who developed this symptom. The chest pain terminated before the ST elevation returned to baseline in all but two patients. In 24 of the 31 patients, the angina resolved within 3 minutes after exercise. The duration of angina was 5 minutes or less in 25 of the 31 patients. The chest discomfort was mild-to-moderate in all but one patient, who had severe chest pain.

Examples of Exercise-induced ST Elevation

In figure 1 is shown a patient who developed 1.5 mm of ST elevation in V₁-V₃ (V₂ is reproduced) immediately after exercise at a heart rate of 110 beats/min, or 65% of his predicted maximum. Leads I, X and Z were unchanged during exercise. Leads aVₑ and Y normalized the early repolarization seen on the control tracing. Within 4 minutes after exercise, the ST elevation in lead V₂ returned to the pre-exercise isoelectric baseline.

Exercise-induced inferior ST elevation is shown in figure 2. At a heart rate of 153 beats/min, or 85% of the predicted maximum, 2 mm of ST elevation occurred in leads II, III, aVₑ and Y immediately after exercise. Laterally 1 mm of ST depression occurred in lead I. Anteriorly in lead V₂ there was no spatial ST shift. By 6 minutes after the exercise there was complete ST resolution back to the control ECG.

One patient (fig. 3) exercised to a heart rate of 180 beats/min, or 97% of his predicted maximum. As exercise ended, a 3-mm ST elevation was noted in leads V₅, V₆, X, Y and Z. Within 15 seconds the elevations in leads V₅ and V₆ totally resolved, while elevations in X and Y partially resolved. At the same time, a 4-mm ST elevation in leads II and III but not aVₑ was recorded. Lead V₂ showed ST depression at this time. By 2 minutes after exercise, all elevations except that

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<td>15</td>
<td>46</td>
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in lead Z had returned to the control isoelectric PR baseline.

Patient 5 (table 2) had rest angina that occurred with emotional stress, postprandially and occasionally with exertion. The patient was repeatedly shown to have transient ST elevation at rest (fig. 4), sometimes accompanied by arrhythmias and, rarely, atrioventricular block. The rest angina was exacerbated by propranolol and relieved by nitrates. The stress test of this patient showed ST elevation in leads Z and V5-6 (fig. 5), but not in leads II or III, which were elevated during the rest angina. Coronary angiography revealed normal coronary arteries. During this procedure no attempt was made to elicit spasm. However, because of the clinical characteristics, this patient was felt to have variant angina, with spasm provokable by exercise. There were no other patients who were felt to have variant angina, either clinically or by angiographically demonstrated coronary artery spasm.

Catheterization Data of Patients Without LVH, Digitalis or Myocardial Infarction

All but one patient had a normal resting ejection fraction (i.e., > 50%). Likewise, the resting wall motion in the right anterior oblique projection was normal in the majority (36 patients). There were nine cases of left ventricular hypokinesis and one case of dyskinesis (tables 1-3). No akinetic segments were noted. Four of the 21 patients with anterior (V1-V5) ST elevation had anterior hypokinesis (tables 1 and 2). Four of the 27 patients with inferior-posterior ST elevation (II, III, aVF, Y and Z) had inferior-posterior wall motion abnormality (three hypokinesis, one dyskinesis) (tables 2 and 3).

Coronary arteriography demonstrated six patients without significant coronary artery obstructions (tables 1-3). Of the remaining 40 patients, 12 had one-vessel, 13 had two-vessel and 15 had three-vessel coronary artery disease (tables 1-3). In the group with anterior ST elevation, six patients had one-vessel, seven had two-vessel and six had three-vessel disease (tables 1 and 2). Those patients with inferior posterior ST elevation included six with one-vessel, eight with two-vessel and nine with three-vessel disease (tables 2 and 3).

Patients with LVH and Digitalis Therapy (table 4)

The mean age of this group of patients was 50 years. All patients were male. No patient had valvular heart disease. The resting ECGs of all patients showed ST- and T-wave changes secondary to the LVH or
I

F

V2

X

Y

Z

Control  Immediate  Post  4 min.
Exercise  Post  Exercise

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digitalis. One patient had resting hypertension and had a hypertensive response to exercise. Two patients had significant resting wall motion abnormalities (hypokinesis and dyskinesis) and one of these patients had a hypotensive response to exercise. All patients had additional ST elevation $\geq 1$ mm during exercise and all but one had ST depression during exercise. There were four patients with anterior (leads $V_1-V_3$), one with lateral (lead X) and one with posterior (lead Z) ST elevation. Three of the four patients with anterior ST elevation had normal wall motion. There was one patient with normal coronary arteries, one with one-vessel, two with two-vessel and two with three-vessel coronary artery disease.

Correlation of Exercise ST Elevation and Location of Disease

In the group of 46 patients without LVH or digitalis therapy, 21 developed anterior elevation, three developed lateral elevation and 27 developed inferior-posterior elevation (fig. 6). The total number of patients with anterior, lateral and inferior-posterior ST elevation exceeds 46 because elevation occurred in several different sets of leads in some patients (table 2). Almost half of the cases with ST elevation in leads $V_1-V_3$ had right and an equal number had circumflex (or obtuse marginal) coronary artery disease. Eighty-six percent had left anterior descending obstruction, which was significantly more common than right and circumflex disease. Fourteen of the 18 patients with only anterior ST elevation (table 1) had proximal anterior descending obstructions, while four had midanterior descending obstructions. Thirteen of the 21 patients with anterior ST elevation (tables 1 and 2), including 11 of the 18 patients with anterior ST elevation and proximal left anterior descending obstruction, developed reciprocal ST depression. In the six patients with LVH, three of four (75%) with anterior

FIGURE 1. Selected resting (control), immediate postexercise and recovery (4 minutes postexercise) ECG leads from a patient with anterior ST elevation.
ST elevation had either a significant proximal left anterior descending or left main obstruction.

Exercise-induced ST elevation in lateral or inferoposterior locations did not localize disease as did anterior elevation (fig. 6). Right and circumflex coronary obstructions occurred with approximately equal frequency. Separation of the group with inferior-posterior ST elevation into two subgroups with strictly posterior (lead Z) and strictly inferior (leads II, III, aVF, and Y) ST elevation did not improve the anatomic correlation of ST elevation with obstruction. Likewise, separation of the group with inferoposterior ST elevation into those with a dominant right and those with a dominant left coronary artery anatomy did not help to locate the obstruction anatomically.

If the criterion for significant net exercise-induced ST elevation were changed from $\geq 0.05$ mv (0.5 mm) to $\geq 0.1$ mv (1 mm), the number of patients who qualified (tables 1–3) would drop from 46 to 34. In this more select group there was no real change in the correlation of anterior ST elevation, since nine patients (53%) had right, nine (53%) had circumflex and 15 (88%) had left anterior descending coronary artery obstructions. Use of the more stringent criterion caused no change in anatomic distribution of coronary disease in the patients with lateral ST elevation. However, the patients who had 1 mm of inferior-posterior elevation tended to equalize the distribution of right (13 patients, 65%), circumflex (12 patients, 60%) and left anterior descending obstructions (12 patients, 60%).

Deletion of those patients who had resting electrocardiographic abnormalities in the same lead in which ST elevation occurred decreased the number of patients who qualified from 46 to 37 (tables 1–3). In the remaining 37 patients there was no change in the correlation with anterior ST elevation: six of 14 (43%) had right, 12 of 14 (86%) had left anterior descending, and six of 14 (43%) had circumflex obstructions. Likewise, there was no change in correlation of the distribution of coronary disease with either lateral or inferior-posterior ST elevation (lateral: two of three (67%) had right, one of three (33%) had left anterior descending, and two of three (67%) had circumflex obstructions; inferior-posterior: 14 of 25 (56%) had right, 10 of 25 (40%) had left anterior descending, and 13 of 25 (52%) had circumflex obstructions).

**Discussion**

Exercise-induced ST elevation is not common. In this study, the 6.6% incidence of exercise-induced ST elevation after infarction, mostly occurring over the area of infarction, comes from a review of a large population, and is slightly higher than previously reported incidences. On the other hand, the low incidence
Table 2. Data on Patients with ST Elevation in Leads V1-3, II, III, aVF, Y, Z and V4-6, X and L

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<th>Pt</th>
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*Bruce protocol.

Abbreviations: A = after exercise termination; ANT = anterior; B = before exercise termination; CIRC = circumflex coronary artery; D = distal; DYSK = dyskinesis; HYPO = hypokinesis; INF = inferior; LAD = left anterior descending coronary artery; LM = left main; M = mid; Mod = moderate; NL = normal; OM = obtuse marginal branch of the left circumflex coronary artery; P = proximal; POST = posterior; RCA = right coronary artery; T = termination of exercise; ↑ = ST elevation; ↓ = ST depression; $\dot{V}O_2$ = oxygen consumption.

H.C. (8-17-77)

(1.7%) of exercise-induced ST elevation in the absence of previous infarction is similar to that in other reports. Fortuin and Friesinger reported an incidence of 2% in catheterized patients with previous infarction and 1% in those without documented infarct.18 Others have reported incidences of 3% infarct-related and 0.5% noninfarct-related exercise-induced ST elevation.9 The differences in frequency of ST elevation may relate to the criterion of 0.5 mm for significant ST elevation rather than the conventional 1 mm used by previous investigators.9, 18 Use of the more stringent criterion would have reduced the frequency slightly, but would not have altered any of the conclusions about the anatomic correlation of disease with ST elevation.

The predictive value of 0.5-mm ST elevation (40 of 46, 87%) is comparable to that of ST depression in a symptomatic population.19 Since 46% of the patients had elevation in V1-V3 and 96% had no elevation or depression in V4, these data suggest that multiple-lead systems that incorporate V1-V3 are more sensitive than the more commonly used single-lead systems. Chaitman et al.20 arrived at a similar conclusion when they demonstrated the improved sensitivity and efficiency of several types of multiple-lead systems over a single V4 lead.

Clinically there were no distinguishing characteristics with regard to age, sex or past medical history which served to separate patients with exercise-induced ST elevation from those with ST depression or

Figure 3. Selected resting (control), exercise-terminated, immediate postexercise and recovery (2 minutes postexercise) ECG leads from a patient with inferior-posterior and lateral ST elevation.
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<td>1.0 V₁, II, III, F</td>
<td>2.5B-2A</td>
<td>2.5B-2A</td>
<td>Mild-Mod</td>
<td>NL</td>
<td>90 P, M</td>
<td>NL</td>
<td>100 P</td>
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<td></td>
</tr>
<tr>
<td>1.5 I, L, X, V₁₋₄</td>
<td>2.0 III</td>
<td>T-1A</td>
<td>0.5B-3A</td>
<td>Mod</td>
<td>INF HYPO</td>
<td>75 P</td>
<td>80 P</td>
<td>99 P</td>
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<td></td>
</tr>
<tr>
<td>1.5 V₁₋₄</td>
<td>2.0 II, III, F, Y, Z, V₁₋₄</td>
<td>8.5-10A</td>
<td>—</td>
<td>—</td>
<td>NL</td>
<td>NL</td>
<td>NL</td>
<td>NL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.0 V₁₋₂</td>
<td>2.0 V₆₋₆, Z</td>
<td>T-15A</td>
<td>1A-10A</td>
<td>Mod</td>
<td>NL</td>
<td>NL</td>
<td>NL</td>
<td>NL</td>
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<td></td>
</tr>
<tr>
<td>2.0 II, III, F, Y</td>
<td>1.0 L</td>
<td>T-8A</td>
<td>0.5B-3A</td>
<td>Mod</td>
<td>NL</td>
<td>95 LM</td>
<td>90 P</td>
<td>80 P</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

those with coronary disease. Approximately one-third of the patients with ST elevation, but without LVH or digitalis, had elevated resting blood pressures, although less than 25% had a hypertensive response to exercise. Significant left ventricular dysfunction secondary to ischemia probably accounted for the drop in blood pressure during exercise in six of the patients. Since three of the six patients developed ST elevation ≥ 3 mm during exercise, the degree of ischemia or left ventricular dysfunction may be related to the degree of elevation. However, more patients must be studied before the exact relationship between the height of ST elevation and the degree of left ventricular dysfunction can be determined.

The majority of patients developed ST elevation along with angina pectoris. The angina that occurred in these patients was mostly mild to moderate in severity and lasted only a few minutes after the cessation of exercise. The last two characteristics, together with an absence of any history of rest angina, argue against variant angina pectoris, which Prinzmetal described as often severe, of longer duration, cyclic and recurring daily at similar times at rest or during routine activity.

Some degree of resting electrocardiographic abnormality was present in almost half of the patients in this study (excluding those with LVH or digitalis), although this was most commonly a minor, non-specific ST-T-wave change. Abnormal resting ECGs without the use of digitalis or valvular heart disease reportedly increase the frequency of diagnosis of coronary artery disease when the postexercise ECG shows ST depression. Considering the group of 46 patients with exercise-induced ST elevation, a resting
TABLE 3. Data on Patients with ST Elevation in Leads II, III, aVF, Y and Z

<table>
<thead>
<tr>
<th>Pt</th>
<th>Age (yrs)</th>
<th>Sex</th>
<th>Blood pressure (mm Hg)</th>
<th>Heart rate (beats/min)</th>
<th>ECG</th>
<th>Blood pressure (mm Hg)</th>
<th>Heart rate (beats/min)</th>
<th>Estimated VO2 (ml/min/kg)</th>
<th>Percent predicted VO2</th>
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<tbody>
<tr>
<td>1</td>
<td>48</td>
<td>M</td>
<td>128/82</td>
<td>105</td>
<td>[2.0 V2,3]</td>
<td>160/80</td>
<td>178</td>
<td>34*</td>
<td>95</td>
</tr>
<tr>
<td>2</td>
<td>56</td>
<td>M</td>
<td>100/72</td>
<td>90</td>
<td>[0.5 III, F, Y]</td>
<td>140/70</td>
<td>134</td>
<td>29*</td>
<td>81</td>
</tr>
<tr>
<td>3</td>
<td>59</td>
<td>M</td>
<td>120/68</td>
<td>54</td>
<td>NL</td>
<td>120/70</td>
<td>148</td>
<td>33*</td>
<td>106</td>
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<tr>
<td>4</td>
<td>63</td>
<td>M</td>
<td>130/82</td>
<td>58</td>
<td>NL</td>
<td>180/90</td>
<td>155</td>
<td>25</td>
<td>82</td>
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<td>158</td>
<td>18</td>
<td>46</td>
</tr>
<tr>
<td>6</td>
<td>65</td>
<td>M</td>
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<td>89</td>
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<tr>
<td>7</td>
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<td>F</td>
<td>125/80</td>
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<td>NL</td>
<td>160/90</td>
<td>155</td>
<td>12*</td>
<td>57</td>
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<td>8</td>
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<td>150/94</td>
<td>90</td>
<td>[1.5 V1,2]</td>
<td>140/85</td>
<td>132</td>
<td>18</td>
<td>58</td>
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<tr>
<td>9</td>
<td>54</td>
<td>M</td>
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<td>129</td>
<td>18</td>
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<tr>
<td>10</td>
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<td>75</td>
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<td>278/86</td>
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<tr>
<td>11</td>
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<td>F</td>
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<td>101</td>
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<td>96</td>
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<td>12</td>
<td>62</td>
<td>F</td>
<td>160/80</td>
<td>78</td>
<td>NL</td>
<td>200/90</td>
<td>182</td>
<td>18*</td>
<td>88</td>
</tr>
<tr>
<td>13</td>
<td>58</td>
<td>M</td>
<td>146/82</td>
<td>85</td>
<td>[1.0 V4,6]</td>
<td>170/90</td>
<td>176</td>
<td>33*</td>
<td>105</td>
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<td>14</td>
<td>61</td>
<td>M</td>
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<tr>
<td>15</td>
<td>52</td>
<td>M</td>
<td>118/70</td>
<td>84</td>
<td>NL</td>
<td>150/50</td>
<td>165</td>
<td>31</td>
<td>90</td>
</tr>
<tr>
<td>16</td>
<td>54</td>
<td>M</td>
<td>138/88</td>
<td>76</td>
<td>[1.0 III, F, Y]</td>
<td>200/90</td>
<td>155</td>
<td>32</td>
<td>94</td>
</tr>
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<td>17</td>
<td>42</td>
<td>M</td>
<td>136/80</td>
<td>78</td>
<td>NL</td>
<td>200/90</td>
<td>174</td>
<td>23</td>
<td>59</td>
</tr>
<tr>
<td>18</td>
<td>50</td>
<td>M</td>
<td>152/100</td>
<td>75</td>
<td>NL</td>
<td>182/96</td>
<td>144</td>
<td>18</td>
<td>49</td>
</tr>
<tr>
<td>19</td>
<td>62</td>
<td>M</td>
<td>160/80</td>
<td>75</td>
<td>[1.0 V2,3]</td>
<td>100/60</td>
<td>135</td>
<td>12</td>
<td>40</td>
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<tr>
<td>20</td>
<td>45</td>
<td>F</td>
<td>150/90</td>
<td>94</td>
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<td>[0.8 V1,2]</td>
<td>230/110</td>
<td>153</td>
<td>43</td>
<td>121</td>
</tr>
</tbody>
</table>

*Bruce protocol.

Abbreviations: A = after exercise termination; ANT = anterior; B = before exercise termination; CIRC = circumflex coronary artery; D = distal; DYSK = dyskinesis; HYPO = hypokinesis; INF = inferior; LAD = left anterior descending coronary artery; LM = left main; M = mid; Mod = moderate; NL = normal; OM = obtuse marginal branch of the left circumflex coronary artery; P = proximal; POST = posterior; RCA = right coronary artery; T = termination of exercise; ↑ = ST elevation; ↓ = ST depression; VO2 = oxygen consumption.

ECG that showed nonspecific ST-T-wave changes or was abnormal predicted significant coronary disease in 23 of 24 cases (96%). A normal resting ECG was associated with coronary artery obstructions in only 17 of the other 22 patients (77%). Consideration of only those cases in which a normal resting electrocardiographic lead showed exercise ST elevation reduced the total number of patients, but not the correlation of elevation with location of disease.

Exercise-related ST elevations have been
**TABLE 3.** (Continued)

<table>
<thead>
<tr>
<th>ECG</th>
<th>Exercise</th>
<th>Angina</th>
<th>Catheterization</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ST↑ (mm)</td>
<td>ST↑ duration (min)</td>
<td>Duration (min)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>—</td>
<td>1.2 Z</td>
<td>5B–10A</td>
<td>—</td>
</tr>
<tr>
<td>—</td>
<td>0.8 Z</td>
<td>6B–3A</td>
<td>0.5B–3A</td>
</tr>
<tr>
<td>1.0 V₄₋₅, X</td>
<td>0.5 II, III, F, Y</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>—</td>
<td>0.7 V₂₋₅, II, III, F, Y</td>
<td>4B–2A</td>
<td>—</td>
</tr>
<tr>
<td>—</td>
<td>0.9 II, III, F, Y</td>
<td>T–1A</td>
<td>—</td>
</tr>
<tr>
<td>2.0 V₄₋₅, X</td>
<td>0.5 Z</td>
<td>T–4A</td>
<td>0.5B–4A</td>
</tr>
<tr>
<td>0.5 V₂₋₅, V₄, X</td>
<td>0.5 Z</td>
<td>1B–2A</td>
<td>—</td>
</tr>
<tr>
<td>1.0 V₂₋₅</td>
<td>1.0 Z</td>
<td>1B–5A</td>
<td>1B–5A</td>
</tr>
<tr>
<td>—</td>
<td>1.0 Z</td>
<td>T–2A</td>
<td>1B–T</td>
</tr>
<tr>
<td>0.8 V₂₋₅, X</td>
<td>0.5 Z, R</td>
<td>4B–2A</td>
<td>0.5B–0.5A</td>
</tr>
<tr>
<td>—</td>
<td>1.0 Z</td>
<td>T–10A</td>
<td>T–6A</td>
</tr>
<tr>
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<td>1.0 Z</td>
<td>1B–1</td>
<td>1B–1A</td>
</tr>
<tr>
<td>1.0 V₂₋₅, X, Y</td>
<td>1.5 Z</td>
<td>9B–10A</td>
<td>—</td>
</tr>
<tr>
<td>2.0 V₂₋₅, I, L, X</td>
<td>1.0 Z, III</td>
<td>8B–10A</td>
<td>9B–3A</td>
</tr>
<tr>
<td>1.0 V₂₋₅, X, Y</td>
<td>1.0 Z</td>
<td>5B–6A</td>
<td>—</td>
</tr>
<tr>
<td>0.9 III</td>
<td>1.0 Z, R</td>
<td>1A–10A</td>
<td>1B–0.5A</td>
</tr>
<tr>
<td>3.0 V₂₋₅, X</td>
<td>1.0 Z, R</td>
<td>T–3A</td>
<td>1B–2A</td>
</tr>
<tr>
<td>—</td>
<td>0.8 Z</td>
<td>T–2A</td>
<td>—</td>
</tr>
<tr>
<td>0.6 V₂₋₅, X</td>
<td>0.5 II, III, F, Y</td>
<td>T–1A</td>
<td>—</td>
</tr>
</tbody>
</table>

Demonstrated in several circumstances, including an occasional normal patient,
variant angina, after a recent myocardial infarction, in patients with abnormal ventricular function with or without a ventricular aneurysm and in patients with significant coronary disease but no resting abnormality of ventricular function or wall motion. With the exception of 16 patients (six normal and the 10 patients with wall motion abnormalities) 30 cases (65%) included in this report fall into the latter group. One patient with normal coronary angiograms was felt to have variant angina clinically, with spasm provokable by exertion. The leads that showed ST elevation at rest in this patient did not show elevation during exercise.

The mechanism of the ST alteration may relate to severe transmural ischemia, a reciprocal change from ST depression or a wall motion abnormality that occurs in the absence of ischemia. Bayley and Prinzmetal and his associates partially ligated large coronary arteries and by altering the degree of
obstruction concluded that severe, transmural ischemia causes ST elevation, while less severe, subendocardial ischemia causes ST depression. In general, during severe ischemia associated with ST elevation, myocardial cells repolarize more rapidly than normal and there is a current flow from injured to uninjured myocardium. The ST elevation is both real and apparent from the downward offset of the TQ segment (i.e., baseline downshift), which is compensated for by most capacitator-coupled electrocardiographs. In addition, the TQ-ST deflections are directly related to duration of ischemia, and ST eleva-

**TABLE 4. Data on Patients with ST Elevation and Left Ventricular Hypertrophy or Digoxin**

<table>
<thead>
<tr>
<th>Pt.</th>
<th>Age (yrs)</th>
<th>Sex</th>
<th>Blood pressure (mm Hg)</th>
<th>Heart rate (beats/min)</th>
<th>ECG (mm)</th>
<th>Blood pressure (mm Hg)</th>
<th>Heart rate (beats/min)</th>
<th>VO2 (ml/min/kg)</th>
<th>Percent predicted VO2 (ml/min/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>49</td>
<td>M</td>
<td>118/72</td>
<td>45</td>
<td>↓0.5 V3-6, X</td>
<td>150/70</td>
<td>97</td>
<td>32</td>
<td>92</td>
</tr>
<tr>
<td>2</td>
<td>64</td>
<td>M</td>
<td>144/80</td>
<td>82</td>
<td>↑1.0 V1-2</td>
<td>190/90</td>
<td>152</td>
<td>26*</td>
<td>88</td>
</tr>
<tr>
<td>3</td>
<td>50</td>
<td>M</td>
<td>210/110</td>
<td>67</td>
<td>↓1.5 V5-6, X</td>
<td>220/120</td>
<td>105</td>
<td>9.6*</td>
<td>28</td>
</tr>
<tr>
<td>4</td>
<td>33</td>
<td>M</td>
<td>118/70</td>
<td>63</td>
<td>↑0.5 V2-3, I, L</td>
<td>160/60</td>
<td>163</td>
<td>36</td>
<td>82</td>
</tr>
<tr>
<td>5</td>
<td>61</td>
<td>M</td>
<td>142/90</td>
<td>60</td>
<td>↑0.5 V1-3, X</td>
<td>120/70</td>
<td>115</td>
<td>13</td>
<td>39</td>
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<tr>
<td>6</td>
<td>43</td>
<td>M</td>
<td>132/84</td>
<td>95</td>
<td>↑0.5 V3-2</td>
<td>160/80</td>
<td>160</td>
<td>18</td>
<td>47</td>
</tr>
</tbody>
</table>

*Bruce protocol.

Abbreviations: A = after exercise termination; ANT = anterior; B = before exercise termination; CIRC = circumflex coronary artery; D = distal; DYSK = dyskinesia; HYPO = hypokinesia; INF = inferior; LAD = left anterior descending coronary artery; LM = left main; M = mid; Mod = moderate; NL = normal; OM = obtuse marginal branch of the left circumflex coronary artery; P = proximal; POST = posterior; RCA = right coronary artery; T = termination of exercise; † = ST elevation; ↓ = ST depression; VO2 = oxygen consumption.
EXERCISE-INDUCED ST ELEVATION/Longhurst and Kraus

<table>
<thead>
<tr>
<th></th>
<th>ST‡</th>
<th>V₁₋₃</th>
<th>%</th>
<th>V₄₋₆, X, L</th>
<th>%</th>
<th>II, III, F, Y, Z</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAD</td>
<td></td>
<td>n = 21</td>
<td></td>
<td></td>
<td>n = 3</td>
<td></td>
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<tr>
<td>RCA</td>
<td>10</td>
<td>48</td>
<td></td>
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<td>67</td>
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<td>70</td>
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<td>86*</td>
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<td>2</td>
<td>67</td>
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<td>17</td>
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</tbody>
</table>

* $x^2 = 6.39$, p < .05

**Figure 6.** Correlation of anatomic location of coronary artery disease (CAD) with electrocardiographic ST elevation (ST‡) in leads V₁; V₂₋₃; V₄₋₆; X, L; II, III, aV₁, Y and Z in patients without left ventricular hypertrophy, digitalis or infarction. n = total number of patients with ST‡ in each set of leads; RCA = right coronary artery; LAD = left anterior descending coronary artery; CIRC = left circumflex coronary artery. See text for details of statistical analysis.

*ST elevation is specifically related to the size of the ischemic area.* The majority of cases included in this report, especially those with ST elevation in leads V₁₋₃, had significant obstructions in proximal portions of vessels supplying large amounts of myocardium. These obstructions became flow-limiting during exercise. This presumably resulted in a large area of transmural ischemia and ST elevation. We cannot rule out some degree of ST elevation as a reciprocal manifestation of ST depression, because more than two-thirds of the patients had both elevation and depression. Experimentally, ST depression reciprocal to ST elevation can be produced.* Conversely, significant ST elevation secondary to ST depression is quite rare, probably due to a lesser degree of ischemia associated with the ST depression. Although several studies show a definite relationship between wall motion abnormality (without ischemia) and ST elevation, the mechanism involved is not known. Only a small proportion of the patients in this study had a wall motion abnormality that might correlate with the exercise-induced ST elevation. However, since biplane angiography and wall motion studies during exercise were not done, it was not possible to rule out an exercise-induced wall motion abnormality that contributed to the ST elevation.

An important finding in this study was that in patients without a history of infarction, LVH or

---

**Table 4.** (Continued)

<table>
<thead>
<tr>
<th>Exercise</th>
<th>Catheterization</th>
</tr>
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<tbody>
<tr>
<td>ECG</td>
<td>Wall motion (mm)</td>
</tr>
<tr>
<td>ST*</td>
<td>Duration (min)</td>
</tr>
<tr>
<td></td>
<td>Duration (min)</td>
</tr>
<tr>
<td>2.5 V₁₋₃</td>
<td>1.0 X</td>
</tr>
<tr>
<td>X, L</td>
<td></td>
</tr>
<tr>
<td>II, III, F</td>
<td>1.5 V₁₋₃</td>
</tr>
<tr>
<td>1.5 Y</td>
<td>3.0 V₁₋₃</td>
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<td></td>
<td>1.0 V₁₋₃</td>
</tr>
<tr>
<td>3.0 V₂₋₃</td>
<td>1.0 Z</td>
</tr>
<tr>
<td>X</td>
<td>3.0 V₁₋₂</td>
</tr>
</tbody>
</table>

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digitalis, exercise-induced anterior ST elevation accompanied significant and usually proximal left anterior descending coronary artery disease. Bobba et al. and Hegge et al.24, 35 suspected this association, but did not have enough patients without previous myocardial infarction to test their data statistically. Additionally, neither report accounted for wall motion abnormalities that independently might have induced ST elevation. The small number of cases and the lack of an extensive electrocardiographic monitoring system has precluded other studies, from making any statistical association of anterior ST elevation with anterior descending disease. Our data also suggest that even in the presence of LVH, anterior ST elevation during exercise may predict a significant proximal left anterior descending obstruction. However, more patients must be studied before a definite conclusion can be reached about this latter group of patients.

Posterior-inferior exercise-induced ST elevation did not accurately locate coronary artery disease. There are not enough cases of anterior-lateral elevation in this report to determine the usefulness of these leads. Other investigators using chest leads V3-V6 or modified leads V5 and V6 suggest that ST elevation in these leads accompanied left anterior descending more often than circumflex obstructions.

In conclusion, there appears to be a small but important group of patients who have exercise-induced ST elevation in the absence of a myocardial infarction. The majority of these patients have coronary artery disease. Elevation that is directed anteriorly (i.e., located in leads V1-V4) often accompanies a significant, often proximal left anterior descending coronary artery obstruction, but inferior-posterior ST elevation does not correlate with coronary artery disease.

Acknowledgments

The authors express their appreciation to Michael M. Dehn and Dr. Donald G. Pansegrau for their valuable assistance in locating patient records and to Dr. C. Gunnar Blomqvist and Dr. Jere H. Mitchell for their careful review of the manuscript and critical suggestions for its formulation. Appreciation is also extended to Scott Fulgham for his technical assistance and to Sharon Kennedy and Jan Wright for secretarial help.

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Occurrence of Circulating Heart-reactive Antibodies in a Population of Cardiac Transplant Recipients
Correlation with Cardiac Rejection and Subsequent Course

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SUMMARY To determine to what extent cardiac allograft transplantation induces the production of heart-reactive antibody or antibodies (HRA), we assayed pre- and postoperative sera from 68 cardiac transplant recipients. During the first postoperative month, HRA was detected in 63% of transplant patients, but in only 25% of 40 cardiac surgical controls ($p < 0.01$). The incidence of detectable preoperative HRA did not differ in the two groups (13% transplant vs 10% nontransplant patients).

To evaluate whether HRA may serve as a monitor of cardiac rejection, we further analyzed sera during 90 episodes of rejection in 65 patients, as diagnosed by endomyocardial biopsy. HRA was present in 65% of first rejection episodes, 62% of all episodes, and in at least one episode in 69% of patients rejecting. HRA generally rose before initial rejection, peaked near rejection, and decreased gradually with rejection therapy. In many patients, HRA appeared to be an early signal of posttransplant immune activation. A relatively neutral role for circulating HRA with respect to clinical outcome was suggested.

We conclude that HRA appears after cardiac transplantation, despite immunosuppression, in a frequency and intensity too great to be explained on the basis of pericardiectomy alone. Because HRA does not appear in all transplant patients during rejection episodes, a rising HRA titer cannot be used as a sole clinical indicator of impending rejection.

IMMUNOFLUORESCENCE ASSAY of circulating heart-reactive antibody or antibodies (HRA) was proposed more than 8 years ago by Ellis, Zabriskie and colleagues as a noninvasive method to monitor cardiac rejection.\(^1\)\(^4\) Data supporting this proposal came from animal studies as well as from a few patients with limited survival, showing the appearance of HRA with cardiac allograft rejection and the disappearance of HRA with rejection therapy.\(^2\)\(^3\) Even though the assay is noninvasive and was claimed to be capable of detecting rejection earlier than other methods, the occurrence of HRA after cardiac transplantation and its value in monitoring early signs of rejection have not yet been clearly defined.

HRA has been found in varying incidence in association with the postpericardiectomy syndrome, the postmyocardial infarction syndrome, after blunt or penetrating chest trauma, in rheumatic fever, recurrent idiopathic pericarditis, cardiomyopathies, and various other disease states, in addition to cardiac graft rejection.\(^5\)\(^\text{-}^\text{11}\) The presence and role of HRA in these various cardiac disease states have also been the subject of extensive reviews.\(^10\)\(^\text{-}^\text{11}\)

HRA has been best described in the postpericardiectomy syndrome, and has been shown to be nonspecies specific and partially organ-specific.\(^8\)\(^\text{-}^\text{9}\) Absorption studies have shown that HRA binds to heterologous as well as autologous heart tissue, to skeletal muscle as well as to cardiac muscle, and, to a lesser degree, to smooth muscle. Absorption with muscle but not with other organs neutralized serum containing HRA.

The role of HRA in cardiac rejection, as in other

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Exercise-induced ST elevation in patients without myocardial infarction.
J C Longhurst and W L Kraus

Circulation. 1979;60:616-629
doi: 10.1161/01.CIR.60.3.616

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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the World Wide Web at:
http://circ.ahajournals.org/content/60/3/616

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