Diagnostic Accuracy of Exercise ECG Lead Systems in Clinical Subsets of Women

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SUMMARY  The diagnostic accuracy of 14-lead exercise electrocardiography was evaluated in 112 women who had no history of myocardial infarction and underwent coronary angiography. The sensitivity of ST-segment displacement of 0.1 mV or more in any of 14 ECG leads was 0.79 for coronary artery stenosis of at least 70%; the specificity was 0.66. Results were similar using bipolar ECG leads CC₆ and CM₆ or 11 standard ECG leads. The ST-segment shifts that occurred only during exercise were associated with a 77% false-positive rate (10 of 13). Down-sloping ST-segment depression did not provide more diagnostic information than horizontal ST-segment depression in the three clinical subsets of women.

In women with typical angina pectoris, ST-segment depression of at least 0.15 mV for 0.08 second after the J point or a final treadmill time less than 360 seconds was predictive of proximal left or multivessel coronary artery disease. In the women with probable angina or nonspecific chest pain, this finding was not of diagnostic value. ST-segment elevation of 0.1 mV or more in leads V₁₋₂ or aV₇ predicted proximal stenosis of at least 80% in the left anterior descending coronary artery in all six women with typical angina pectoris.

Maximal exercise testing in women with typical angina provides important diagnostic information when 11 standard ECG leads are recorded. In women with probable angina or nonspecific chest pain, diagnostic exercise testing is less useful and bipolar leads CC₆ and CM₆ are sufficient for most clinical purposes.

THE DIAGNOSIS of coronary disease in women with chest pain is a difficult problem in clinical medicine. Exercise stress testing in women has a relatively low diagnostic yield for obstructive coronary disease compared with that in men, especially when symptoms are atypical or nonspecific.¹ ¹ Symptomatic women who have a positive test have a lower risk of coronary artery disease than do men, and have fewer coronary events.¹ ¹¹

Different ECG leads have been used in exercise studies in women.³ ⁶ ⁷ ⁸ Data on the predictive accuracy of individual ECG leads in clinical patient subsets are often not stated, and some ECG leads may be associated with more false-positive results than others. In this study, we evaluated the diagnostic accuracy of 14 ECG leads recorded during and after exercise in 112 women who had no history of myocardial infarction and underwent coronary angiography.

Material and Methods

Patient Population

The patients were a prospective series of 112 women, mean age 49 years (range 29–64 years), who underwent a maximal stress test using 14 ECG leads within 1 week before coronary angiography. The indication for cardiac catheterization was typical angina in 41 women, probable angina in 28 women and nonspecific chest pain in 43 women. Typical angina pectoris was defined as a substernal discomfort precipitated by exertion, relieved by rest or nitroglycerin or both, and with typical radiation to either shoulder, jaw or inner arm. Probable angina pectoris had most of the features of typical angina pectoris, but in some aspects was not entirely typical (e.g., chest pain in unusual location or not always relieved by nitroglycerin, or inconstant precipitating factors). Nonspecific chest pain was defined as chest pain that did not meet the criteria for typical or probable angina pectoris and included chest pain unrelated to activity and unrelieved by nitroglycerin or rest or both.

Patients who had a history of myocardial infarction, valvular heart disease, left ventricular hypertrophy, bundle branch block or patients who were taking digitalis preparations were excluded. Patients who had a systolic click or evidence of mitral valve prolapse at left ventriculography were also excluded. Cardiac medication except for sublingual nitroglycerin was stopped for at least 2 days before the test in 70 patients; 42 women were receiving chronic ß-blocker therapy within 2 days of the treadmill test. The incidence of ST-segment depression in the ECG leads monitored and the final treadmill work time were similar among the women with and without ß blockers. All 53 patients with a negative test achieved at least 85% of their maximal age-predicted heart rate and 36 achieved at least 90%.¹²

Exercise Protocol

All patients performed a maximal treadmill test using a Bruce protocol¹³ modified by a 3-minute warm-up at 1.7 mph and a 5% grade. Blood pressure was measured by cuff each minute throughout the test. A decrease in peak systolic pressure of 10 mm Hg or

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more or an increase in diastolic pressure of 15 mm Hg or more during exercise that was sustained for two or more consecutive determinations was noted. Both criteria are associated with multivessel coronary disease in symptomatic males.14-16

The ECG was monitored continuously and recorded each minute during upright exercise and for 5 minutes after exercise in the sitting position. The most common reason for stopping exercise was chest pain in women with typical angina (18 of 41, 44%) and exhaustion in women with probable angina (11 of 28, 39%) or nonspecific chest pain (31 of 43, 72%).

Exercise ECG Lead System

The 14-lead ECG consisted of the 11 standard leads (minus aVr) and bipolar leads CCa, CMb and ML (negative lead, manubrium; positive lead, left flank). The sequence and duration of ECG recordings have been described.17-20 The baseline from which changes were measured was taken from a line joining two consecutive PQ junctions. The magnitude of J-point shift and ST-segment shift 0.08 second after the J point was measured using a 7 × magnifying glass calibrated in tenths of a millimeter. Test results were reviewed by a second observer and differences were resolved by a joint study of the record. Each exercise test was interpreted without knowledge of the clinical history or coronary angiographic results. The depth and slope of ST-segment depression were coded during and after exercise in each lead. Forty-two women had ST-T-wave abnormalities on the rest ECG.12 Seventeen women had horizontal or downsloping ST-segment depression >0.05 mV; 25 women had isoelectric or negative T waves. The ECG criteria for a positive test in any lead were horizontal or downsloping ST-segment depression ≥0.1 mV for 0.08 second or ST-segment elevation ≥0.1 mV in at least three consecutive complexes compared with the rest tracing.

Cardiac Catheterization

Selective coronary angiography was performed using a percutaneous transfemoral approach; cranio-caudal and caudocranial sagittal views were recorded routinely to avoid superimposition of the proximal left coronary vessels.21 A stenosis ≥70% of the arterial intraluminal diameter was considered significant. A proximal stenosis of a large diagonal or marginal branch was considered as a stenosis of the left anterior descending or circumflex coronary arteries, respectively. Stenoses of a nondominant right coronary artery were not considered in determining the extent of disease. Twenty-nine patients had one-vessel disease, eight had two-vessel disease and five had three-vessel disease; 21 women had obstructive lesions in the proximal left anterior descending coronary artery. Forty-eight women had normal coronary arteries at angiography, 16 had mild coronary disease and no stenosis ≥50% and six had stenoses of 50–69%.

The left ventricle was opacified in the 30° right anterior oblique position. Left ventricular wall motion was assessed qualitatively by an experienced cardiovascular radiologist; 96 patients had a normal left ventricular contraction pattern, 12 had segmental hypokinesis and four had an akinetic left ventricular segment.

Data Analysis

The sensitivity and specificity of different degrees of ST-segment shift for important coronary disease and the corresponding likelihood ratio for a normal and abnormal test result were calculated for individual leads, for the standard 11 leads, for three bipolar leads (CCa, CMb and ML) and for all 14 ECG leads. The false-positive rate of specific ECG patterns was determined in individual clinical patient subsets. The definitions used were: sensitivity = true positives/(true positives + false negatives); specificity = true negatives/(true negatives + false positives); likelihood ratio of an abnormal test = sensitivity/(1 - specificity); likelihood ratio of a normal test = specificity/(1 - sensitivity); false positive rate = false positives/all positive tests. Intergroup and intragroup differences were examined using a chi-square test. Parametric differences were determined using the t test.

Results

Women with typical angina had a higher incidence of ST-T-wave abnormalities on the rest ECG than did women with probable angina or nonspecific chest pain ($p < 0.01$) (table 1). The presence of ST-T-wave abnormalities on the rest ECG did not significantly change the sensitivity or specificity of the exercise ECG lead groups or the predictive value of a positive

<p>| Table 1. Clinical and Angiographic Characteristics of the Test Population |
|-----------------------------|------------------------|----------------------|------------------------|------------------------|</p>
<table>
<thead>
<tr>
<th></th>
<th>Mean age (years)</th>
<th>No. with rest ST-T-wave abnorm.</th>
<th>No. of pts who had coronary artery stenosis ≥ 70%</th>
<th>No. with proximal LAD stenosis ≥ 70%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical angina</td>
<td>41</td>
<td>52</td>
<td>24</td>
<td>0</td>
</tr>
<tr>
<td>Probable angina</td>
<td>28</td>
<td>47</td>
<td>5</td>
<td>18</td>
</tr>
<tr>
<td>Nonspecific chest pain</td>
<td>43</td>
<td>49</td>
<td>13†</td>
<td>42†</td>
</tr>
<tr>
<td>Total</td>
<td>112</td>
<td>49</td>
<td>42</td>
<td>70</td>
</tr>
</tbody>
</table>

*p < 0.05 vs typical or probable angina.

†p < 0.01 vs typical or probable angina.

Abbreviations: LAD = left anterior descending coronary artery.
or a negative test in the three clinical subgroups. The prevalence of obstructive coronary disease was 75% (31 of 41) in women with typical angina, 36% (10 of 28) in women with probable angina and 2% (one of 43) in women with nonspecific chest pain (p < 0.001). Multivessel coronary disease was uncommon in women with probable angina and was not observed in women with nonspecific chest pain.

Exercise Test Results by ECG Leads Recorded

The classic criteria of exercise-induced horizontal or downsloping ST-segment depression ≥0.1 mV or ST-segment elevation ≥0.1 mV for 0.08 second after the J point resulted in a sensitivity of 0.71 (30 of 42) and a specificity of 0.73 (51 of 70) using the standard 11-lead ECG (table 2). Leads I and aV_{L} were the least sensitive, followed by leads V_{1}, V_{2} and leads II, III, aV_{F} and V_{S}. The sensitivity of unipolar leads V_{S} or V_{A} was 0.57 (27 of 42). The specificity of leads I, aV_{L} and V_{R} ranged from 0.91-1.00, compared with 0.80-0.84 for inferior leads II, III and aV_{F} or lateral leads V_{4}–V_{6}. Nineteen of 21 patients with proximal left anterior descending coronary disease and 10 of 13 patients with multivessel disease were detected using the 11-lead ECG (table 3).

Of the 42 women with coronary disease, lead CC_{S} detected 24 (57%), lead CM_{S} 26 (62%) and lead ML 17 (40%). Of the 70 women without disease, lead CC_{S} was negative in 62 (89%), lead CM_{S} in 52 (74%) and lead ML in 56 (80%). Overall sensitivity was 0.74 and specificity was 0.70 for the three simultaneously recorded leads (similar to results obtained with the 11-lead ECG). The three bipolar ECG leads were positive in three patients in whom the 11-lead ECG was negative; all three were false-positive tests. The 11-lead ECG was positive in three patients in whom the three bipolar leads were negative; two of the three patients had coronary disease.

The sensitivity and specificity for important ST-segment shifts in the 14-lead exercise ECG diagnostic of obstructive coronary disease were 0.79 and 0.66, respectively. The addition of a slowly upsloping ST segment ≥0.2 mV 0.08 second after the J point to the criteria for positivity did not substantially change the sensitivity or specificity for obstructive coronary disease. The sensitivity increased from 0.79 to 0.81 and specificity decreased from 0.66 to 0.64.

The average number of ECG leads with horizontal or downsloping ST-segment depression ≥0.1 mV for 0.08 second after the J point or ST-segment elevation ≥0.1 mV was comparable in patients with or without coronary disease (fig. 1). The results were similar when patients were classified according to clinical presentation.

In women with typical angina, ST-segment depression ≥0.15 mV or a treadmill time less than 360 seconds (Bruce stage II) predicted proximal left coronary or multivessel coronary artery disease (fig. 2). In women with probable angina, the high false-positive rate of important ST-segment depression decreased the value of this finding.

Relation of the False-positive Rate to Time of ST-segment Displacement

The false-positive rate was significantly higher for ST-segment shifts that occurred only during exercise. Of 52 women with a positive ECG in leads CC_{S}, CM_{S} or ML, eight of nine (89%) were falsely positive if the ST-segment shift occurred only during exercise, 12 of 36 (33%) if the ST-segment shift persisted in the recovery period and one of seven (14%) if the ST-segment shift was recorded in the recovery period (p < 0.01) (table 4). The results were similar with 11 or 14 ECG leads.

ST-segment Elevation

All six patients with ST-segment elevation ≥0.1 mV had 80% or greater stenosis of the proximal left anterior descending coronary artery. Only one patient had multivessel disease. The ST-segment elevation occurred in leads V_{1}–V_{3} in three patients (fig. 3), in the lateral leads (I, aV_{L}, V_{4}–V_{6}, CC_{S}, CM_{S}) in two patients and in both lead groups in one patient. There was no ST-segment elevation in the inferior leads. In one woman, variant angina was suspected because of a positive ergonovine test; in a second patient, an akinetic wall motion abnormality was present at cardiac catheterization. Thallium-201 uptake in the anteroseptal region during exercise was decreased in each of the four women who had a rest-exercise myocardial perfusion scan.

Three patients had ST-segment elevation ≥0.05 mV but <0.1 mV. All three had multivessel coronary disease ≥70% and a stenosis ≥80% of the proximal left anterior descending coronary artery. All nine patients with exercise-induced ST-segment elevation ≥0.05 mV had typical angina. Eight had associated horizon-
Table 2. Exercise Test Results by ECG Leads Recorded*

<table>
<thead>
<tr>
<th></th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>aV_L</th>
<th>aV_F</th>
<th>V_1</th>
<th>V_2</th>
</tr>
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<tbody>
<tr>
<td>Sensitivity</td>
<td>2/42</td>
<td>14/42</td>
<td>9/42</td>
<td>2/42</td>
<td>11/42</td>
<td>4/42</td>
<td>5/42</td>
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<tr>
<td></td>
<td>(0.05)</td>
<td>(0.33)</td>
<td>(0.21)</td>
<td>(0.05)</td>
<td>(0.26)</td>
<td>(0.10)</td>
<td>(0.12)</td>
</tr>
<tr>
<td>Specificity</td>
<td>70/70</td>
<td>59/70</td>
<td>59/70</td>
<td>70/70</td>
<td>56/70</td>
<td>70/70</td>
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<tr>
<td></td>
<td>(1.0)</td>
<td>(0.8)</td>
<td>(0.84)</td>
<td>(1.0)</td>
<td>(0.8)</td>
<td>(1.0)</td>
<td>(1.0)</td>
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<tr>
<td>LR abnormal test</td>
<td>∞</td>
<td>2.06</td>
<td>1.312</td>
<td>∞</td>
<td>1.3</td>
<td>∞</td>
<td>∞</td>
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<tr>
<td>LR normal test</td>
<td>1.05</td>
<td>1.253</td>
<td>1.063</td>
<td>1.05</td>
<td>1.08</td>
<td>1.11</td>
<td>1.14</td>
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Predictive value of an abnormal test

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<th></th>
<th>Typical angina</th>
<th>2/2</th>
<th>10/10</th>
<th>7/10</th>
<th>2/2</th>
<th>8/12</th>
<th>4/4</th>
<th>5/5</th>
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<tr>
<td></td>
<td></td>
<td>(1.0)</td>
<td>(0.77)</td>
<td>(0.7)</td>
<td>(1.0)</td>
<td>(0.07)</td>
<td>(1.0)</td>
<td>(1.0)</td>
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<tr>
<td></td>
<td>Probable angina</td>
<td>0/0</td>
<td>4/8</td>
<td>2/5</td>
<td>0/0</td>
<td>3/7</td>
<td>0/0</td>
<td>0/0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(indet.)</td>
<td>(0.5)</td>
<td>(0.4)</td>
<td>(indet.)</td>
<td>(0.43)</td>
<td>(indet.)</td>
<td>(indet.)</td>
</tr>
<tr>
<td></td>
<td>Nonspecific chest pain</td>
<td>0/0</td>
<td>0/4</td>
<td>0/5</td>
<td>0/0</td>
<td>0/6</td>
<td>0/0</td>
<td>0/0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(indet.)</td>
<td>(0)</td>
<td>(0)</td>
<td>(indet.)</td>
<td>(0)</td>
<td>(indet.)</td>
<td>(indet.)</td>
</tr>
</tbody>
</table>

Predictive value of a normal test

<table>
<thead>
<tr>
<th></th>
<th></th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>(0.26)</td>
<td>(0.25)</td>
<td>(0.23)</td>
<td>(0.26)</td>
<td>(0.26)</td>
<td>(0.27)</td>
<td>(0.28)</td>
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<tr>
<td></td>
<td>Probable angina</td>
<td>18/28</td>
<td>14/20</td>
<td>15/23</td>
<td>18/28</td>
<td>14/21</td>
<td>18/28</td>
<td>18/28</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(0.64)</td>
<td>(0.7)</td>
<td>(0.65)</td>
<td>(0.64)</td>
<td>(0.67)</td>
<td>(0.64)</td>
<td>(0.64)</td>
</tr>
<tr>
<td></td>
<td>Nonspecific chest pain</td>
<td>42/43</td>
<td>38/39</td>
<td>37/38</td>
<td>42/43</td>
<td>36/37</td>
<td>42/43</td>
<td>42/43</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(0.98)</td>
<td>(0.97)</td>
<td>(0.97)</td>
<td>(0.97)</td>
<td>(0.97)</td>
<td>(0.98)</td>
<td>(0.98)</td>
</tr>
</tbody>
</table>

*Criteria for positive test: horizontal or downsloping ST-segment depression ≥ 0.1 mV for 0.08 second after the J point or ST-segment elevation ≥ 0.1 mV.  
Abbreviations: indet. = indeterminate; LR = likelihood ratio.

tal or downsloping ST-segment depression ≥0.1 mV in other leads.

Downsloping ST-segment Depression

The predictive value of downsloping ST-segment depression in the three clinical subsets of women was similar to that of horizontal ST-segment depression. The predictive value of downsloping vs horizontal ST-segment depression ≥0.1 mV for obstructive coronary disease was 0.79 (11 of 14) vs 0.89 (25 of 28) for women with typical angina, 0.50 (three of six) vs 0.46 (six of 13) for women with probable angina and 0 (neither of two) vs 0.0 (none of 11) for women with nonspecific chest pain (NS).

The predictive value of downsloping vs horizontal ST-segment depression ≥0.1 mV for multivessel coronary disease was 0.29 (four of 14) vs 0.55 (10 of 18) for women with typical angina, 0.17 (one of six) vs 0.0 (none of 13) for women with probable angina, and 0 (neither of two) vs 0.0 (none of 12) for women with nonspecific chest pain (NS).

Hemodynamic Response to Exercise

The final treadmill work time was significantly less in women with typical angina than in women with probable angina or nonspecific chest pain (413 ± 148 seconds vs 512 ± 132 or 517 ± 87 seconds, p < 0.005). In general, ST-segment depression started earlier in patients with more extensive coronary disease, although there was considerable overlap (fig. 4).

Only one of 112 (0.9%) women had a decrease in peak systolic blood pressure during exercise. She had nonspecific chest pain, normal coronary arteries and normal left ventricular function at cardiac catheterization.

Twenty-seven women had an abnormal increase in diastolic blood pressure during exercise. Of 11 with typical angina, 10 (91%) had obstructive coronary disease and three (27%) had multivessel disease. In contrast, only one of six women with probable angina (17%) and none of 10 with nonspecific chest pain who had this finding had coronary artery disease (p < 0.05).

Table 3. Sensitivity of Lead Systems for High-risk Coronary Artery Disease in Women

<table>
<thead>
<tr>
<th></th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>aV_L</th>
<th>aV_F</th>
<th>V_1</th>
<th>V_2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proximal LAD disease (n = 21)</td>
<td>2 (0.10)</td>
<td>11 (0.52)</td>
<td>5 (0.24)</td>
<td>2 (0.10)</td>
<td>9 (0.43)</td>
<td>4 (0.19)</td>
<td>4 (0.19)</td>
</tr>
<tr>
<td>Multivessel disease (n = 13)</td>
<td>1 (0.8)</td>
<td>4 (0.31)</td>
<td>1 (0.13)</td>
<td>0</td>
<td>2 (0.10)</td>
<td>1 (0.08)</td>
<td>1 (0.08)</td>
</tr>
<tr>
<td>Three-vessel disease (n = 5)</td>
<td>0</td>
<td>2 (0.40)</td>
<td>1 (0.20)</td>
<td>0</td>
<td>1 (0.20)</td>
<td>0</td>
<td>1 (0.20)</td>
</tr>
</tbody>
</table>

Abbreviation: LAD = left anterior descending coronary artery.
Chest Pain

The occurrence of chest pain during exercise predicted coronary disease in all 14 women who had typical angina, compared with three of eight (38%) with probable angina and none of three with non-specific chest pain. The predictive value of this finding was not enhanced in any of the groups if a significant ST-segment shift accompanied chest pain. Chest pain was predictive of multivessel coronary disease in only six of 18 women (33%) with typical angina.

Discussion

The specificity of important exercise-induced ST-segment shifts for obstructive coronary disease is lower in women than in men. In a review of nine studies correlating exercise-induced ST-segment shifts with angiographic findings, sensitivity ranged from 0.50–0.89 and specificity from 0.63–0.92 (table 5). A potential source of interstudy variability is the choice of exercise ECG lead group recorded and the population of women examined. In most studies, the sensitivity and specificity of individual leads are not reported, nor are the patients stratified according to the clinical presentation. We previously described the diagnostic accuracy of 14 exercise ECG leads in several clinical subsets of men. The present study describes our findings in three clinical subsets of women who had no history of myocardial infarction.

Exercise Test Results

The sensitivity of important ST-segment shifts for coronary disease increased with the number of ECG leads recorded. ST-segment displacement occurred in 79% of women with coronary disease when 14 ECG leads were recorded, similar to the 84% sensitivity we reported in men. The specificity of the 14-lead exercise ECG was less in women (66%) than in men (82%). Others have reported similar findings using single- or multiple-lead exercise ECG recordings. The sensitivity and specificity of ST-segment shifts diagnostic of obstructive coronary disease were similar for leads CC5, CM5, ML and the standard 12-lead ECG. The three bipolar ECG leads require five electrode placements, compared with 10 for the 12-lead ECG.

The diagnostic accuracy of ST-segment changes that occurred only during exercise was low compared with changes that persisted or occurred during the recovery period. Only 23% of the 13 women who had
horizontal or downsloping ST-segment depression $\geq 0.1$ mV during exercise had coronary disease. Lesbre et al.\textsuperscript{a} and Broustet et al.\textsuperscript{7} reported predictive values of 29\% (two of seven) and 63\% (five of eight), respectively, for ST-segment shifts that occurred only during exercise in women.

The configuration of the ST segment during or after exercise is a useful diagnostic guide in predicting coronary and multivessel coronary disease in men.\textsuperscript{23-25} In symptomatic men, a slowly upsloping ST segment depressed $\geq 0.2$ mV 0.08 second after the J point is predictive of coronary disease.\textsuperscript{26-28} In symptomatic women, this criterion decreases specificity. In symptomatic men, downsloping ST-segment depression $\geq 0.1$ mV 0.08 second after the J point is more specific for obstructive and multivessel coronary disease than a similar degree of horizontal ST-segment depression.\textsuperscript{29,30} In our symptomatic population of women, downsloping ST-segment depression had the same diagnostic importance as horizontal ST-segment depression for obstructive and multivessel coronary disease.

The prevalence of ST-segment elevation $\geq 0.1$ mV was 5\% (six of 120) in our study. This finding was specific for coronary disease and was not associated with false-positive results. Lesbre et al.\textsuperscript{a} reported a prevalence of 1\% in 150 symptomatic women who underwent stress testing using a single lead, CM$_4$. In our study, the ST-segment was elevated most often in leads V$_1$; only two of 12 (2\%) had this finding in lead CM$_4$. Bipolar lead CM$_4$ is relatively insensitive in detecting ST-segment elevation.\textsuperscript{30-32}

The incidence of systolic hypotension during exercise was 0.9\% in our study. Morris et al.\textsuperscript{14} and Levites et al.\textsuperscript{15} reported an incidence of 2.3\% in men and 2.7\% in men and women, respectively. Decreased systolic blood pressure during progressive exercise is specific for multivessel coronary disease in symptomatic men,\textsuperscript{14,15} but is an uncommon and nonspecific finding in women. Sheps et al.\textsuperscript{16} found that an exercise-induced increase in diastolic blood pressure was specific for severe coronary disease in men and women. In our study, this finding was associated with obstructive coronary disease in 91\% of women with typical angina but only 6\% of women with probable angina or nonspecific chest pain.

### Diagnostic Accuracy in Clinical Subsets

#### Typical Angina

The pretest risk for coronary disease was 0.75 in women with typical angina pectoris. The post-test risk for a patient with a positive test was 0.83 using leads CC$_6$, CM$_4$ and ML or 11 leads. The predictive value of individual leads among the multiple ECG lead group ranged from 0.7 for the inferior leads to 0.91 for lead CC$_6$. The predictive value of a negative test in any of the 14 ECG leads was 0.50.

The degree of ST-segment depression and final treadmill work time was predictive of proximal or multivessel coronary disease, confirming results we

### Table 4. False-positive Rate Stratified by Lead System and Occurrence of Important ST-segment Displacement

<table>
<thead>
<tr>
<th>Lead system</th>
<th>False-positive rate for ST-segment shift</th>
<th>CC$_6$, CM$_4$ and ML</th>
<th>11 leads</th>
<th>14 leads</th>
</tr>
</thead>
<tbody>
<tr>
<td>In exercise only</td>
<td>89% (8/9)</td>
<td>67% (8/12)</td>
<td>77% (10/13)</td>
<td></td>
</tr>
<tr>
<td>During and after exercise</td>
<td>33% (12/36)</td>
<td>34% (11/32)</td>
<td>38% (14/37)</td>
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</tr>
<tr>
<td>After exercise only</td>
<td>14% (1/7)</td>
<td>0 (0/5)</td>
<td>14% (1/7)</td>
<td></td>
</tr>
<tr>
<td>$p$</td>
<td>&lt; 0.01</td>
<td>&lt; 0.05</td>
<td>&lt; 0.03</td>
<td></td>
</tr>
</tbody>
</table>
obtained in a male population with a high disease prevalence. The number of positive ECG leads was not useful in separating women with mild or no disease from those with more severe coronary disease, in contrast to data obtained in a similar subset of men.

**Probable Angina**

The pretest risk for coronary disease was 0.36 in women with probable angina pectoris. The post-test risk for patients with a positive test was only 0.5 using bipolar leads CC₅, CM₅, and ML and 0.45 using 11 leads. The high false-positive rate in women with probable angina reduced the diagnostic usefulness of ST-segment shifts in this subset of patients regardless of the lead system recorded. Our results support the prognostic findings of Manca et al., who reported a 5-year cumulative survival of 96.4% in 144 women who had atypical angina and horizontal or downsloping ST-segment depression ≥0.1 mV for 0.08 second

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of women</th>
<th>Lead system</th>
<th>Prevalence of CAD</th>
<th>Exercise test result</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Sensitivity</td>
</tr>
<tr>
<td>Caru et al.¹</td>
<td>168</td>
<td>12</td>
<td>29%</td>
<td>0.73</td>
</tr>
<tr>
<td>Cahen et al.²</td>
<td>100</td>
<td>12</td>
<td>41%</td>
<td>0.88</td>
</tr>
<tr>
<td>Sketch et al.³</td>
<td>56</td>
<td>12</td>
<td>18%</td>
<td>0.50</td>
</tr>
<tr>
<td>Detry et al.⁴</td>
<td>45</td>
<td>12</td>
<td>40%</td>
<td>0.89</td>
</tr>
<tr>
<td>Linhart et al.⁵</td>
<td>98</td>
<td>CM₅</td>
<td>24%</td>
<td>0.71</td>
</tr>
<tr>
<td>Lesbre et al.⁶</td>
<td>150</td>
<td>CM₅</td>
<td>27%</td>
<td>0.66</td>
</tr>
<tr>
<td>Broustet et al.⁷</td>
<td>84</td>
<td>CM₅, ML₅</td>
<td>25%</td>
<td>0.50</td>
</tr>
<tr>
<td>Barolsky et al.⁸</td>
<td>92</td>
<td>CM₅, XYZ</td>
<td>33%</td>
<td>0.60</td>
</tr>
<tr>
<td>Weiner et al.⁹</td>
<td>580</td>
<td>12 of 14 hospitals used multiple leads</td>
<td>29%</td>
<td>0.76</td>
</tr>
<tr>
<td>Present study</td>
<td>112</td>
<td>12, CC₅, CM₅, ML</td>
<td>37%</td>
<td>0.79</td>
</tr>
</tbody>
</table>

Abbreviation: CAD = coronary artery disease.
in any of the 12 standard ECG leads during or after exercise.

Nonspecific Chest Pain

The pretest risk for coronary disease was 0.02 in women with nonspecific chest pain. Multivessel coronary disease was not observed. In a larger study of 1397 women with nonspecific chest pain who underwent coronary angiography in the CASS study,29 6% had obstructive coronary disease, 2% had multivessel coronary involvement and 0.6% had left main or three-vessel coronary disease. Clearly, noninvasive diagnostic tests for coronary disease will have a low diagnostic yield in this patient subset and perhaps should not be performed if the sole reason is to identify extensive and severe coronary disease.

Strengths and Limitations of the Present Study

The predictive accuracy of significant ST-segment shifts was strongly influenced by the patient subset examined, regardless of the lead system used. The concept of analyzing noninvasive test results in terms of clinical subsets was not applied in many of the earlier studies in women.1,3,4,9 The rate of false-positive or false-negative results in the earlier studies (table 5) relates to a clinical population in which the overall prevalence of coronary disease was 0.18–0.41. Thus, the diagnostic accuracy of the results would apply to a clinical subset of women with probable angina pectoris but not to women with definite angina pectoris or nonspecific chest pain.

The lead system recorded during and after exercise can influence the sensitivity and specificity for obstructive coronary disease.20 In four studies using the standard 12-lead ECG during exercise, sensitivity ranged from 0.50–0.89 and specificity from 0.63–0.92, comparable to the values obtained in two other studies using lead CM, with which sensitivity and specificity ranged from 0.66–0.71 and 0.77–0.78, respectively (table 5).1–4 In the present study, both lead groups were recorded at the same time in the same patients. The 11-lead ECG was more sensitive than lead CM, in detecting ST-segment elevation and depression (0.71 vs 0.57); the specificity was similar.

The 14-lead exercise ECG was associated with 24 false-negative results. Mitral valve prolapse is a well-known cause of false-positive stress tests.34 We excluded patients who had a systolic click or angiographic evidence of mitral valve prolapse, but we did not routinely perform echocardiography. The echocardiogram may be a more sensitive test for mitral valve prolapse than uniplane left ventriculography in the 30° right anterior oblique position, and it is possible that a few patients with mitral valve prolapse were not detected in the present study.35,36

Hyperventilation can cause electrocardiographic changes that resemble myocardial ischemia in as much as 15% of patients with normal coronary arteries.1,9,37 We did not record continuous tracings during hyperventilation. The technique may be useful in detecting a small number of patients with false-positive stress tests, particularly women with atypical or nonspecific chest pain.

In conclusion, the diagnostic importance of exercise test variables in women differs from that in men. Women with typical angina appear to be the only clinical subset in which exercise testing is potentially useful. Although thallium-201 imaging49–51 and exercise radionuclide ventriculography52–54 or exercise echocardiography55–57 may provide more definitive diagnostic information than stress electrocardiography, these newer tests have not been shown to be diagnostically useful in clinical subsets of women with a low prevalence of disease. Diagnostic noninvasive tests on a routine clinical basis are not indicated in women with nonspecific chest pain because of the low prevalence of coronary and multivessel coronary disease and the current absence of the definitive diagnostic noninvasive test.

Bipolar leads CC and CM, are sufficient for diagnostic purposes in women who have probable angina or nonspecific chest pain and who have not had a myocardial infarction. Although the 12-lead ECG provides similar data, it requires 10 rather than four electrode placements. However, the 11- or 14-lead ECG is recommended in women with typical angina or when variant angina or infarction have occurred and ST-segment elevation is likely.
References


Enhanced Atrioventricular Conduction in Patients Without Preexcitation Syndrome: Relation to Heart Rate in Paroxysmal Reciprocating Tachycardia

DAVID G. BENDITT, M.D., MICHAEL L. EPSTEIN, M.D., CARL E. ARENTZEN, M.D., JOLENE M. KRIETT, M.D., AND GEORGE J. KLEIN, M.D.

SUMMARY We studied the electrophysiologic characteristics of atrioventricular (AV) nodal conduction in patients with reciprocating tachycardia (RT) without ventricular preexcitation, and the relation of these characteristics to RT cycle length (CL). Thirty-five symptomatic patients who had a normal PR interval (0.13–0.20 second) during sinus rhythm underwent detailed intracardiac electrophysiologic study during which ventricular preexcitation was excluded, and the RT mechanism was determined. RT was due to reentry using an accessory AV pathway capable of conduction only in the retrograde direction (concealed AP) in 13 patients (37%) and to reentry within the AV node in 22 (63%). Dynamic properties of AV conduction (assessed by degree of AH prolongation during progressive increase in atrial pacing rate) were normally distributed (p < 0.005); 12 patients (34%) fulfilled the criteria for enhanced AV conduction (EAVC).

The patients with EAVC had a shorter RT CL than did patients without EAVC (294 ± 43.3 msec vs 360 ± 68.1 msec, p < 0.01). However, CL differences were primarily due to the influence of EAVC in the subgroup of patients with RT using a concealed AP (EAVC CL, 274 ± 35.1 msec; without EAVC, 326 ± 15.7 msec, p < 0.005). The RT CL in patients with reentry within AV node was not measurably influenced by concomitant EAVC (EAVC, 314 ± 43.8 msec; without EAVC, 376 ± 76.8 msec) (NS).

This study suggests that despite the presence of a normal PR interval during sinus rhythm, dynamic AV conduction responses can vary widely in patients with RT. In patients with RT using a concealed AP, but not in those with reentry within the AV node, coexisting diminished physiologic AV conduction slowing may be associated with more rapid tachycardia rates.

THE VENTRICULAR RATE is a principal factor in the hemodynamic effects and severity of symptoms in patients with paroxysmal supraventricular tachyarrhythmias. Improved understanding of the determinants of heart rate during supraventricular tachycardias may lead to more effective application of antiarrhythmic therapy.

The relation between the electrophysiologic properties of atrioventricular (AV) conduction and the tachycardia rate in patients with certain supraventricular tachyarrhythmias is controversial. Gallagher et al., studying patients with Wolff-Parkinson-White (WPW) syndrome, and Benditt et al., studying patients with Lown-Ganong-Levine (LGL) syndrome, reported that tachycardia rates were faster in patients who had diminished conduction delay within the AV node, which was termed enhanced AV nodal conduction (EAVC). Bauerfeind et al., evaluating patients with reciprocating tachycardia (RT) due to reentry within the AV node, could not substantiate a relation between electrocardiographic and electrophysiologic descriptors of AV nodal function and the associated tachycardia rate.

To further evaluate these apparently divergent views, we examined the ventricular response during supraventricular tachyarrhythmias in patients without ventricular preexcitation.

Methods

Patient Selection

The patients were selected according to the following criteria: (1) history of documented symptomatic paroxysmal regular narrow QRS tachycardia; (2) normal PR interval (0.13–0.20 second) documented by

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P Guiteras, B R Chaitman, D D Waters, M G Bourassa, J M Scholl, R J Ferguson and P Wagniart

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