Differences in Electrocardiographic Response To Exercise of Women and Men: A Non-Bayesian Factor

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SUMMARY We evaluated the ability of ST-segment analysis during submaximal exercise tolerance testing (85% predicted age-adjusted heart rate) to diagnose the presence of significant coronary artery stenosis (≥75% cross-sectional area narrowing) in a group of 85 men and 92 women with chest pain syndromes and no previously documented myocardial infarctions. Disease prevalence by selective coronary angiography was 36% for men and 33% for women (NS). Predictive value of a positive exercise test (PV(+ET)) as defined by 1 mm ST-segment depression 0.08 second after the J point was significantly higher for men than for women (77% vs 47%, p < 0.05). Predictive value of a negative test (PV(-ET)) was not significantly different for men (81%) and women (78%). Analysis of the 66 men and 66 women not taking digitalis preparations again showed that PV(+ET) was significantly higher for men than for women (90% vs 45%, p < 0.01).

Multivariate analysis showed that patients with angiographically significant coronary disease had significantly lower attained heart rates and shorter exercise duration than those without significant stenosis, independent of ST-segment responses. A discriminant function using ST-segment response, attained heart rate and a sex-dependent ST-segment response factor was developed. Duration of exercise was not an independent predictor by our analysis. This function improved the PV(+ET) and PV(-ET) for the total group and for the women; for men, the PV(-ET) improved, while the PV(+ET) fell slightly. This function has not yet been used prospectively.

In patients with chest pain and no previously documented myocardial infarction, men have a significantly higher PV(+ET) than women, which cannot be accounted for simply by a difference in disease prevalence (i.e., Bayes' theorem).

EXERCISE TESTING has been a commonly used tool for the evaluation of cardiac status for over 20 years. Despite its extensive use as a screening test for asymptomatic patients, a diagnostic test for patients with symptoms of ischemic heart disease, and as a functional test for patients with known cardiac disease, the usefulness, accuracy, and even basic methods for interpretation of the test remain controversial.

Proper use of any test involves definition of the patient populations in which the diagnostic yield will be greatest. The use of exercise testing for diagnosis of coronary atherosclerotic heart disease in women with chest pain has also been controversial. Some authors have found that women have a higher rate of false-positive exercise tests than men, while others feel that there is no difference between the sexes in the exercise electrocardiographic response. We examined the electrocardiographic response to exercise of symptomatic men and women with regard to the diagnosis of coronary atherosclerotic heart disease.

Methods

Study Group

The records of the cardiac catheterization and cardiac function laboratories at Grady Memorial Hospital from 1971-1977 were reviewed, and all patients evaluated for chest pain who had both coronary angiography and acceptable exercise tests within 6 months were identified. Patients with valvular heart disease, including mitral valve prolapse, congenital heart disease, idiopathic hypertrophic subaortic stenosis, left bundle branch block on the ECG, a history of chest surgery, or a previously documented myocardial infarction were excluded from the study. The diagnosis of a previous myocardial infarction was based on the finding of at least two of the following criteria: 1) chest pain for longer than 20 minutes that was felt to represent cardiac ischemia; 2) electrocardiographic findings of acute myocardial infarction, including the development of Q waves or the loss of R voltage; and 3) increased serum cardiac enzyme (CPK, LDH or SGOT) levels to at least two times the upper limit of normal.

Exercise Tests

All patients during this period underwent a graded treadmill exercise test using a modified Bruce protocol that included a low-level, stage 0, exercise warm-up of 3 minutes (1.0 mph, 5% grade), and then progressively increased work loads at 3-minute intervals according to the Bruce protocol. All patients were continuously monitored by four electrocardiographic leads: Frank orthogonal leads X, Y and Z, and a CM4 lead. Recordings were made before exercise in the supine and upright positions. Recordings were also made during the last 30 seconds of each exercise stage, immediately at the termination of exercise in the supine position, and at 2, 5 and 8 minutes after exercise. Blood
pressure and heart rate were recorded at each of these points. Treadmill duration score (TDS) in minutes was recorded, but this did not include the 3-minute warm-up (stage 0). Oxygen consumption during exercise was determined by analyzing a timed collection of expired air. Blood lactates at rest, at peak exercise, and 5 minutes after cessation of exercise were measured as previously described.\(^a\)

An exercise test was included in the study if any of the following occurred: 1) the patient reached 85% of the maximal age-adjusted heart rate during exercise;\(^a\) 2) evidence for a maximal exercise performance based upon plateauling of the oxygen consumption values, and at least a threefold increase in baseline serum lactate levels; 3) the development of chest discomfort with exercise; 4) the development during exercise of ST-segment depression > 1 mm below the isoelectric line 0.08 second after the J point in at least one electrocardiographic lead (in the presence of preexercise ST-segment depression, an additional 2 mm of depression was required); 5) a decrease in systolic blood pressure ≥ 20 mm Hg with exercise; 6) the occurrence of a potentially dangerous arrhythmia (e.g., ventricular tachycardia) with exercise. The objective criteria for stopping the exercise test were 1, 2, 4, 5, or 6; the subjective criterion for stopping was 3.

The exercise tests were evaluated by two of us, and the interpretations compared with the original interpretation before final classification. Significant ST-segment changes are as described above.

Cardiac Catheterization

All patients underwent cardiac catheterization with selective coronary angiography in our laboratory. The angiograms were evaluated by at least two of us and then compared with the original interpretation before final classification. Lesions were described as to their location in the left main coronary artery, the distribution of the anterior descending coronary artery and its branches, and the distribution of the left circumflex coronary artery and its branches. Lesions were classified as insignificant if there was 50% cross-sectional area narrowing, questionably significant if there was 50–74% cross-sectional area narrowing and significant if there was ≥ 75% cross-sectional area narrowing of the vessel involved.

Analysis and Definitions

A patient was classified as having a true-positive exercise test if the test showed ischemic ST-segment changes as described above and the coronary angiograms showed significant coronary atherosclerotic disease, i.e., ≥ 75% cross-sectional area narrowing (50% decrease in internal diameter) in at least one coronary vessel. A true-negative exercise test showed no significant ST-segment changes with exercise, in a patient with no significant atherosclerotic lesions. False-positive exercise tests were tests in which electrocardiographic criteria previously mentioned were present, but the coronary angiograms demonstrated no significant lesions. False-negative exercise tests were those in which the electrocardiographic criteria were not present, but the coronary angiograms showed at least one significant, i.e., ≥ 75% cross-sectional area narrowing, coronary atherosclerotic lesion.

The predictive value (PV) of a positive exercise test (+ET) is defined as:

\[
\frac{\text{Number of patients with (+ET) and significant coronary disease}}{\text{Number of patients with (+ET)}} \times 100
\]

Similarly, the PV of a negative exercise test (−ET) is defined as:

\[
\frac{\text{Number of patients with (−ET) and no significant coronary disease}}{\text{Number of patients with (−ET)}} \times 100
\]

Basically, the PV states how often the test result matches the actual disease state.

Sensitivity of the exercise test was defined as:

\[
\frac{\text{Number of patients with (+ET) and significant coronary disease}}{\text{Number of patients with significant coronary disease}} \times 100
\]

Specificity of the exercise test was defined as:

\[
\frac{\text{Number of patients with (−ET) and no significant coronary disease}}{\text{Number of patients with no significant coronary disease}} \times 100
\]

The prevalence of coronary atherosclerotic disease (P[D]) is given as:

\[
\frac{\text{Number of patients with significant coronary disease}}{\text{Number of patients in study group}} \times 100
\]

Statistical methods included chi-square analysis, multidimensional contingency table analysis, analysis of variance, and discriminant analysis, all performed using standard, statistical computer programs.

Results

Study Group

After a retrospective search of all patients who underwent coronary angiography at our institution, 177 patients who met the criteria for this study were found. The group consisted of 85 men and 92 women. There was no statistically significant difference between the men and women in age, P[D], use of digitalis, or the overall rate of (+ET) and (−ET) (table 1). There was no significant difference between the men and women in the distribution of one-, two- or three-vessel disease, or the presence of multivessel disease (fig. 1). Eighty-five percent of the men and 88% of the women had one or more of the objective criteria for stopping the exercise test. Table 2 lists the number of men and women who had each of the criteria. The remaining patients had subjective, exercise-induced
chest pain as the only reason for terminating the exercise test.

Thirty-one of the 85 men (36%) and 30 of the 92 women (33%) had significant stenosis of at least one coronary artery. Five of the 85 men (6%) and two of the 92 women (8%) had significant occlusion of the left main coronary artery. Four men (5%) and four women (4%) had significant disease of only the right coronary artery. Twenty-six men (31%) and 38 women (41%) had significant changes in their ST segment with exercise (table 3).

**True-positive Exercise Tests**

Twenty of 26 men and 18 of 38 women who had significant ST-segment depression with exercise had significant narrowing of at least one coronary vessel (table 3). Thus the PV (+ET) was 77% and 47% for men and women, respectively, a rather marked difference \( (p < 0.05) \) (see table 4). The mean TDS for patients with true-positive exercise tests was 4.1 ± 2.7 (± SD) for men and 3.1 ± 1.8 minutes for women \( (p < 0.001) \) (table 5). Maximal exercise heart rate

**DISTRIBUTION OF CORONARY ATHEROSCLEROTIC DISEASE**

![Graph showing distribution of coronary atherosclerotic disease](image)

**FIGURE 1. Distribution of coronary atherosclerotic disease determined by coronary angiography within 6 months of the treadmill exercise test. There was no statistical difference for one-, two- or three-vessel disease between males and females.**

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**TABLE 1. Characteristics of Study Group**

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>85</td>
<td>92</td>
<td>NS</td>
</tr>
<tr>
<td>Age—mean (years)</td>
<td>49</td>
<td>50</td>
<td>NS</td>
</tr>
<tr>
<td>Range (years)</td>
<td>26–65</td>
<td>27–66</td>
<td></td>
</tr>
<tr>
<td>Prevalence of disease</td>
<td>36%</td>
<td>33%</td>
<td>NS</td>
</tr>
<tr>
<td>Percent with positive exercise test</td>
<td>31%</td>
<td>41%</td>
<td>NS</td>
</tr>
<tr>
<td>Use of digoxin</td>
<td>22%</td>
<td>28%</td>
<td>NS</td>
</tr>
</tbody>
</table>

**TABLE 2. Basis for Acceptable Exercise Tolerance Test**

<table>
<thead>
<tr>
<th></th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>( 85% ) maximal heart rate</td>
<td>56* 62*</td>
</tr>
<tr>
<td>Oxygen consumption and lactate</td>
<td>30 23</td>
</tr>
<tr>
<td>Chest pain with exercise</td>
<td>46 50</td>
</tr>
<tr>
<td>ST-segment depression</td>
<td>24 38</td>
</tr>
<tr>
<td>Decreased blood pressure</td>
<td>1 3</td>
</tr>
<tr>
<td>Ventricular arrhythmia</td>
<td>8 5</td>
</tr>
</tbody>
</table>

\*Column figures will not add to number of study patients because many patients met several criteria.

**TABLE 3. Results of Exercise Testing and Coronary Angiography in Male and Female Patients Using ST Segment Alone or a Multiple Variable Discriminant Function**

<table>
<thead>
<tr>
<th>Sex</th>
<th>Coronary angiography</th>
<th>Exercise testing</th>
<th>ST segment only</th>
<th>Multiple variable discriminant function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (n = 85)</td>
<td>Positive</td>
<td>Positive</td>
<td>20</td>
<td>23</td>
</tr>
<tr>
<td></td>
<td>Negative</td>
<td>11</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Female (n = 92)</td>
<td>Positive</td>
<td>18</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Negative</td>
<td>12</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Positive</td>
<td>20</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Negative</td>
<td>42</td>
<td>47</td>
<td></td>
</tr>
</tbody>
</table>

(beat/min) showed no significant difference between men and women with true-positive tests (137 ± 22 and 132 ± 27, respectively) (table 6).

**False-negative Exercise Tests**

Eleven of 59 men (19%) and 12 of 54 women (22%) who had no or minimal ST-segment changes to exercise had significant coronary artery narrowing (table 3) (NS). The TDS was 5.7 ± 3.0 minutes for males and 3.4 ± 2.2 minutes for females in the false-negative group \( (p < 0.001) \) (table 5). In this group, the maximal heart rate was 140 ± 27 beats/min for males and 135 ± 23 beats/min for females (NS) (table 6). The distribution of coronary artery disease in the false-negative group is of interest. Among the men with false-negative exercise tests, five had one-vessel disease (three left anterior descending coronary artery, one left circumflex coronary artery, and one right coronary artery), four had two-vessel disease (two left anterior descending coronary artery and left circumflex coronary artery, and two left anterior descending coronary artery and right coronary artery), and two had three-vessel disease. Among the women with false-negative exercise tests, nine had one-vessel disease (six left anterior descending coronary artery, one left circumflex coronary artery, and two right cor-
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had significant ST-segment depression and 166 (p < 0.001) (table 5). The average maximal heart rate for the same group was 147 ± 29 beats/min for males and 166 ± 15 beats/min for females (NS) (table 6).

**False-positive Exercise Tests**

Six of 26 men (23%) and 20 of 38 women (53%) who had significant ST-segment depression with exercise had no significant coronary lesion. The average TDS for the false positives was 6.2 ± 2.6 minutes for males and 5.2 ± 1.5 minutes for females (p < 0.001) (table 5). The average maximal heart rate for the same group was 147 ± 29 beats/min for males and 166 ± 15 beats/min for females (NS) (table 6).

**True-negative Exercise Tests**

Forty-eight of 59 men and 42 of 54 women who had no ST-segment changes with exercise were without significant stenosis of even one coronary vessel. Thus, the PV (−ET) is 81% for men and 78% for women (table 4). The mean TDS was 7.1 ± 2.9 minutes for males and 5.3 ± 1.9 minutes for females in the true-negative group (p < 0.001) (table 5). The average maximal heart rate was 161 ± 23 beats/min for males and 154 ± 20 beats/min for females (NS) (table 6).

**Other Factors**

The study group was selected on the basis of the criteria given above. Two unexpected findings were the equal prevalence of coronary disease in both men and women and the lower PV (+ET) in the women. A number of characteristics of the group were analyzed to determine if they could explain these findings. As the group is broken into subgroups, it is more difficult to prove statistically significant differences.

**Digitalis**

Digitalis preparations are known to cause altered ST-segment changes at rest and with exercise.60 Sixty-six men and 66 women in our study were not taking any digitalis preparation. The findings in these patients are given in table 7. The PV (+ET) was 90% for the men and only 45% for the women (p < 0.01) not taking digitalis. Hence, the PVs differ markedly between sexes. The PV (−ET) was 78% for men and 77% for women (NS).

**Resting ECG**

Sixty-two percent of the men and 62% of the women had some abnormality of the resting ECG. There was no statistically significant difference in PV (+ET) or PV (−ET) in patients with normal vs those with abnormal resting ECGs within the same sex.

**Blood Pressure**

Hypertension may contribute to the high rate of positive ST-segment responses by increasing myocardial oxygen demands. In our group, however, the mean resting blood pressure (BP) was 132/84 mm Hg for men and 139/84 mm Hg for women (NS). Twenty-eight of the 86 men (33%) and 35 of the 92 women (38%) had a systolic BP > 140 mm Hg and/or a diastolic BP > 90 mm Hg at rest. This difference in the prevalence of resting hypertension was not significant. Mean peak systolic pressure with exercise was 177 mm Hg for the men and 179 mm Hg for the women. Differences in BP between men and women did not appear to account for the difference in ST-segment response.

**Comparison by TDS and Heart Rate**

The TDS is higher for male and female patients with negative coronary angiograms regardless of the

### Table 4. Predictive Value of Exercise Testing Using ST-segment Depression Alone or a Discriminant Function

<table>
<thead>
<tr>
<th></th>
<th>Males (n = 85)</th>
<th>Females (n = 92)</th>
<th>All subjects (n = 177)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PV (+ET)</td>
<td>77% (70%)</td>
<td>47% (59%)</td>
<td>59% (64%)</td>
</tr>
<tr>
<td>PV (−ET)</td>
<td>81% (85%)</td>
<td>78% (85%)</td>
<td>80% (85%)</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>65% (74%)</td>
<td>60% (73%)</td>
<td>62% (74%)</td>
</tr>
<tr>
<td>Specificity</td>
<td>89% (81%)</td>
<td>68% (76%)</td>
<td>78% (78%)</td>
</tr>
</tbody>
</table>

Abbreviations: PV(+ET) = predictive value of a positive test; PV(−ET) = predictive value of a negative test.

### Table 5. Average Treadmill Duration Score (Minutes) for Patient Groups

<table>
<thead>
<tr>
<th></th>
<th>Angiogram positive</th>
<th>Angiogram negative</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Positive ET</td>
<td>Negative ET</td>
</tr>
<tr>
<td>Males</td>
<td>4.1 ± 2.7</td>
<td>5.7 ± 3.0</td>
</tr>
<tr>
<td>Female</td>
<td>3.1 ± 1.8</td>
<td>3.4 ± 2.2</td>
</tr>
</tbody>
</table>

Values are ± sd.

Males vs females: p < 0.001 by analysis of variance.

The difference for coronary angiogram positive or negative is significant whether the exercise test is positive or negative: p < 0.0001 by analysis of variance.

Abbreviation: ET = exercise test.
TABLE 6. Average Maximal Heart Rate (beats/min) for Patient Groups

<table>
<thead>
<tr>
<th></th>
<th>Angiogram positive</th>
<th>Angiogram negative</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Positive ET</td>
<td>Negative ET</td>
</tr>
<tr>
<td>Male</td>
<td>137</td>
<td>140</td>
</tr>
<tr>
<td></td>
<td>± 22</td>
<td>± 27</td>
</tr>
<tr>
<td>Female</td>
<td>132</td>
<td>135</td>
</tr>
<tr>
<td></td>
<td>± 27</td>
<td>± 23</td>
</tr>
</tbody>
</table>

Values are ± SD.
No significant difference in response for male vs female (analysis of variance).
The difference for coronary angiogram positive or negative is significant whether the exercise test is positive or negative: \( p < 0.0001 \) by analysis of variance.
Abbreviation: ET = exercise test.

ST-segment response \( (p < 0.001) \) (table 5).
A similar difference is found with respect to maximal heart rate, i.e., both males and females achieve higher mean maximal heart rates in the absence of coronary artery disease than males and females who do have coronary disease \( (p < 0.0001) \) (table 6). This difference in heart rate was seen regardless of the exercise test ST-segment response.

Patients in this study with chest pain who had normal coronary angiograms could walk longer on a standard treadmill protocol and could achieve higher heart rates than chest pain patients who had significant coronary atherosclerosis.

Discriminant Function Analysis

The contributions of four variables were evaluated with respect to the diagnosis of coronary atherosclerosis by discriminant analysis. The results (table 8) indicate that maximal heart rate and ST-segment depression were highly significant \( (p = 0.000001) \) in discriminating between chest pain patients who have and those who do not have coronary atherosclerosis. Another significant contributor to the discriminant function is the sex-dependent ST-segment response \( (p = 0.03) \), although its F value was much less than the F values for heart rate and ST segment alone (table 8). The sex-dependent ST-segment variable contributes a shift to the discriminant score only if the patient is a female with a positive ST-segment response. Finally the TDS does not contribute significantly to the discriminant score \( (F \text{ value } 1.43, \text{ NS}) \) (table 8). Therefore, the TDS is not included in the final discriminant function.

Comparison of ST Segment Alone and Discriminant Score

The results on PV of using the discriminant score as an alternative to ST segment alone are given in tables 3 and 4. For male and female subjects combined, there was improvement over the “ST segment alone” results in PV (+ET) and PV (−ET): 59% to 64% and 80% to 85%, respectively (table 4). Similarly, for all subjects, the sensitivity increased from 62% to 74% using the discriminant score. No change was noted in the specificity for all subjects.
The greatest single value of the discriminant score in this study was among females. The number of true positives increased from 18 to 22 and the number of false positives decreased from 20 to 15 (table 3). This improvement is shown also in table 4, where PV (+ET) for females increased from 47% to 59%. PV (−ET), sensitivity and specificity improved in females when the discriminant score was used.
Males did not benefit from use of the discriminant score: PV (+ET) decreased from 77% to 70%, while PV (−ET) increased from 81% to 85%. Sensitivity for males increased from 65% to 74%, but specificity declined from 89% to 81% (table 4).
Whether use of this discriminant function in a prospective study will be useful is not known.

Discussion

The role of exercise testing in the diagnosis of coronary atherosclerotic heart disease in women is unclear. Several investigators have reported a high rate of ST-segment changes in women with exercise. Astrand et al. reported in 1965 on a group of 117 women and 87 men selected for a general health survey, who had bicycle exercise tests performed at 8-year intervals. At both exercise tests the women had a higher rate of ST-segment changes with exercise than the men. Positive exercise tolerance tests were seen in 16% of the women and 6% of the men at the first testing, and in 27% of the women and 13% of the men 8 years
later. This finding was surprising in view of the presumed lower incidence of coronary atherosclerotic heart disease in women than men in this asymptomatic population. Lepeschkin6 also noted a higher overall rate of ST-segment changes in women with exercise.

Profant,4 in a study of 144 healthy women tested with a graded treadmill exercise test found 33% with significant ST-segment depression by visual inspection. Cummings5 studied 357 normal women with a bicycle ergometer test. Significant ST-segment changes with exercise occurred in 25% of women 20–39 years of age, 50% of women 40–59 years of age, and 66% of women over 60 years of age. In none of these groups was there any documentation of the patients’ coronary status by angiography.

Bartell’s11 study of 650 patients who had coronary angiography and exercise tolerance tests found only 133 without significant coronary disease. Eleven of these patients without coronary artery disease had significant ST-segment changes with exercise despite the lack of coronary narrowing. Six of these patients (55%) were women, although women accounted for only 23% of the population, suggesting a true difference in the response of the women to exercise. This study, however, failed to report the sex distribution of the coronary disease. Thus, different disease prevalence could have explained at least part of the sex difference. The importance of the prevalence of the disease being tested for in the interpretation of the results of any testing procedure (Bayes’ theorem) has been reviewed by several authors.12–14

Sketch15 studied a group of 195 men and 55 women with chest pain, using exercise testing and coronary angiography. He found that PV (+ET) for men was 89%, but only 33% for women. The prevalence of coronary artery disease was 53% in the men and 18% in the women. How much the difference in disease prevalence contributed to the higher rate of false-positive tests in women is not clear.

Detry and associates16 also noted that false-positive and false-negative exercise test results were strongly influenced by sex. Again, the prevalence of disease was different for males (80%) than for females (43%). Thus, it is not possible to determine from either the Sketch or the Detry data whether women have more false-positive results to exercise testing apart from the effects of coronary atherosclerotic disease prevalence, or whether this Bayesian factor accounts for the total difference.

Linhart17 studied “98 consecutive females” with both exercise testing and coronary angiography. Eighty-nine of the 98 (91%) had recurrent chest pain. The coronary disease prevalence was 24%. No directly comparable group of males was reported, but in a nonconcurrent group consisting of 80% males, the rates of false-positive and false-negative tests were said to be similar. Linhart concluded that the electrocardiographic response of women was similar to that of men, even though the PV (+ET) (52%) for his women was low and similar to that reported in the present study (47%).

Ryan,17 in a study of 404 women with chest pain and no previously documented coronary or other heart disease, showed a 27% prevalence of disease documented by angiography. The PV (+ET) was only 49%; the PV (−ET) was 82%, findings very similar to those of the present study. On the other hand, exercise testing missed half of the patients with coronary artery disease, and over one-third of those with multivessel disease were not identified.

The difficulty in interpreting the results of these studies as to whether women have a higher rate of false-positive ST-segment changes with exercise, is to decide whether this is a true difference in response to exercise or merely a Bayesian disease distribution effect. To clarify this problem, we have studied a very specific subgroup of patients who presented with chest pain. To emphasize the possible diagnostic role of exercise testing in evaluating patients with chest pain, only patients with no previously documented myocardial infarctions were included. The present study showed no significant difference between the disease prevalence for men and women in this select subset of patients. Yet, there was a highly significant difference in the rate of false-positive exercise tolerance tests in the women as shown in their lower PV (+ET). This difference was even more striking when male–female differences were examined in patients who did not take digitalis preparations. No difference in the rate of true-negative or false-negative exercise tests was found between the men and women. These results suggest that there is a separate difference, beyond disease prevalence, in electrocardiographic response to exercise in males compared to females with regard to false-positive tests. No difference in false-negative response between males and females is suggested by this study or any of the previously mentioned studies.

**Conclusions**

These results concerning the diagnosis of the cause of chest pain in women with no previously documented myocardial infarction have several clinical implications. Women, whose coronary atherosclerotic disease prevalence in the general population of most Western countries is lower than that of men, tend to have more false-positive exercise tests on this basis. In addition, some other female attributes, either anatomic or physiologic, appear to add to the number of false-positive results, as reported in this study. Thus, the discovery of a (+ET) in the clinical evaluation of a female patient with chest pain would add little to the diagnostic accuracy. Even with the addition of other variables in the discriminant score, the PV (+ET) for women only rose to 59% — slightly better than flipping a coin.

Should exercise testing for the diagnosis of coronary artery atherosclerosis in women with chest pain but no previously documented myocardial infarction ever be done? While the PV (+ET) in such a patient group is of dubious value, even without the addition of a discriminant score, the PV (−ET) is quite high.18

Some significant coronary disease will be missed by
negative treadmill results, but in this study, no patient with left main disease was missed and only two of the eight men and one of the six women with three-vessel disease were not identified. Therefore, we suggest that exercise testing for the diagnosis of significant coronary artery disease continue to be used in women with chest pain as one of the clinical tools currently available.

If the goal is not only diagnosis, but also the identification of patients who should go on to coronary arteriography for possible coronary artery surgery, the results of exercise testing are more encouraging. Few surgical candidates would be missed, using currently accepted criteria for operative indications. As the criteria for surgical therapy change, this may not hold true.

The addition of other exercise testing variables in the determination of a discriminant score to classify women patients in this study appeared to improve predictive accuracy of the test. Male patients in this study, however, did not benefit from such analysis. Other investigators are actively evaluating the use of multiple exercise test measurements, in addition to ST-segment response, and this technique holds promise for the improvement of the predictive power of exercise testing.19

Acknowledgment

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