Women with chest pain: is exercise testing worthwhile?

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Abstract

Objective—To determine the diagnostic value of the exercise tolerance test (ETT) in women presenting with chest pain.

Design—Prospective study of all women presenting to a centre with chest pain between 1987 and 1993 who were assessed by an ETT and coronary angiography.

Setting—The outpatient clinic of one consultant cardiologist in a tertiary referral centre.

Patients—All women referred to this outpatient clinic with chest pain were screened. For inclusion, patients had to perform ETT and undergo coronary angiography. Of the 347 referred during this period, 142 were excluded because they were unable to perform ETT or because of Q waves or other abnormalities on their resting electrocardiogram.

Results—Overall the sensitivity of the ETT was 68% and the specificity was 61%, with a positive predictive value of 0.61 and a negative predictive value of 0.68. There were 42 false positive and 31 false negative ETT results (36% of the study group). The predictive value of a negative test was higher in younger women (<52 years) than in the older group (≥52 years) (P = 0.004), but the positive predictive value in the two groups was not significantly different. The predictive value of a negative test was also higher in those with two or fewer risk factors than in those with three or more risk factors (P = 0.001). The negative predictive value for those women above 52 years with three or more risk factors (24% of the study group) was only 0.25. Lack of chest pain during ETT was associated with a higher negative predictive value in the younger group than in the older women (P = 0.006).

Conclusions—in women with chest pain use of the ETT was a misleading predictor of the presence or absence of coronary disease in 36% of these patients. In particular, a negative test in older women with three or more risk factors had a very low predictive value. The inclusion of risk factors and division by age can, however, be used to identify a population at intermediate risk for coronary artery disease in whom the ETT result has the highest diagnostic utility.

(Heart 1996;76:156–160)

Keywords: exercise test; women; chest pain; coronary angiography.

Coronary disease is a common cause of morbidity and mortality in women, and is the commonest cause of death in those over the age of 65 years. According to the Framingham study the prevalence of coronary artery disease in younger women is lower than in men, but the death rates of the two sexes converge in late middle age. Women with chest pain account for a considerable proportion of cardiac referrals.

Exercise testing has been a widely used screening procedure for the assessment of cardiac status for over 30 years. None the less, the value of this procedure in the screening of women to predict the presence of obstructive coronary disease has been the subject of considerable controversy. The usual electrocardiographic criteria applied in exercise testing seem less valuable in women than in men. In symptom free women "significant" ST segment changes are up to three times more common than in men. In addition, symptomatic women with a positive exercise tolerance test (ETT) have a lower prevalence of coronary artery disease and fewer coronary events than men.

We have previously shown that a diagnosis of normal coronary arteries was five times more likely in women referred with chest pain than in a matched population of men. To a great extent, the apparent differences in predictive accuracy between men and women reflect not much more than a clinical proof of Bayes theorem, whereby the predictive accuracy of a test is dependent on the prevalence of the disease in the population being studied. It has also been suggested, however, that in patients with chest pain the higher positive predictive value of exercise testing in men compared with women cannot be fully explained by a difference in disease prevalence. In current clinical practice the ETT result is a key factor in the decision to perform an invasive investigation and unless coronary angiography were without significant risk or cost it could not become the primary diagnostic test for patients with chest pain.

The aim of this study was to describe the results of exercise testing as a diagnostic test for the presence or absence of coronary disease in women. We aimed to identify subgroups of women in whom ETT was especially useful or particularly misleading.

Patients and methods

We screened all women referred to one cardiologist’s outpatient clinic with chest pain who underwent coronary angiography over the
period 1987–1993. All women included in the study had both an ETT and coronary angiography. Exclusion criteria included pathological Q waves or left or right bundle branch block on the electrocardiogram at presentation; organic valvar or congenital heart disease; previous angiographically documented coronary artery disease; and inability to perform ETT, either because of disability or symptoms. The presence of recognised risk factors for coronary disease, including a family history (first degree relative with coronary artery disease), diabetes mellitus (diet or drug controlled), hypertension, raised cholesterol (random total cholesterol ≥ 6·5 mmol/l, or taking lipid lowering medication), or smoking (at the time of referral) was documented for all patients. When risk factor profiles were incomplete, follow up was undertaken using notes from other hospitals and GPs or by asking the patients. We analysed electrocardiograms (ECG) obtained at the original referral or at the first consultation at this centre. All exercise ECGs were analysed in this department, and were regarded as positive when they showed horizontal or downsloping ST segment depression of 1 mm from the baseline 80 ms after the J point. Coronary angiograms were analysed by the same consultant cardiologist throughout, and coronary artery disease was diagnosed when there was luminal stenosis greater than 50% of any epicardial coronary artery.

ANALYSES
The following formulae were applied to the test results:

Sensitivity = true positives/(CAD+)
Specificity = true negatives/(CAD−)
Positive predictive value = true positives/(ETT+)
Negative predictive value = true negatives/(ETT−)

where (CAD+) is the number of patients with coronary disease, (CAD−) is the number of patients with normal coronary arteries, (ETT+) is the number of patients with a positive ETT, and (ETT−) is the number of patients with a negative ETT.

The predictive value of a test represents the frequency with which the test result matches that of the disease state.

For more detailed analysis, women were divided into two age groups; less than 52 years and 52 years and above. This division is arbitrary, but takes account of data from the Nurses’ Health Study of 121 700 women, in whom the median age for the menopause ranged from 52·4 years in non-smokers to 50·4 years in heavy smokers. Women were also subdivided according to how many of the five risk factors they had, as well as by the presence of chest pain at ETT.

Statistical analysis was undertaken using the χ² test, with Fisher’s exact test for groups with sample numbers of five or less.

Results
ALL WOMEN
Three hundred and forty seven women were

<table>
<thead>
<tr>
<th>Period</th>
<th>No. of patients</th>
<th>CAD+</th>
<th>CAD−</th>
<th>ETT+</th>
<th>ETT−</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;52 years</td>
<td>76 (23%)</td>
<td>15 (7%)</td>
<td>21 (10%)</td>
<td>61 (33%)</td>
<td>10 (6%)</td>
</tr>
<tr>
<td>52 or over</td>
<td>79 (27%)</td>
<td>24 (9%)</td>
<td>22 (8%)</td>
<td>65 (39%)</td>
<td>10 (6%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>RF</th>
<th>No. of patients</th>
<th>CAD+</th>
<th>CAD−</th>
<th>ETT+</th>
<th>ETT−</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>47 (23%)</td>
<td>15 (7%)</td>
<td>21 (10%)</td>
<td>61 (33%)</td>
<td>10 (6%)</td>
</tr>
<tr>
<td>1RF</td>
<td>30 (15%)</td>
<td>8 (4%)</td>
<td>16 (8%)</td>
<td>52 (28%)</td>
<td>10 (6%)</td>
</tr>
<tr>
<td>2RF</td>
<td>3 (1%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>3RF</td>
<td>3 (1%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>4RF</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

**P = 0·001 for 0·2 v ≥ 3 RF groups.
PV, predictive value; pos, positive; neg, negative.

Table 1 Details of study population

<table>
<thead>
<tr>
<th>Total</th>
<th>205</th>
<th>56-6 (range 25-93)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAD:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>One vessel</td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>Two vessel</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>Three vessel</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Risk factors:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family history</td>
<td>123 (60%)</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>83 (40%)</td>
<td></td>
</tr>
<tr>
<td>Raised cholesterol</td>
<td>114 (56%)</td>
<td></td>
</tr>
<tr>
<td>Smoker</td>
<td>75 (37%)</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>15 (7%)</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>21 (10%)</td>
<td></td>
</tr>
<tr>
<td>1RF</td>
<td>47 (23%)</td>
<td></td>
</tr>
<tr>
<td>2RF</td>
<td>65 (32%)</td>
<td></td>
</tr>
<tr>
<td>3RF</td>
<td>46 (22%)</td>
<td></td>
</tr>
<tr>
<td>4RF</td>
<td>10 (10%)</td>
<td></td>
</tr>
<tr>
<td>5RF</td>
<td>3 (1%)</td>
<td></td>
</tr>
</tbody>
</table>

Table 2 Exercise test results in all women (n = 205)

<table>
<thead>
<tr>
<th>No. of risk factors</th>
<th>All (n = 205)</th>
<th>0–2 (n = 136)</th>
<th>≥ 3 (n = 69)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity (%)</td>
<td>61</td>
<td>63</td>
<td>56</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>68</td>
<td>76</td>
<td>79</td>
</tr>
<tr>
<td>Pos PV</td>
<td>0·61</td>
<td>0·56</td>
<td>0·67</td>
</tr>
<tr>
<td>Neg PV</td>
<td>0·68</td>
<td>0·80</td>
<td>0·45**</td>
</tr>
</tbody>
</table>

Percentage figures given in brackets are for the whole study group.

Percentage of women with coronary artery disease according to risk factors (RF) and age.

- 0–2 RF
- 3–5 RF
- Total

Percentage of women with coronary artery disease according to risk factors (RF) and age.

Percentage of women with coronary artery disease according to risk factors (RF) and age.

- 0–2 RF
- 3–5 RF
- Total

Percentage of women with coronary artery disease according to risk factors (RF) and age.
Table 3 Exercise test results in all women according to presence or absence of pain during test

<table>
<thead>
<tr>
<th>Chest pain (n = 80)</th>
<th>No chest pain (n = 125)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specificity (%)</td>
<td>64</td>
</tr>
<tr>
<td>Sensitivity (%)</td>
<td>86</td>
</tr>
<tr>
<td>Pos PV</td>
<td>0.71*</td>
</tr>
<tr>
<td>Neg PV</td>
<td>0.78</td>
</tr>
</tbody>
</table>

*P = 0.08. PV, predictive value; pos, positive; neg, negative.

The positive predictive value was 0.80 in the lower risk factor group and only 0.45 in the others (P = 0.001). Eighty women had chest pain during the ETT, of whom 48 (60%) had significant ST segment depression (table 3). Fifty-nine (47%) of the 125 patients who were pain-free had a positive test. The specificity for the exercise test in those with chest pain was 64% and the sensitivity was 86%, compared with 60% and 56% respectively in the pain-free group. The positive predictive value was higher in those with chest pain compared with those with no pain (0.71 vs 0.53 respectively), although this did not reach statistical significance (P = 0.08). There was also a trend of higher negative predictive value in the pain group (0.78) than in the pain-free patients (0.64).

Table 4 Exercise results in women divided according to age and number of risk factors

<table>
<thead>
<tr>
<th></th>
<th>Less than 52 years (n = 69)</th>
<th>52 years or older (n = 136)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0-2 (n = 49)</td>
<td>≥ 3 (n = 20)</td>
</tr>
<tr>
<td>ETT</td>
<td>28</td>
<td>21</td>
</tr>
<tr>
<td>ETT -</td>
<td>41</td>
<td>28</td>
</tr>
<tr>
<td>CAD +</td>
<td>19</td>
<td>11</td>
</tr>
<tr>
<td>CAD -</td>
<td>50</td>
<td>38</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>70</td>
<td>66</td>
</tr>
<tr>
<td>Sensitivity (%)</td>
<td>68</td>
<td>73</td>
</tr>
<tr>
<td>Pos PV</td>
<td>0.46</td>
<td>0.08</td>
</tr>
<tr>
<td>Neg PV</td>
<td>0.85*</td>
<td>0.80</td>
</tr>
</tbody>
</table>

*P = 0.004. †P = 0.008. ‡P = 0.001.

Table 5 Exercise test results in women divided according to age and chest pain at exercise

<table>
<thead>
<tr>
<th></th>
<th>Younger (&lt; 52 yr)</th>
<th>Older (≥ 52 yr)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Chest pain (n = 28)</td>
<td>No chest pain (n = 41)</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>79</td>
<td>65</td>
</tr>
<tr>
<td>Sensitivity (%)</td>
<td>67</td>
<td>70</td>
</tr>
<tr>
<td>Pos PV</td>
<td>0.60</td>
<td>0.39</td>
</tr>
<tr>
<td>Neg PV</td>
<td>0.83</td>
<td>0.87*</td>
</tr>
</tbody>
</table>

*P = 0.006.

Discussion
Although coronary artery disease is common in women, presentation with chest pain is much more common. Identifying those with coronary artery disease among women with chest pain is a common clinical problem. The ETT has become one of the main methods used to evaluate women with chest pain, and in order to decide who should undergo further investigation. It is simple to perform, widely available, and the mortality is low.14-15 However, if conventional ECG criteria alone are used women have a high false positive rate.44 So although the sensitivity of the ETT is generally shown to be as good as in men,12-16,17 the specificity is lower. Another disadvantage as a screening procedure is that a significant proportion of patients will not be suitable for the test and this was well illustrated by our study in which 27% (92 of 347) of patients did not have a test. These problems may contribute to the selection bias that exists against women when referral for coronary angiography is being considered.18-20 Unfortunately, practical and financial considerations prevent the use of tests such as nuclear imaging, which has greater sensitivity and specificity,16,17,20 as the universal method for investigating these patients.

This study set out to identify which subgroups of women referred to a tertiary referral centre for assessment of their chest pain benefit most from exercise testing as a means of deciding who should undergo coronary angiography. One limitation of the study is that it is based on a "selected" population, because we are unable to take into account...
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