Diagnostic Value of History and Maximal Exercise Electrocardiography in Men and Women Suspected of Coronary Heart Disease

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SUMMARY Coronary arteriographic data have been compared in 278 patients (231 males and 47 females) with the ECG response to a maximal exercise test and with the history (myocardial infarction — MI, typical or atypical angina pectoris — AP). The sensitivity and specificity of exercise ECG were similar in males and females. False negative ECG responses were frequent in males (40%) and false positive ECG responses were frequent in females (38%). This difference between sexes was essentially due in our patients to the higher prevalence of CHD in males (80%) than in females (43%).

In the absence of a previous MI, a history of typical AP was associated with coronary heart disease (CHD) in 94% of males and 62% of females. Atypical AP was rarely associated with CHD (18% in males; 11% in females). When typical AP was associated with an abnormal exercise ECG, CHD was highly probable in males (98%) and present in 75% of females. In presence of atypical AP with a normal exercise ECG, CHD was unlikely in males (11%) and in females (8%).

We conclude that exercise ECG has limited value for the diagnosis of CHD. In men with typical AP, exercise ECG often confirms the diagnosis but a negative ECG exercise does not rule out CHD because of the high incidence of false negative responses. In males and females with atypical AP, an abnormal response to exercise is difficult to interpret owing to a high incidence of false positive responses.

EXERCISE ELECTROCARDIOGRAPHY (ECG) is a well-established method for the diagnosis of coronary heart disease (CHD). Its value has been differently assessed from correlative studies with arteriographic data and the validity of exercise ECG has more recently been questioned especially in women. Clinically, however, the results of an exercise test are not only interpreted without taking into account the patient’s history and complaints. The purpose of the present study was to estimate the actual contribution of exercise ECG to the overall diagnosis of CHD and thus to define its advantages and limitations. The patient’s history and the ECG recorded during a test of maximally tolerated exercise were compared with the angiographic findings in a group of 278 patients.

Material

Of the 278 patients that were studied, 231 were males (mean age 48 years, range 27–65) and 47 were females (mean age 49 years; range 33–64). This group included a series of patients from January 1971 to November 1975 who had a coronary arteriographic study and within one month prior to the arteriography underwent a maximal exercise test. The majority of the exercise tests were performed one to five days before the coronary arteriography. Those patients with bundle branch block, valvular heart disease and those receiving digitalis less than three weeks before the exercise test were excluded.

The reasons for having these patients undergo exercise tests and coronary arteriography were: 1) the diagnosis of CHD in patients with complaints of typical or atypical angina pectoris (AP); 2) the presence of typical or atypical AP in patients with a previous well-documented acute myocardial infarction — MI (table 1).
on paper every minute. A twelve lead ECG was recorded during exercise every five minutes, at the maximal exercise level and at the third and sixth minute of the recovery. Expiratory gases were usually collected during the last minutes of exercise and analyzed as previously reported.18

All ECG records were analyzed independently from the arteriographic data by one of the authors. The ECG were visually analyzed and the amount of ST-segment depression or elevation was measured in every lead at the J point with the PR level used as zero reference. The ST-segment abnormalities already present at rest were subtracted from the observed changes. The ECG response to exercise was considered as abnormal in presence of: 1) a horizontal or downsloping ST depression ≥ 0.1 mV for at least 0.08 sec; 2) an elevation of the ST segment ≥ 0.1 mV. The ECG abnormalities were usually observed during exercise and were most marked at the maximal exercise level. Only five of the 214 abnormal ECG responses were observed only after exercise. The mean maximal heart rate was 150 per minute in men and in women.

The coronary arteriography was performed through the femoral artery using preshaped catheters.19 The angiographic studies always began with a left ventricular injection in the right oblique anterior position. As many injections as necessary were made in the left and right coronary arteries to provide adequate films. The major complications of this procedure were two acute MI with no death. An anterior MI occurred at the end of the procedure in a patient with a 75% stenosis of the LAD and a poor distal bed; a patient with a 75% stenosis of the RCA developed an inferior MI 6 hours after the procedure. All films were independently reviewed by one of the authors. The coronary arteriography was considered abnormal in presence of a decrease of 50% in diameter of at least one coronary vessel. C+ = absence of significant coronary lesions; E+ and E- refer to an abnormal and normal ECG response to exercise.

### Table 1. Correlation between Clinical History, Coronary Arteriography and ECG Response to Maximal Exercise

<table>
<thead>
<tr>
<th></th>
<th>Age (yr)</th>
<th>Maximal HR</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(N)</td>
<td>Range</td>
<td>True positives</td>
<td>True positives</td>
</tr>
<tr>
<td><strong>Men</strong></td>
<td></td>
<td></td>
<td>negatives</td>
<td>negatives</td>
</tr>
<tr>
<td><strong>Previous MI</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Typical AP</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All patients</td>
<td>50</td>
<td>23.9</td>
<td>158</td>
<td>90</td>
</tr>
<tr>
<td>AP during the test*</td>
<td>36</td>
<td>23.9</td>
<td>153</td>
<td>94</td>
</tr>
<tr>
<td>Atypical AP</td>
<td>34</td>
<td>24.3</td>
<td>151</td>
<td>71</td>
</tr>
<tr>
<td>Total</td>
<td>84</td>
<td>24.0</td>
<td>143</td>
<td>82</td>
</tr>
<tr>
<td><strong>No previous MI</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Typical AP</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All patients</td>
<td>97</td>
<td>23.9</td>
<td>152</td>
<td>95</td>
</tr>
<tr>
<td>AP during the test*</td>
<td>69</td>
<td>23.2</td>
<td>140</td>
<td>98</td>
</tr>
<tr>
<td>Atypical AP</td>
<td>50</td>
<td>15.5</td>
<td>168</td>
<td>76</td>
</tr>
<tr>
<td>Total</td>
<td>147</td>
<td>22.6</td>
<td>144</td>
<td>40</td>
</tr>
</tbody>
</table>

*In these patients, the exercise test was interrupted because of the onset of typical AP.

Abbreviations: MI = myocardial infarction; AP = angina pectoris; HR = heart rate; C+ = decrease of 50% or more in diameter of at least one coronary vessel; C− = absence of significant coronary lesions; E+ and E− refer to an abnormal and normal ECG response to exercise.

### Results

In the present group of patients, CHD was more frequent in men than in women (80% versus 43%; \( P < 0.001 \); table 1).
All patients with a history of MI had significant CHD. In the absence of a previous MI, symptoms of typical AP were associated with significant CHD in 94% of the men and 62% of the women ($P < 0.01$); these percentages were slightly but nonsignificantly higher in the patients who experienced typical AP during the exercise test itself (96% in men and 71% in women). When the complaints were atypical, CHD was present in 18% of the men and 11% of the women.

The maximal heart rate (HR) was always lower in patients with a history of typical AP since the exercise test was often interrupted for the onset of AP (table 1); the latter was observed in 71% (105/147) of the men and 54% (15/28) of the women with a history of typical AP. In men with a history of atypical AP, the mean maximal HR was 151 in those with a previous MI and 165 in those without a previous MI ($P < 0.001$); these HR correspond to 89% and 96% of the predicted maximal HR. In women with a history of atypical AP, the mean maximal HR was 162 which corresponds to 93% of the predicted maximal HR.

In all 278 patients (231 men and 47 women), the sensitivity of ECG during maximal exercise was 86% (176/204) and the specificity 70% (52/74). The sensitivity and specificity of exercise ECG were slightly higher in men than in women (table 1). False negative ECG responses were more frequent in men (40% vs 19%; $P < 0.10$) while the false positive ECG responses were more frequent in women (38 vs 7%; $P < 0.001$). Among the men without a previous MI, false negative responses were frequent (56%) when typical AP was present; false positive responses were frequent in men (67%) when the complaints were atypical. It is apparent from table 1 that the differences existing between sexes and those among a given sex are related to differences in the prevalence of CHD. In our patients, when CHD was uncommon (women; men or women without AP) the false positive responses were frequent and when CHD was frequent (men; men with AP) the false negative responses were frequent.

The false positive responders (table 1; fig. 1) had in both sexes a significantly higher maximal HR than the true positives responders (165 vs 144 in men, $P < 0.001$; 172 vs 136 in women, $P < 0.001$). In men and in women this difference is largely due to the fact that the true positive responders include many patients with typical AP and a low maximal HR; the majority of the men with a false positive response belong to the group of patients with a history of atypical AP and in this group, the maximal HR of false positive responders is slightly less than that of true positive responders (164 versus 168).

The false negative responders (table 1; fig. 1) had in both sexes a significantly lower maximal HR than the true negatives responders (156 vs 166 in men, $P < 0.001$; 142 vs 153 in women, $P < 0.001$).

Since significant coronary lesions were seen in all patients with a history of MI, exercise ECG has a limited diagnostic value in this subgroup. Therefore the diagnostic value of exercise ECG in the patients without a previous MI will now be examined.

In these patients (table 2), when typical AP is associated with an abnormal ECG response to exercise, 98% (86/88) of the men and 75% (15/20) of the women have significant CHD. When atypical complaints are associated with a normal ECG response to exercise, only 11% (4/35) of the men and 8% (1/13) of the women have significant coronary lesions. In the presence of a discrepancy between history and exercise ECG (abnormal ECG with atypical complaints or normal ECG with typical AP), 42% (10/24) of the men and women were re-evaluated.

### Table 2. Correlation between Exertional ECG, History and Arteriographic Data in Patients without Previous Myocardial Infarction

<table>
<thead>
<tr>
<th>History of atypical AP</th>
<th>Exertional ECG</th>
<th>All patients</th>
<th>Patients with AP during the test</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Men</strong></td>
<td></td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>Yes</td>
<td>Abn</td>
<td>86/88</td>
<td>98</td>
</tr>
<tr>
<td>F. R.</td>
<td>5/9</td>
<td>50</td>
<td>1/3</td>
</tr>
<tr>
<td>No</td>
<td>Abn</td>
<td>5/15</td>
<td>33</td>
</tr>
<tr>
<td>F. R.</td>
<td>4/35</td>
<td>11</td>
<td>-</td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td></td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>Yes</td>
<td>Abn</td>
<td>15/20</td>
<td>75</td>
</tr>
<tr>
<td>F. R.</td>
<td>1/6</td>
<td>17</td>
<td>1/2</td>
</tr>
<tr>
<td>No</td>
<td>Abn</td>
<td>1/6</td>
<td>17</td>
</tr>
<tr>
<td>F. R.</td>
<td>1/13</td>
<td>8</td>
<td>-</td>
</tr>
</tbody>
</table>

**Abbreviations:** Abn = abnormal; NI = normal.

### Table 3. Type of ECG Response to Exercise and Arteriographic Data

<table>
<thead>
<tr>
<th>ECG response to exercise</th>
<th>Number of diseased vessels (stenosis ≥ 50%)</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Men</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>35</td>
<td>10</td>
<td>7</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>ST depression ≥ -0.1 mV</td>
<td>12</td>
<td>28</td>
<td>52</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>ST elevation ≥ +0.1 mV</td>
<td>-</td>
<td>9 (3)*</td>
<td>11 (5)</td>
<td>10 (4)</td>
<td></td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>17</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>ST depression ≥ -0.1 mV</td>
<td>9</td>
<td>8</td>
<td>3</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>ST elevation ≥ +0.1 mV</td>
<td>1 (1)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

*The numbers in parentheses indicate the patients with ST elevation who had a significant ST depression in another reciprocal lead.
TABLE 4. ST-Segment Elevation during Exercise and Left Ventriculography (N = 231 men)

<table>
<thead>
<tr>
<th>Left ventriculography</th>
<th>ST segment elevation ≥ 1 mm during exercise</th>
<th>Patients with a previous MI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All patients (N) (%)</td>
<td>(N) (%)</td>
</tr>
<tr>
<td>Normal</td>
<td>6/108 (5.6)</td>
<td>1/13 (7.7)</td>
</tr>
<tr>
<td>Hypokinesia</td>
<td>2/48 (4.2)</td>
<td>1/20 (5.0)</td>
</tr>
<tr>
<td>Akinesia</td>
<td>10/44 (22.7)</td>
<td>9/30 (30.0)</td>
</tr>
<tr>
<td>Diskinesia</td>
<td>12/22 (54.5)</td>
<td>12/21 (57.1)</td>
</tr>
</tbody>
</table>

17% (2/12) of the women have significant CHD (table 2). These correlations are not significantly different in the patients who experienced typical AP during the exercise test.

ECG abnormalities during exercise were not significantly related to the number of diseased vessels (table 3). Of the men with single vessel disease 79% (37/47) had an abnormal exercise ECG vs 90% (60/67) of those with triple vessel disease. In patients with a previous MI, however, ST-segment changes with exercise were more frequent in those with three vessel disease (31/35; 89%) than in those with single vessel disease (9/14; 64%; P < 0.05).

In men (table 3) ST-segment elevation during exercise was not frequent, but when present was highly specific for CHD (30/30; 100%). The majority (23/30; 77%) of these patients had a prior MI; among the seven other patients, four suffered from variant angina pectoris. The occurrence of ST-segment elevation during exercise was often accompanied by impaired left ventricular function (table 4). After an MI, the onset or aggravation of ST-segment elevation during exercise was associated in 21 of 23 cases (92%) with an akinetic or dyskinetic left ventricular segment.

The degree of the ST-segment depression also influences the data (table 5). A 100% specificity was noted for a 0.4 mV depression of the ST segment but this finding had a very low sensitivity.

Discussion

It is important to discuss first whether or not the exercise tests performed by the patients were really maximal. The mean maximal HR of men (150) and women (150) correspond to ± 85% of their predicted maximal HR; this rather low percentage of the predicted maximal HR is essentially due to the inclusion of patients with a history of typical AP. Many of these patients experienced typical AP during the exercise test and the latter prevented their predicted maximal HR from being reached. The patients without previous MI and with complaints of atypical AP reached 93% (women) and 96% (men) of their predicted maximal HR, which indicates that the intensity of the exercise was sufficient to elicit near-maximal to maximal HR. In patients with a previous MI but atypical AP, the maximal HR was lower (± 85% of the predicted maximal HR); similar values of maximal HR have been observed previously in such patients.21 It should be remembered that all our patients were instructed to exercise until the onset of symptoms or until subjective exhaustion and that they all cooperated very well. From a clinical point of view, the exercise tests were therefore really maximal since the patients were unable to exercise further; this raises the question whether or not predicted values of maximal HR measured in completely asymptomatic subjects are applicable to patients referred for symptoms of atypical AP.

Many previous reports correlating exercise ECG with coronary arteriography included a significant number of patients with a history of MI as well as a small and variable percentage of women. The sensitivity (86%) and specificity (70%) of exercise ECG observed in all patients in our study are in general agreement with previous studies using similar methods.1-4, 7, 8 Our data, as well as those of others,6-14 clearly indicate, however, that the diagnostic value of exercise ECG varies according to the history and the sex of the patients.

Patients With a Previous MI

In our group of men, a history of MI was always associated with significant coronary lesions.22 Our data in women do not allow any valid conclusion because this subgroup was too small. The existence of myocardial infarction with normal coronary arteries has been documented in women.23

ST-segment changes with exercise in post-MI patients were more frequent in patients with three vessel disease than in those with single vessel disease (89% vs 64%; P < 0.05) and they were more frequently recorded in patients with residual AP (90% vs 71%). These data may help explain the poorer prognosis of post-MI patients with an abnormal ECG response to exercise.21

The onset or the aggravation of an ST-segment elevation during exercise was observed in 23 patients with a history of MI; 21 of these patients (92%) had akinetic or dyskinetic left ventricular segments. This association already mentioned by others22-24 is of clinical importance and appears to be more specific than the association between the persistence of an ST-segment elevation on the resting ECG and the presence of left ventricular asynergic zones.25-28

Patients Without a Previous MI

In men, the clinical diagnosis correlated very well with the arteriographic data since 94% of those with typical AP had significant CHD while 82% of those with atypical complaints had normal coronary arteries. In women, the clinical diagnosis is much less reliable since only 62% of the women with typical AP had significant CHD. No satisfactory explanation has yet been offered for angina-like symptoms with normal coronary arteries in women although their prognosis appears to be good.26-28 The occurrence of AP during the exercise test itself had no more diagnostic value than the presence of a history of typical AP.

Our data in patients with typical AP are practically identical with those previously reported by others in larger groups of men and women.25, 29, 30 The prevalence of CHD in
our patients with atypical AP appears to be low since other
studies have indicated a prevalence of CHD varying from 26
to 46%; 22, 28, 30 In these studies, the patients with chest pain
but whose clinical diagnosis was "normal or probably nor-
mal" were considered separately from those with atypical
AP, which was not done in the present study due to the
smaller number of patients. When the patients quoted by
Welch et al.29, 30 as normal, probably normal and atypical
AP are pooled together, their prevalence of CHD is 12% in
women and 18% in men, which is similar to our findings.

In patients without previous MI, the sex does not
significantly influence the sensitivity (91% in males; 89% in
females) nor the specificity (74% in males; 63% in females)
of exercise ECG. Sketch et al.11 also reported equal sensi-
tivity and specificity in men and women. The lower sensitivi-
ty (51% in males and 45% in females) observed by these
authors could partly result from their lower maximal heart
rate.

False positive and false negative results are strongly in-
fluenced by the sex. False positive results were frequent in
women (38%) and rarely observed in men (7%) while false
negative results were frequent in men (40%) and much less
frequent in women (19%). Sketch et al.11 made similar obser-
vations but offered no satisfactory explanation for their find-
ings. It should be recalled here that the significance of a
diagnostic test depends not only on its accuracy but also on the
prevalence of the disease in the population under study.

When a disease is frequent many false negative results are
observed; conversely, when a disease is rare, many false
positive results are observed.14, 28 The differences between
sexes have therefore to be examined taking into account the
prevalence of CHD, which in the present population is low in
women and high in men (43% vs 80%; P < 0.001). This
difference is largely responsible for the difference in the
relative frequency of false positive and false negative results.

The influence of the prevalence of the disease is also
clearly apparent when men and women are considered
separately. As previously observed,4 false positive results
were more frequent (67%) in the men with atypical com-
plaints (low prevalence of CHD); they were practically ab-
sent (2%) in the men with typical AP (high prevalence of
CHD). Conversely, false negative responses were frequent
(56%) in men with typical AP (high prevalence of CHD) and
unfrequent (11%) in men with atypical complaints (low
prevalence of CHD). The same trend has also been observed
in women although the number of cases is smaller. It is in-
teresting to note that 80% of false positive responses were
observed in women with atypical complaints (very low
prevalence of CHD).

The aforementioned explanation fits very well with our
data and probably helps to explain the very high incidence of
positive responses observed in so-called "healthy middle-
aged" women.24, 30 Assuming a prevalence of CHD of 10% in
such women, and applying our values of sensitivity (89%) and
specificity (63%) in women without MI, one can calculate that 42.2%
of all women tested would have a positive response to exercise. The calculated result is close to the
published results.24, 30 Among these positive responses, 70%
would be falsely positive.

In both sexes, the false positive responses are associated
with significantly higher maximal HR than the true positive
responses while the false negative responders have lower
maximal HR than the true negative responders. These find-
ings are difficult to interpret correctly due to the small
numbers of both false positive and false negative responses
and to the wide range of maximal HR in all groups (fig. 1).
The latter precludes a consideration of the maximal HR as a
major factor directly responsible for the false positive
responses in men or for the false negative responses in
women. In women, it is tempting to incriminate the high
maximal HR as being responsible for the false positive
responses but the maximal HR was above 175 (highest value
observed in true positive responses) in only three instances.

In men, the negative ECG responses were always falsely
negative when the maximal HR was below 135; this may
help explain only four of the 24 (17%) false negative
responses. It can therefore be concluded that very low or
very high maximal HR possibly play a role in a few cases of
false negative responses in men or false positive responses in
women but that this factor is probably not a major one due
to the many cases where its role cannot be incriminated.

The combination of history and exertional ECG allows a
better diagnostic approach to patients suspected of CHD. In
men, the diagnosis of CHD is highly probable when both
history and exercise ECG are positive (98% of true positive)
while it is unlikely when atypical complaints are associated
with a normal ECG response to exercise (89% of true
diagnostic). When there is a discrepancy between history and
exercise ECG, it is not possible to establish in men a reliable
diagnosis without performing coronary arteriography. In
such cases, the probability of having CHD varies from 33 to
56%, which is in agreement with previously published
series.1, 2, 30

In women, the diagnosis of CHD should be considered
only when typical complaints are associated with an abnor-
mal ECG response to exercise. In such cases, coronary
arteriography should be performed since 25% of these
women have normal coronary arteries. In other conditions,
namely a discrepancy between the history and the exercise
ECG, or when both are negative, the presence of CHD is
very unlikely in women.

Finally, the significance of the degree of ST-segment
depression should be mentioned. The more the ST segment
is depressed, the more likely is the presence of significant
CHD. Very abnormal responses to exercise are indeed
highly specific but they are infrequently observed.1, 5, 30

We conclude from the present study that exercise ECG
has a limited value for the diagnosis of CHD. In men with
typical AP, exercise ECG most often confirms the diagnosis
but a negative ECG response does not rule out the diagnosis
of CHD. In men with atypical complaints, exercise ECG is
difficult to interpret owing to the numerous false positive
responses. In women, the diagnosis of CHD cannot be estab-
lished reliably from the history nor from the ECG
response to exercise; when the complaints are atypical, exer-
cise ECG has no value in women because of the numerous
false positive responses.

Acknowledgment

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