Postexercise Electrocardiogram in Screening for Latent Ischemic Heart Disease*
A Study with Clinical Follow-up Observation

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Double Master’s exercise tests were performed in the course of general or periodic examinations on 1,375 patients without angina pectoris. These patients were either asymptomatic or had nonspecific chest pain, and patients with angina pectoris or previous myocardial infarction were specifically excluded. Initial tests were negative in 1,269 (92 percent) and positive in 106 (8 percent). Follow-up information (average duration 30 months) was obtained from clinical reexamination in 833 patients. Of 763 patients with negative tests, 740 (97 percent) were well at last follow-up, 16 (2 percent) had developed clinical signs of ischemic heart disease and seven (1 percent) were dead. Of 70 patients with positive exercise tests, only 21 (30 percent) were living and well at last follow-up, while 42 (60 percent) had signs of ischemic heart disease and seven (10 percent) were dead. It appeared that the double Master’s exercise test may have been a valuable adjunct in screening essentially asymptomatic patients for ischemic heart disease. A negative exercise test in such patients seemed to be associated with low rate of development of clinical ischemic heart disease in immediate future months, while a positive exercise test frequently seemed to presage clinical disease in this group of patients.

INTRODUCTION

Detection of latent coronary artery disease remains one of the most important and difficult problems of modern medicine. A laboratory method which is suitable to include in the periodic examination of asymptomatic patients must be simple, inexpensive and without significant risk. The exercise and postexercise electrocardiograms fulfill these criteria, and previous studies attest to their diagnostic value.1-7 The recent study of Robb and Marks7 using life insurance statistics showed an excellent prognostic value for the postexercise electrocardiogram in relation to death rate from coronary disease. However, there is little if any data available on the value of the postexercise electrocardiogram in screening essentially asymptomatic patients in clinical practice and on the prognosis of patients found to have positive and negative results in such screening.3 While various types of exercise, maximal and submaximal, have been used to elicit ischemic electrocardiographic changes, the double Master’s two-step test1 seems most practical for most physicians to perform in their offices and is a type of exercise to which most patients are already accustomed.

The present study was undertaken to answer two basic questions: (1) what is the incidence of positive double Master’s tests in patients presenting at the physician’s office without angina pectoris and (2) is a positive response in such patients of sufficient value to warrant a diagnosis of ischemic heart disease and a bad prognosis?

MATERIALS AND METHODS

The subjects consisted of all patients who had double Master’s tests performed in a private practice medical clinic during the years 1955 through 1964. There was a total of 1,375 patients (1,189 men and 206 women). None had angina pectoris or previous myocardial infarction which could be diagnosed from clinical examination. Of the patients, 754 (55 percent) were asymptomatic, 580 (42 percent)
had nonspecific types of chest pain, and a small minority (41 patients or 3 percent) had symptoms suggestive of, but not diagnostic for, angina pectoris. Clinical evaluation prior to testing was done by a cardiologist or competent internist, and no patients with clinical angina pectoris were tested. Patients with any abnormality of resting electrocardiograms similarly were not tested. The average age of patients was 45 years (range 17 to 88). Thus, the postexercise electrocardiogram was used as an aid in screening patients for ischemic heart disease in the course of general and periodic examinations in the internist's office when such a diagnosis could not be made from clinical examination.

Follow-up information was available in 833 of these patients when they again presented for reexamination at the same clinic or sought medical attention for illness, and all follow-up findings are results of actual reexamination. No attempts were made to obtain information by questionnaire or other means from patients who did not return. It was recognized that this might introduce some bias into follow-up results. However, it was felt that limiting follow-up results to patients actually reexamined might produce more accurate reassessment diagnoses and might yield information not available from studies by questionnaire, life insurance statistics, and other indirect means of follow-up.

Double Master's two-step exercise tests were performed by the standard technique4 no sooner than one hour after the preceding meal in comfortable air-conditioned rooms. Postexercise electrocardiograms consisted of leads V4, V5, V6 and II taken immediately, two minutes and six minutes after exercise. Criteria for positivity were straight-line or downwardly-sloping ischemic type S-T segment depression of more than 0.5 mm.4,5,7 In practice, when truly ischemic type S-T segment depression occurred, it was almost always 1 mm or more. Attempts to quantitate degree of changes, as in the studies of Robb and Marks4,7 were not done.

RESULTS

The overall incidence of positive tests in this group of patients was 8 percent. Incidence of positive results was lowest in completely asymptomatic patients (3 percent positive results), higher in those with nonspecific chest pain (11 percent positive results), and highest in those few patients having symptoms suspicious of angina (46 percent positive results). The percentage of positive tests also increased progressively with each decade through age 69 (Table 1).

Table 1—Incidence of Positive Tests by Age Group

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>No. of Patients</th>
<th>Patients with Negative Tests</th>
<th>Patients with Positive Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 20</td>
<td>4</td>
<td>4 (100%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>20-29</td>
<td>54</td>
<td>53 (98%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>30-39</td>
<td>330</td>
<td>348 (99%)</td>
<td>4 (1%)</td>
</tr>
<tr>
<td>40-49</td>
<td>513</td>
<td>481 (94%)</td>
<td>32 (6%)</td>
</tr>
<tr>
<td>50-59</td>
<td>345</td>
<td>300 (87%)</td>
<td>45 (13%)</td>
</tr>
<tr>
<td>60-69</td>
<td>102</td>
<td>79 (77%)</td>
<td>23 (23%)</td>
</tr>
<tr>
<td>70-79</td>
<td>6</td>
<td>5 (83%)</td>
<td>1 (17%)</td>
</tr>
<tr>
<td>80-89</td>
<td>1</td>
<td>1 (100%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Total</td>
<td>1,375</td>
<td>1,269 (92%)</td>
<td>106</td>
</tr>
</tbody>
</table>

Table 2 lists pertinent data on the groups of patients with negative and positive results. Besides the higher incidence of nonspecific chest pain in the positive groups, the mean blood pressures were slightly higher than in the negative group, as was mean serum cholesterol. These differences were of minimal degree and borderline statistical significance (p values of mean differences 0.01 to 0.05). Follow-up information was available in approximately the same percentage of negative and positive groups, and the average duration of follow-up was similar for the two groups.

Subsequent exercise tests were done after the first in 383 patients and the results of these subsequent tests are recorded in Table 3. It will be noted that 7 percent of patients having a negative test on one occasion later had a positive response, a phenomenon not too difficult to explain on a basis of possible subsequent development of significant coronary stenosis. It is somewhat more difficult to explain why nine out of 22 patients with initial positive tests subsequently showed negative responses. These often followed cessation of smoking, weight reduction, control of low grade hypertension and periods of physical training, however.

Of particular interest is the fate of 833 patients who had follow-up examinations subsequent to exercise testing. The average duration of follow-up

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living and free of clinical coronary disease, 42 (60 percent) had developed typical angina or had sustained a myocardial infarction and 7 (10 percent) had died. All of the deaths in the positive group were from myocardial infarction except two. One of these patients died from postoperative pulmonary embolism and had extensive coronary atherosclerosis with major branch stenosis at autopsy. The other died of a brain stem infarct and was found at autopsy to have severe coronary atherosclerosis with extreme narrowing of the anterior descending branch and a previously unrecognized old anterior myocardial infarction.

**DISCUSSION**

The results of submaximal exercise testing in the present series yielded approximately 8 percent positive results in patients presenting without angina pectoris or previous myocardial infarction. It should be remembered that the present study was conducted upon patients presenting at a physician's office for periodic examinations, because of atypical chest pain, or both (ie, frequently symptoms of nonspecific chest pain were elicited in patients appearing for periodic examination). Incidence of positive results in such a group of patients may not reflect expected incidence for other groups or populations. Brody, for example, found truly ischemic type of postexercise ST segment depressions in 23 of 756 men patients, mostly business executives, undergoing periodic examinations. Nonetheless, in the present group of patients positive postexercise electrocardiograms were clearly more frequent in patients with nonspecific chest pain, and were most frequent in those few cases in which the examiner had some suspicion of angina but could not be certain from clinical examination. Positive tests were more frequent after age 40, a distribution pattern which parallels the known frequency of coronary artery disease.

The prognosis as to development of clinical coronary disease and as to life for patients having negative tests was far better than for those having initially positive tests, a finding in agreement with the results of Robb and Marks' obtained by follow-up of male life insurance applicants given a standard double Master's two step test. Follow-up results in the present study were limited to those patients actually reexamined. This probably made for greater diagnostic accuracy over follow-up by indirect methods, particularly as regards incidence of angina pectoris and less severe myocardial infarcts, but may well introduce some bias in analysis of follow-up results. Of Brody's 23 asymptomatic patients with truly positive postexercise electrocardiograms

<table>
<thead>
<tr>
<th>Table 3—Results of Subsequent Exercise Test*</th>
<th>(383 Patients Having Two or More Tests)</th>
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<tbody>
<tr>
<td></td>
<td>Results of subsequent test</td>
</tr>
<tr>
<td></td>
<td>Negative No., %</td>
</tr>
<tr>
<td>Negative results on initial test (361 patients)</td>
<td>336 (93)</td>
</tr>
<tr>
<td>Positive results on initial test (22 patients)</td>
<td>9 (41)</td>
</tr>
</tbody>
</table>

*Average interval between first and last exercise test was 28 months (range 1-113) in both the initially negative and the initially positive groups.

was 30 months (range 1 to 121 months) in this group, and average follow-up duration was the same for both negative and positive groups. In the negative group 21 percent of patients were followed up to 1 year, 29 percent 1 to 2 years, 20 percent 2 to 3 years, 13 percent 3 to 4 years, and 17 percent over 4 years, while comparable figures for the positive group were 25 percent, 27 percent, 18 percent, 10 percent, and 20 percent respectively. The follow-up assessment was by actual physician examination. The condition at last evaluation is given in Table 4.

Of 763 patients with negative tests, 740 (97 percent) were living and free of evidence of overt coronary disease at last follow-up, 16 (2 percent) had clinical evidence of coronary disease (either typical angina or a myocardial infarction) and 7 (1 percent) were dead. One of these deaths was due to proved myocardial infarction. Another patient died suddenly and five died from causes unrelated to coronary disease. Of 70 patients who had positive double Master's exercise tests and a subsequent examination only 21 (30 percent) were
ograms six patients subsequently developed myocardial infarction and ten developed angina, for a clinical coronary disease rate of 70 percent.\(^3\)

The findings in all three series seem to be indirect evidence that significant coronary atherosclerosis is the most common cause of a positive test. Yet, Demany and co-workers\(^4\) found a poor correlation between the postexercise electrocardiogram and the presence or severity of coronary artery disease by coronary cinearteriography, with false negative tests occurring in the presence of arteriographic demonstrable coronary artery disease and false positive results in patients with arteriographic normal coronary arteries. The possibility remains, however, that some of these discrepancies may be explained by the presence of disease in vessels too small for adequate visualization by usual arteriographic techniques. It has been suggested that exercise electrocardiography may supply information on myocardial behavior at the cellular level, while arteriography demonstrates only the pathology present in large coronary arteries.\(^7\)

Numerous types of exercise testing have been tried to refine the discrimination of exercise and postexercise electrocardiography. Bellet and Roman\(^8\) found that a maximal exercise treadmill test yielded a higher percentage of positive tests than did the standard double Master's test. Patients undergoing these tests will have to be followed adequately to determine if results of these exercise tests are more or less valid than the two-step test.

It is of interest that some patients with a clearly positive postexercise electrocardiogram when tested initially, subsequently showed negative tests. In all cases these were patients who undertook some therapeutic measures between the two tests. These included cessation of smoking, weight reduction, control of hypertension, reduction of hyperlipidemias, and programs of physical training. That this reversal is possible would lend support to the hypothesis that ST changes in the postexercise electrocardiogram are a function of myocardial oxygen supply and demand, with supply being determined by multiple factors including presence or absence of major branch stenosis, degree of patency of collateral channels, and physiologic and anatomic status of smaller coronary arteries.

The high incidence of myocardial infarction subsequent to the test in essentially asymptomatic patients with positive postexercise electrocardiograms would seem to indicate that a positive test denotes the presence of significant ischemic heart disease for which preventive therapeutic measures should as a rule be undertaken. Certainly an attempt should be made to correct any known risk factors present.

**References**


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