TODAY'S PRACTICE OF CARDIOPULMONARY MEDICINE

Evaluating the Positive Exercise Stress Test in the Asymptomatic Individual*

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Over the past decade, exercise electrocardiography has become increasingly popular as a noninvasive approach to the detection of coronary artery disease. Initial studies suggested that stress testing offered a means of identifying coronary disease in a high proportion of symptomatic individuals while yielding a low rate of false-positive results. Based upon those results and the current interest in preventive health care, exercise testing has been applied increasingly to large numbers of people in the asymptomatic population. Healthy middle-aged men were exhorted to have a stress test before undertaking an exercise program. Some public agencies, such as police departments, required all officers to have periodic exercise test "screening." Commercial "stress test centers" were organized and encouraged anyone who could read their advertisements to undergo stress testing "for safety's sake." With the growing popularity of exercise testing for the population at large, a new problem rapidly acquired importance: how to manage the further care of an individual with "positive" stress electrocardiographic findings, but with no cardiac symptoms, and perhaps even no coronary risk factors.

Importance of Pre-test Probability of Disease (Bayes' Theorem)

This dilemma forced physicians to assess more critically the theoretical and clinical foundations upon which was based the early optimism regarding the utility of exercise electrocardiography. Two essential concepts evolved. On the one hand, the initial studies supporting the usefulness of stress testing largely involved symptomatic or "at risk" populations¹ and were not necessarily applicable to asymptomatic individuals. On the other hand, application of statistical principles revealed that the expectation of obtaining useful information concerning the probable presence of coronary disease in a subject was determined in part by how likely he was to have the disease before he was tested. In other words, in those persons who are very likely or very unlikely to have coronary disease based upon considerations other than the stress ECG, the interpretation of this test as either "positive" or "negative" does not alter substantially the probability of their truly having disease.

This statistical concept is based on Bayes² theorem which states that the predictive accuracy of a test depends not only on its sensitivity (proportion of those with disease who have a "positive" test) and specificity (proportion of those without disease who have a "negative" test), but also on the prevalence of the disease in the population tested.²-⁵ As can be seen from Figure 1, asymptomatic people of

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**Figure 1.** Relationship between age, sex, and anginal symptoms, and risk of presence of coronary artery disease (CAD). Reproduced with permission from Epstein.*
Table 1—Relationship of Test Results to Prevalence of Disease and Sensitivity and Specificity of Test (Hypothetical Example) *

<table>
<thead>
<tr>
<th>Total No. Subjects (1,000)</th>
<th>Positive Exercise ECG</th>
<th>Negative Exercise ECG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (95%)</td>
<td>950</td>
<td>95 (10% false positive)</td>
</tr>
<tr>
<td>Coronary Disease (5%)</td>
<td>50</td>
<td>30 (60% true positive)</td>
</tr>
</tbody>
</table>

*Consider disease prevalence 5 percent, sensitivity 60 percent, specificity 90 percent.

all ages and both sexes have a low prevalence of coronary disease. Based upon an average coronary disease prevalence of 5 percent and typical sensitivity and specificity rates for stress ECG testing of 60 percent and 90 percent, respectively, Table 1 demonstrates the diagnostic difficulty encountered with stress testing in asymptomatic populations. Even though the false-positive tests are only 10 percent of all the tests, because the overwhelming majority of the people being tested are normal, the absolute number of false-positive results greatly outweighs the absolute number of true-positive. Thus, in this hypothetical example, about three-fourths of asymptomatic individuals with abnormal stress ECGs will, in fact, not have coronary disease.

Given this limitation of the exercise ECG in asymptomatic subjects, it would appear that in many circumstances such testing is not justified. Routine screening of random groups of apparently healthy subjects may cause unnecessary anxiety and result in further testing and expense in an unacceptably large number of people. In certain instances, however, such screening of asymptomatic subjects for coronary disease may be justified. The most obvious example is those, such as airline pilots, whose cardiac health is crucial to the safety of many others. Among such groups, even though many false-positive tests will result, exercise stress testing does identify individuals with a considerably increased risk of coronary disease and the development of its clinical manifestations.

Analysis of a Positive Exercise ECG

For those asymptomatic subjects in whom a stress ECG is deemed appropriate, a positive test should be approached in a systematic, individualized manner. There is a range of options that can be pursued in this regard, including more critical analysis of the “positive” test result itself, further noninvasive testing and coronary angiography; which course is most appropriate depends upon each patient’s circumstances. For example, in the case of an airline pilot, it might be decided that the best hope of preserving the patient’s job, consistent with passenger safety, would be to proceed directly to coronary angiography despite the invasive nature and considerable expense of this study. An occasional asymptomatic patient may experience such anxiety from learning of his “positive” stress test that the definitive answer afforded by coronary angiography is required to settle to his satisfaction the issue of whether or not he has coronary disease. Such instances are the exception, however, and for most asymptomatic people with a “positive” stress ECG, further noninvasive evaluation is indicated.

A reasonable way to begin further evaluation is to examine the nature of the positive test in more detail. As always, of course, one must be certain that the ECG response to stress is not rendered uninterpretable by the presence of such factors as digitalis or other drugs, left bundle branch block, left ventricular hypertrophy or nonspecific ST-segment abnormalities in the control tracing. If ischemic changes develop during the early phase of an exercise test (eg, at heart rates under 130/min) there is significantly more likelihood that they represent real disease than if the same changes develop at a high level of exertion. The depth of ST-segment depression during stress is also an important factor in assessing the probability that the test abnormality truly represents ischemic disease. As Figure 2 demonstrates, in an individual with a 5 percent pretest likelihood of coronary disease, 1 mm ST-segment depression during exercise raises the post-test likelihood of disease only to about 15 percent, whereas 2.5 mm ST-segment depression elevates the post-test likelihood of disease to about 65 percent. In the presence of 1 mm ST-segment depression, both patient and physician may not feel further testing is indicated, whereas the more marked ECG abnormality presents a stronger case for further evaluation. Other factors that increase the predictive accuracy of a positive exercise ECG are the occurrence of ischemic ST-segment changes in multiple leads, the prolonged persistence of the alteration post-exercise (six minutes or more) and associated findings during stress such as arrhythmias and drop in blood pressure. A further consideration is whether the positive test has developed in the setting of a previously negative test. In a large study of asymptomatic subjects, this development was accompanied by an 85 percent incidence of subsequent clinical coronary disease.

Further Evaluation

After evaluating the foregoing considerations and

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other factors such as age, sex and coronary risk factors, additional noninvasive testing is usually indicated if probable presence of coronary disease is high. The logic of this approach is that other diagnostic studies, though also only indicating probability rather than certainty regarding presence of disease, are additive to the initial test in terms of predicting the existence of disease. In the situation of asymptomatic persons with positive stress ECGs, this may be of significant utility, as demonstrated in Figure 3. As noted in the previous example, in an asymptomatic individual with a 5 percent probability of coronary disease, a positive stress ECG can increase the likelihood to 15 percent. This 15 percent likelihood becomes the new pretest probability of disease for the second diagnostic test. When an exercise thallium myocardial perfusion scintigram is used as the second test, a positive result would increase the likelihood of disease to about 60 percent. Thus, a significant likelihood of disease may be demonstrated for those asymptomatic individuals in whom both tests are positive. On the other hand, Figure 3 also demonstrates that a “negative” thallium stress scintigram in the face of a 15 percent post-positive exercise ECG likelihood of disease lowers the probability of disease to near 0 percent. Indeed, several small studies have demonstrated that a negative exercise thallium perfusion scintigram is highly reliable in distinguishing those persons with a positive stress ECG who have disease from those subjects with a positive test without disease.\(^\text{11,12}\)

Exercise thallium perfusion scintigraphy has been presented as a reliable second noninvasive test because of its wide availability. Several other noninvasive approaches for identification of coronary

![Figure 2](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21277/)  
**Figure 2.** Relationship of extent of exercise-induced ST-segment depression and likelihood of coronary artery disease (CAD) (see text). ST = ST-segment depression. Adapted from Epstein.\(^6\)

![Figure 3](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21277/)  
**Figure 3.** Demonstration of the use of two tests to enhance confidence in the results of testing. The post-test likelihood of disease based on the first test is used as the pre-test likelihood of disease for the second test, which yields a likelihood of disease post both tests (see text). CAD = coronary artery disease. ECG Ex = stress ECG test. Ti scan = thallium exercise perfusion scan. SEN = sensitivity. SPEC = specificity. Adapted from Epstein.\(^6\)

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artery disease have also been developed and may be more widely utilized in the future. In a recent report, the presence of coronary artery calcification detected by fluoroscopy has been noted to correlate highly (92 percent predictive accuracy) with angiographically significant coronary artery disease in asymptomatic patients with positive exercise ECGs. Comparative rest and exercise radionuclide ventriculography can reveal areas of abnormal ventricular wall motion during the stress of exercise that are not present at rest and which often signify ischemic disease. Where this study is available, its predictive value for the presence of coronary disease has been as good as or better than thallium perfusion scintigraphy. A new clinical tool, cardiokymography, using changes in an electromagnetic field induced by ventricular wall motion to detect ischemia-induced segmental asynergy, has shown early promise as another noninvasive method of detecting the presence of coronary disease.

**SUMMARY**

Exercise electrocardiography to detect coronary disease yields a probability of its presence or absence rather than an absolute "yes" or "no" answer. Because of the high frequency of false-positive results in asymptomatic individuals, only select persons in this group should be tested. When testing is indicated, the conventional stress ECG is a readily available technique of reasonable cost in time and money and thus is an appropriate initial method. Additionally, stress ECGs can be performed for other indications and the results of all such studies must be interpreted with care. A normal treadmill result in a person with no coronary symptoms is highly reassuring of the absence of high risk coronary artery disease. A positive test must be viewed with caution. If the individual is young and without risk factors, the presence of disease is very unlikely, often obviating further evaluation in favor of long-term observation for other indications of coronary disease. Should the positive stress ECG be associated with multiple risk factors, or should it induce significant anxiety, further noninvasive testing is usually indicated, and is best implemented by exercise thallium perfusion scintigraphy. If this test is also positive, coronary angiography is a reasonable consideration. Only when personal or public safety require certainty regarding the presence or absence of coronary disease should a positive stress test in an asymptomatic individual lead directly to coronary angiography. Through application of the basic concepts concerning interpretation of the results of a stress ECG and utilization of the test in a discriminating manner relative to each patient's circumstances, maximum utility and cost-effectiveness in patient evaluation can be achieved.

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