Resuscitating the exercise stress test

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ABSTRACT

By incorporating additional data, clinicians can transform the exercise stress test from a poor diagnostic test to a good prognostic one. These additional data include indices of how the patient's heart rate and blood pressure respond to exercise. Computerized measures of electrocardiographic ST-segment changes that adjust for heart rate also show promise.

Clinicians are using the exercise stress test to ask the wrong question

OLD DOESN'T NECESSARILY MEAN obsolete when it comes to medical technology. A case in point is the exercise stress test, used for decades as a test for coronary artery disease. These days, many physicians are turning away from the traditional exercise stress test with echocardiography (ECG), citing its lack of sensitivity, and instead are ordering thallium imaging and other costly, high-tech imaging tests.

Nevertheless, I believe we can resuscitate the exercise stress test if we refine the way we interpret the results, supplement them with additional heart rate and hemostatic information—and use them to answer the right question.

EXERCISE TESTING OFTEN MISSES DISEASE

Study after study has shown that exercise testing that relies on visual interpretations of exercise ECG can miss many cases of coronary artery disease. Sensitivity can be as low as 45%, though specificity is somewhat higher, at around 85%.[1–3]

There are four possible reasons the test performs so poorly.

We are asking the wrong question. Instead of trying to use exercise testing for diagnosis, we should use it to determine prognosis. With coronary disease endemic in our society, many, if not most, patients referred for exercise stress testing have some degree of coronary disease. Exercise stress testing should not be used to diagnose coronary disease, but to predict cardiac events and mortality. These findings should then be used to guide treatment and to educate patients about risk factors.

We are looking for the wrong lesions. An exercise ECG is considered abnormal if it shows 1 mm or more of horizontal or downsloping ST-segment depression 60 to 80 msec after the J point. However, ST-segment abnormalities appear only when the patient has hemodynamically obstructive lesions; stenoses of 50% may not cause stress-induced ischemia.

We are ignoring other important information. Non-electrocardiographic variables such as exercise capacity and heart-rate and blood-pressure changes during exercise can contribute valuable information. These variables are particularly useful when combined into a measure called the chronotropic index.

We are using the wrong methods. We are beginning to show that computerized analyses of ECGs, adjusted for heart rate, may be more accurate and valuable than visual inspections.

IMPROVING EXERCISE TESTING

Measuring exercise capacity

To improve our interpretation of exercise tests, one of the factors we should measure is exercise capacity (essentially, physical fitness). Exercise capacity and improvement in exercise capacity are powerful and independent predictors of survival and survival free of cardiac mortality and morbidity.[4–6]

TABLE 1

Levels of exercise and metabolic equivalents consumed

LEVEL	ESTIMATED METS*	ACTIVITY
Mild	2–3	Baking, slow dancing, writing, playing golf with a cart
Moderate	3–5	Gardening, playing the drums, swimming slowly
Vigorous	6	Dancing
	8	Playing field hockey
	10	Jogging at 10 minutes/mile
	12	Playing squash

*1 metabolic equivalent (MET) is the amount of oxygen consumed during awake rest, about 3.5 mL/kg/min

FROM FLETCHER GF, BALADY G, FROELICHER VF, ET AL. EXERCISE STANDARDS. A STATEMENT FOR HEALTH-CARE PROFESSIONALS FROM THE AMERICAN HEART ASSOCIATION WRITING GROUP. CIRCULATION 1995; 91:580–615.

Exercise capacity is measured in METs, or metabolic equivalents, the amount of oxygen consumed at rest by an awake patient (TABLE 1). Younger people have a markedly higher functional capacity than older people, and men a slightly higher capacity than women.

In a study that followed 3,400 patients for 2 years, we found that low exercise capacity and impaired cardiac perfusion as shown on thallium scans were both strongly predictive of mortality.[7]

Exercise capacity is only one of the factors that should go into an assessment of cardiac health. It does not fill in the whole picture, and in addition, it may be inaccurate for individual patients because it is generally estimated from published tables rather than measured directly by gas-exchange analyses.[8]

Recognizing chronotropic incompetence

A second factor that should be measured is the patient's heart-rate response to exercise. This was suggested more than 20 years ago, after a healthy 51-year-old man suffered sudden cardiac death shortly after passing his exercise stress test with flying colors. The only abnormality had been that his heart rate had not risen above 110 beats per minute during exercise. An autopsy showed severe two-vessel coronary disease with 80% stenosis of the left anterior descending and circumflex arteries.[9]

This event prompted cardiologist Myrvin H. Ellestad and several colleagues to review the records of 2,700 patients. They found that patients with attenuated heart-rate responses to exercise were more likely to suffer acute coronary events than patients with ST-segment depression and normal heart-rate responses.[10]

Ellestad named the phenomenon chronotropic incompetence. The association between chronotropic incompetence and heart disease has been repeatedly confirmed in other studies,[11] and chronotropic incompetence has been shown to be associated with myocardial scarring.[12]

When a patient taking an exercise test fails to reach 85% of his or her age-predicted maximum heart rate, the test is often classified as "nondiagnostic." However, we believe the finding should be considered much more ominous and in most cases, chronotropic incompetence should be considered "evidence of an adverse prognosis."

Exercise capacity is only one of the factors in cardiac health

Unfortunately, simple use of the percent of target heart rate achieved is problematic. Estimated peak heart rates are highly variable in each age group, making it difficult to apply them to individuals. Resting heart rate and physical fitness also strongly affect the patient's ability to reach a predicted peak heart rate.

Calculating the chronotropic index

To solve this problem, Wilkoff has created a simple measure now called the chronotropic index that predicts mortality independent of age, resting heart rate, and metabolic work.[13]

Before exercise, a person has a certain metabolic reserve, which is the difference

Calculating the chronotropic index

IN HEALTHY PERSONS, heart rate increases with exercise in a predictable fashion. Persons whose heart rate fails to increase to the expected level have a higher risk of cardiac morbidity and mortality. The *chronotropic index* can show whether a patient's heart-rate response to exercise is healthy or unhealthy.

The first step is to calculate the patient's *metabolic reserve*. One *metabolic equivalent* (1 MET) is the amount of oxygen a person consumes at rest, typically about 3.5 mL/kg/min. The difference between the peak and resting MET levels is called the *metabolic reserve*.

The estimated MET level at any stage of exercise ($METs_{stage}$) is displayed automatically by computerized treadmills. Using this figure, the clinician can calculate how much of the metabolic reserve the patient has used.

$$\text{Percent metabolic reserve used} = \frac{(METs_{stage} - METs_{rest})}{(METs_{peak} - METs_{rest})} \times 100$$

The second step is to calculate the *heart rate reserve*, the difference between the patient's estimated peak heart rate (220 minus the patient's age) and resting heart rate. The percent heart rate reserve used at a particular stage of exercise is:

$$\text{Percent heart rate reserve used} = \frac{(HR_{stage} - HR_{rest})}{(HR_{peak} - HR_{rest})} \times 100$$

To calculate the *chronotropic index*, divide the percent heart rate reserve used by the percent metabolic reserve used. If the ratio is less than 0.8, the patient's heart rate is lower than expected during exercise, and the patient has a high risk of cardiac morbidity and mortality.

A low chronotropic index predicts mortality independent of age, resting heart rate, and metabolic work

between the level of oxygen consumption at the peak of strenuous exercise (exercise capacity) and resting oxygen consumption. During exercise, this reserve is used up. Analogously, the heart rate reserve can be defined as the difference between the estimated peak heart rate and the resting heart rate. This reserve is also used up as exercise progresses.

At each stage of exercise, we can calculate both the percent of the metabolic reserve used and the percent of the heart rate reserve used, and we can plot these values on a line graph. The slope of this line is called the chronotropic index. (See accompanying article "Calculating the chronotropic index," on this page.)

In healthy adults, the slope is close to 1.0. A ratio below 0.8 is associated with a higher risk of mortality and of severe coronary disease as identified by angiography.[14] Smoking is strongly associated with a low chronotropic index.[15]

Is there more to chronotropic incompetence than ischemia? In early research into the chronotropic index, we could not immediately rule out the possibility that a low chronotropic index was solely a manifestation of myocardial ischemia, and that the ischemia was the true cause of the mortality. In a prospective study of 231 consecutive patients, we adjusted the chronotropic index for myocardial ischemia detected by ECG and for other possible confounding factors. We found that a low chronotropic index and failure to reach 85% of the target heart rate both remained predictive of mortality, independent of ischemia.[16]

Confirming this finding is our recent article in the *Journal of the American Medical Association*,[17] in which we show that a low chronotropic index and failure to reach 85% of the age-predicted maximum heart rate, even when adjusted for evidence of ischemia found on thallium scan, were both associated with a high risk of mortality. A low chronotropic index was as ominous as thallium perfusion defects; the combination was associated with a particularly poor prognosis (**FIGURE 1**).[17]

We do not understand why chronotropic incompetence indicates a poor outcome. It is clearly associated with myocardial ischemia, although we think it is more than just a compensatory mechanism for hearts with heavy ischemic burdens. Subtle alterations in autonomic tone may also contribute.

Measuring blood pressure changes

An exaggerated blood pressure response to exercise (exercise hypertension) is apparently benign. Patients with resting hypertension have a higher likelihood of severe coronary artery disease, but those with exercise hypertension (peak systolic blood pressure during exercise of at least 210 mm Hg in men or 190 mm Hg in women) have a lower likelihood of CAD and thallium perfusion defects.[7] However, a delayed decline in systolic blood pressure after exercise seems to be associated with coronary artery disease.[18]

Computerizing ECG analysis

Standard ST-segment analysis is imprecise because it is performed visually. In addition, measuring the ST segment alone fails to take differences in heart rate into account. Computerized ST-segment measurements adjusted for heart rate may improve the prognostic capabilities of exercise ECGs.

One adjusted ST-segment measure is the ST/heart rate index, the change in ST depression during exercise divided by the difference between peak and resting heart rates. Another is the ST/heart rate slope, which is the slope of the line produced by plotting the change in ST depression against the change in heart rate during exercise.

Some major studies have shown that standard visual ST-segment analyses failed to predict cardiac events, whereas computerized measures adjusted for heart rate did.[19–21] However, other studies have been unable to confirm this.[22–24]

Survival as a function of the chronotropic index and thallium perfusion defects

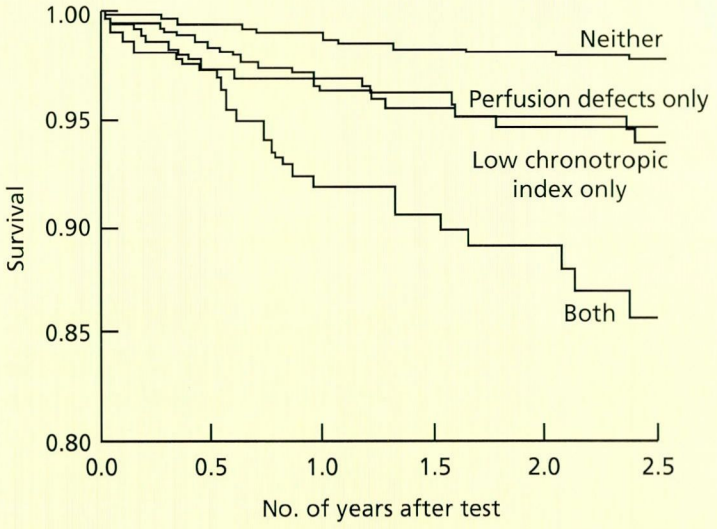

FIGURE 1. A prospective cohort study has found that people with either a low chronotropic index or perfusion defects found with thallium scintigraphy have a higher risk of mortality than people with neither finding. People with both findings have a much lower survival rate.

SOURCE: LAUER MS, FRANCIS GS, OKIN PM, ET AL. IMPAIRED CHRONOTROPIC RESPONSE TO EXERCISE STRESS TESTING AS A PREDICTOR OF MORTALITY. JAMA 1999; 281:524–529.

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