Stress Echocardiography in Known or Suspected Coronary Artery Disease
An Exercise in Good Clinical Practice*

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Exercise testing by treadmill or ergometer is an established, class I-recommended diagnostic procedure for patients with an intermediate probability of coronary artery disease (CAD) (1,2). Exercise testing provides several types of information, including exercise-induced symptoms, exercise-induced heart rate and blood pressure changes, an estimate of exercise capacity, and electrocardiogram (ECG) changes indicative of ischemia, in particular "significant" ST-segment depression, or arrhythmias.

Although all of these data are undoubtedly valuable, the identification of exercise–induced ECG signs of ischemia or the provocation of angina usually is perceived as the most critical information provided by stress testing. Frequently, the presence or absence of these signs of ischemia determines whether coronary angiography is subsequently performed and whether the finding of a coronary stenosis on angiography leads to revascularization. Because exercise tests that use symptoms and changes in ECG as their outcome measures are inexpensive and universally available, they are the initial standard procedure in suspected CAD, unless there are specific patient contraindications, such as an inability to exercise, left bundle branch block, or other conditions precluding performance or meaningful interpretation of the test.

Despite their widespread use, however, nonimaging stress tests have quite limited diagnostic accuracy. This limitation comes strikingly into focus in the important study of Bouzas-Mosquera et al. (3) in this issue of the Journal. In this large study, they analyze the incremental value of exercise stress echocardiography performed in parallel to classic treadmill testing, mostly following the classic Bruce protocol. Patients who had a pathologic treadmill test, either because they developed angina or ST-segment depression (30% of the initial cohort of 5,740 patients), were excluded from further analysis. The remaining 4,004 patients with a negative treadmill test formed the basis for the study. Patients were on average 60 years of age, 16% were diabetics, and 29% had a documented history of CAD; only 9% had sustained a myocardial infarction within 30 days, and 18% had resting wall motion abnormalities. Most patients had a history of chest pain (69%).

With exercise, heart rate increased to an average of 150 beats/min in the nonischemic and 145 beats/min in the ischemic group, with approximately one-fifth of all patients reaching only "submaximal" exercise levels (<85% of age-predicted heart rate). A total of 1 in 6 (16.9%) of these patients with an entirely normal classic treadmill test had an ischemic echocardiographic response (defined as new or worsening wall motion abnormality), a finding that has a major impact on the decision how to further work up and treat such a patient. Ischemia on stress echocardiography more than doubled the rate of cardiac death or myocardial infarction during the next 5 years, although test results did influence further patient management. Thus, one can surmise that the event rate would have been even greater if these patients had not undergone stress echocardiography and had been managed only based on the results of the classic exercise test. On the other hand, a normal stress echocardiogram predicted a low yearly rate of cardiac death or myocardial infarction of 0.84%, and of 0.64% in those who also had a normal resting echocardiogram.

Several technical points deserve comment. Treadmill exercise echocardiography was performed at peak and immediately after stress. Peak stress images were acquired with the patient upright and quickly walking, a technique often considered “not feasible” because of the body motion of the patient (4). However, this and earlier work from these authors (5,6) indicate that, although doubtlessly demanding, it is indeed feasible. For bicycle ergometry, special devices are available that allow tilting the patient to the left side during exercise, thus facilitating peak exercise echocardiography. Obviously, if diagnostic images are achieved, there are important advantages to peak exercise imaging. In classic treadmill exercise echocardiography, the patient terminates exercise and is transferred into a supine position for imaging, which entails a short loss of time in which wall motion abnormalities may fade or disappear. The present work’s authors reported in an earlier study that peak treadmill stress images were more sensitive, especially for multivessel (and thus extensive) ischemia than post-stress images (6,7), which corresponds to data from peak bicycle exercise echocardiography (8).

Remarkably, no patient was excluded from the present analysis because of poor image quality. In only 7 patients, left heart contrast was used (0.2%). In only 5% of patients,
1 or more segments of the left ventricle could not be assessed. Further, although an effort was made to discontinue beta-blocker medication before the test, 5.9% of patients continued on beta-blockers; in fact, ironically, the rate of beta-blocker intake trended greater in the group developing ischemia than in the nonischemic group.

Finally, no severe complication of exercise testing occurred. This finding is in contrast to dobutamine stress echocardiography, where severe adverse event rates of 2 to 3 per 1,000 examinations have been reported (9,10), although certainly at least in part this is attributable to patient selection, with sicker patients undergoing pharmacologic stress rather than physical exercise. Other disadvantages of pharmacologic stress testing are longer duration and the need for intravenous access.

The study’s most important message is the impressive prognostic value of stress echocardiography in these patients tested negative for ischemia by classic treadmill exercise. The overwhelming majority of patients (87%) had a low Duke treadmill score (>5), which is not surprising, given that by definition they had a normal exercise ECG and no symptoms. Such a score has been reported to predict a yearly mortality well below 1% (11). Strikingly, in these patients the combined rate of cardiac death and myocardial infarction increased almost 5-fold (from 2.7% to 12.7%) during the next 5 years if they had ischemia on echocardiography, although they were treated according to the test results. Even the mere presence of resting wall motion abnormalities—before any exercise—already added significantly to clinical and ECG variables.

Similar findings have been reported by Marwick et al. (12), who showed significant incremental risk-stratification value for exercise echocardiography over the Duke treadmill score, especially in the intermediate-risk range. In a recent meta-analysis, the annual rate of hard events (myocardial infarction or cardiac death) after a negative exercise stress echocardiogram, the annual rate of hard events (myocardial infarction or cardiac death) after a negative exercise stress echocardiogram, where severe adverse event rates of 2 to 3 per 1,000 examinations have been reported (9,10), although certainly at least in part this is attributable to patient selection, with sicker patients undergoing pharmacologic stress rather than physical exercise. Other disadvantages of pharmacologic stress testing are longer duration and the need for intravenous access.

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Similar findings have been reported by Marwick et al. (12), who showed significant incremental risk-stratification value for exercise echocardiography over the Duke treadmill score, especially in the intermediate-risk range. In a recent meta-analysis, the annual rate of hard events (myocardial infarction or cardiac death) after a negative exercise stress echocardiogram (no resting or stress-induced wall motion abnormalities) in >3,000 patients was 0.54% (13), similar to the present study with its 0.64% risk. These excellent prognostic data, generated by a safe, rapid, cheap, and radiation-free test, deserve particular emphasis at a time of explosive growth of other tests of yet largely unclear clinical utility, such as noninvasive coronary angiography by multiphase computed tomography, and they reinforce the concept that identification of ischemia is the keystone in the management of CAD.

The study’s findings of course raise the question of whether exercise ECG should be really the stress test of choice in patients as in the present study, relegating the imaging stress tests to second rank, to be used by current recommendations only where the ECG is uninterpretable or inconclusive or the patient is unable to exercise (1,2). True, exercise stress echocardiography has substantial limitations. Many patients cannot exercise well. Moreover, stress and certainly exercise stress examinations are among the most challenging tasks in echocardiography, and diagnostic accuracy is heavily dependent on expert performance and interpretation. However, the latter is true for many, if not all, procedures in cardiology. The present study compellingly supports a larger role for imaging stress tests, in particular exercise stress echocardiography, in coronary risk stratification of patients with intermediate pre-test likelihood of CAD.

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