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Yield of Downstream Tests After Exercise Treadmill Testing

A Prospective Cohort Study

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Objectives The purpose of this study was to estimate the frequency and results of downstream testing after exercise treadmill tests (ETTs).

Background The utility of additional diagnostic testing after ETT is not well characterized.

Methods We followed consecutive individuals without known coronary artery disease referred for clinical ETT at a large medical center. We measured the frequency and results of downstream imaging tests and invasive angiography within 6 months of ETT and the combined endpoint of survival free from cardiovascular death, myocardial infarction, and coronary revascularization.

Results Among 3,656 consecutive subjects who were followed for a mean of 2.5 ± 1.1 years, 332 (9.0%) underwent noninvasive imaging and 84 (2.3%) were referred directly to invasive angiography after ETT. The combined endpoint occurred in 76 (2.2%) patients. The annual incidence of the combined endpoint after negative, inconclusive, and positive ETT was 0.2%, 1.3%, and 12.4%, respectively ($p < 0.001$). Rapid recovery of electrocardiography (ECG) changes during ETT was associated with negative downstream test results and excellent prognosis, whereas typical angina despite negative ECG was associated with positive downstream tests and adverse prognosis ($p < 0.001$). Younger age, female sex, higher metabolic equivalents of task achieved, and rapid recovery of ECG changes were predictors of negative downstream tests.

Conclusions Among patients referred for additional testing after ETT, the lowest yield was observed among individuals with rapid recovery of ECG changes or negative ETT, whereas the highest yield was observed among those with typical angina despite negative ECG or a positive ETT. These findings may be used to identify patients who are most and least likely to benefit from additional testing. (J Am Coll Cardiol 2014;63:1264–74) © 2014 by the American College of Cardiology Foundation

Coronary artery disease (CAD) remains the leading cause of death in men and women. Although advances in cardiovascular imaging have greatly improved our ability to diagnose and treat CAD, the rising costs of noninvasive testing have generated concern regarding its potential overuse (1).

The current American Heart Association and American College of Cardiology guidelines recommend exercise treadmill tests (ETTs) in the initial evaluation for ischemic heart disease in patients who are able to exercise and have a normal electrocardiogram (ECG) at baseline (2,3). In addition to testing for ischemic ECG changes, this test provides other data that have important prognostic implications, such as functional capacity, arrhythmias, and exercise-induced symptoms (4).

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Thus, a common and economically-appealing strategy is to perform ETT as an initial test and then, among patients with positive or inconclusive results, to selectively use noninvasive imaging or invasive angiography to guide further care (5). Although recent studies assessed patterns of downstream

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testing after percutaneous coronary intervention (PCI) (6,7) and use of invasive angiography after stress testing (8), to our knowledge, no data exist on the incidence and results of downstream noninvasive testing after ETT in patients without known CAD.

Therefore, the aim of our study was to identify the frequency and results of downstream testing after ETT and to identify predictors of patients who are most and least likely to benefit from additional testing.

Methods

Population. The study population consisted of all consecutive patients who underwent clinically-indicated ETT at Brigham and Women's Hospital between January 1, 2009, and December 31, 2010. We excluded patients with known CAD; prior coronary artery bypass grafting, PCI, or myocardial infarction (MI); and nonclinical indications for testing such as participation in a research protocol or post–heart transplant evaluation. The Partners Institutional Review Board approved this study.

Clinical information. Demographics, clinical history, medications, and indications for testing were collected prospectively through the use of a standardized patient interview. The electronic medical record, which includes all physicians' notes, was used to identify the presence or absence of the following risk factors: hypertension, diabetes, hyperlipidemia, and family history of CAD. We estimated pre-test probability of CAD by use of the Morise score (9).

Exercise treadmill testing. ETTs were performed with the use of a symptom-limiting Bruce protocol according to established guidelines (2) as part of routine clinical care. The target heart rate was determined as 85% of the maximum predicted heart rate (MPHR) (MPHR = 220 − age). All ST-segment measurements were performed 80 ms after the J point. The Duke Treadmill Score (DTS) was calculated for each patient who completed the Bruce protocol as: exercise time (min) − (5 × maximal ST-segment depression [mm]) − (4 × angina index [0, no angina; 1, angina; 2, angina as reason for stopping test]) (10).

We categorized each test result as positive, negative, or inconclusive through the use of conventional criteria (2). Positive tests were defined as upsloping ST-segment depressions ≥1.5 mm or downsloping or horizontal depressions ≥1.0 mm in at least 2 leads. Inconclusive tests were defined to include any result that may be interpreted as indeterminate and comprised the following categories: 1) negative ECG with reduced sensitivity as the result of submaximal exercise (<85% MPHR and rate-pressure product <25,000); 2) positive ECG with reduced specificity as the result of baseline ECG abnormalities; 3) positive ECG with reduced specificity as the result of rapid recovery of ECG changes, defined as changes that resolve within 60 s; 4) typical angina; 5) inappropriate dyspnea despite negative ECG findings, and 6) clinically significant rhythm disturbances (any sustained arrhythmia or >3 beats of ventricular tachycardia). Typical angina was defined as exertional chest discomfort that was substernal and was relieved with rest or nitroglycerin.

Downstream testing. For each patient, we identified the use of all noninvasive imaging and invasive angiography tests performed within 6 months after ETT through review of the electronic medical record. The decision to undergo further testing was at the discretion of the referring physician. We chose the 6-month cutoff to capture any downstream testing that was probably triggered by the ETT results.

Noninvasive imaging. We included all possible subsequent noninvasive imaging tests available at our institution: nuclear stress tests, stress echocardiograms, coronary computed tomography angiography (CCTA), and stress magnetic resonance imaging (MRI). All tests were performed and reported according to institutional protocols.

We categorized all nuclear stress tests (positron emission tomography and single-photon emission computed tomography [SPECT]) results as follows: negative (summed stress score ≤2); inconclusive (equivocal scan results or negative perfusion imaging with submaximal heart rate response [<85% of MPHR]); and positive for "abnormal" or "probably abnormal" results (11).

We categorized CCTA results as negative for reports of no plaque or stenosis ≤50% and positive for stenosis >70% (or >50% in the left main coronary). We defined as inconclusive for the evaluation of ischemia any studies that were uninterpretable or had moderate (51% to 70%) stenosis, given that such lesions may not be associated with ischemia and have uncertain hemodynamic significance (12).

We categorized cardiac MRI results as negative if no ischemia was detected, inconclusive if image quality precluded interpretation, and positive if ischemia was identified.

We categorized results of echocardiograms as positive, negative, or inconclusive on the basis of the presence or absence of stress-induced wall motion abnormalities. Tests were defined as inconclusive when reduced image quality limited the evaluation or if patients failed to achieve 85% of the MPHR.

Invasive coronary angiography. We defined obstructive CAD as a stenosis ≥50% in the left main coronary artery or ≥70% in any other coronary vessel (13).

Patient follow-up for nonfatal MI and revascularization. We reviewed all patient charts to identify incident nonfatal MI and coronary revascularization, which comprised all PCI and coronary artery bypass grafting procedures. MI was defined by means of universal criteria (14).

Abbreviations and Acronyms

CAD = coronary artery disease
CCTA = coronary computed tomography angiography
DTS = Duke Treadmill Score
ECG = electrocardiogram
ETT = exercise treadmill test
METs = metabolic equivalents of task
MI = myocardial infarction
MPHR = maximum predicted heart rate
MRI = magnetic resonance imaging
PCI = percutaneous coronary intervention
SPECT = single-photon emission computed tomography