What is the best management for patients with evidence of asymptomatic ischemia on exercise stress testing?

LAWRENCE W. RAYMOND, MD, ScM; LEE KAUFMAN, MLS
Carolinas Medical Center, Charlotte, NC

EVIDENCE-BASED ANSWER

Patients with intermediate- or high-risk Duke Treadmill score (DTS) on exercise stress testing (EST) should undergo myocardial perfusion imaging or exercise echocardiography, especially if they have abnormal values of Chronotropic Index or post-EST Heart Rate Recovery.

For patients who have a low-risk DTS, the 4-year mortality is less than 1% to 2%; therefore, risk-factor reduction without further investigation is appropriate (strength of recommendation: **B**, based on cohort studies and consensus guideline). ❑

EVIDENCE SUMMARY

No randomized controlled trials have identified the optimal management of patients with asymptomatic ischemia on EST. EST is not generally recommended for asymptomatic persons because of its limited predictive value. EST may sometimes be useful for predicting mortality risk among patients who plan to begin exercise programs, or whose jobs affect public safety, or who have conditions such as diabetes or chronic renal insufficiency. (1)

For example, a prospective cohort study of 613 patients with suspected coronary artery disease investigated EST duration, presence of angina, and ST-segment depression as predictors of mortality. (2) Patients with asymptomatic ischemia (2 mm of ischemic depression) whose EST lasted 15 minutes (DTS = +5, low risk) had a 5-year cardiac mortality of less than 1%, compared with 2% for those whose EST was tolerated for only 7 minutes (DTS = –3, intermediate risk). (2) (See TABLE for DTS formula.)

FAST TRACK

Patients with a low-risk Duke treadmill score should have a review of their cardiovascular risk factors

CLINICAL COMMENTARY

When a stress test is not normal, discuss with the patient and examine risk factors

Ronald L. Healy, MD
United Medical Center, Cheyenne, Wyoming

Exercise stress testing is performed to assess the risk of heart disease for asymptomatic patients. EST is relatively inexpensive, convenient, and, with the appropriate equipment, easily performed in a physician's office. Although the test is limited in its predictive value, it can be reasonably sensitive when performed on the appropriate population groups.

When the EST result is normal, I review cardiovascular risk factors with the patient and use the opportunity to reinforce the importance of healthy lifestyle modifications. Difficulties arise, however, when an EST result is not normal. Since the patient is at increased risk of cardiovascular morbidity and mortality, I usually recommend further testing. Many options are available, including exercise stress echocardiography, thallium scan, and coronary catheterization. Newer technologies such as MRI and CT scan may be appropriate in some circumstances. I usually base my decision after discussion with the patient, examination of the patient's risk factors, and the preferences and expertise of my local cardiology group. ❑

Later prospective cohort studies (3,4) confirmed that a low-risk DTS was associated with high 5-year survival—eg, 97% among 2758 patients (median age 49, 70% male, 30% prior myocardial infarction, 49% with angina). (3) Those with an intermediate- or high-risk DTS had corresponding survival rates of 90% and 65%, respectively. The DTS was further analyzed in a 5-year follow-up of 9454 patients, 88% of whom were low-risk (75% undergoing screening EST). (4) Most patients (1406 of 1477) with ST-segment depression ≥1 mm had asymptomatic ischemia, only 71 having EST-induced angina. A low-risk DTS was associated with 98% survival, compared with 92% for patients with an intermediate- or high-risk DTS. (4)

Patients with an intermediate-risk DTS, and normal or near-normal perfusion imaging without cardiomegaly, also comprised a low-risk group with 5-year cardiac survival of 99.5%. (5) Post-EST heart rate recovery and the Chronotropic Index are enhancements to the DTS. (6) Used singly or in combination, these tools provided more accurate estimates of 5-year all-cause mortality among 9454 patients referred for EST (TABLE).

Two other prospective cohort studies of middle-aged men with EST showing asymptomatic ischemia did not employ the above enhancements but reported major impact of cardiac risk factors on mortality. Among 25,927 healthy men followed for an average of 8.4 years, the age-adjusted risk of death from all causes of those with asymptomatic ischemia increased from 2-fold (95% confidence interval [CI], 1.1–3.8, $P=.03$) with no risk factors to 4 (95% CI, 2.7–5.4) with 1 risk factor, 5 (95% CI, 3.3–6.9) with 2 risk factors, and 8 (95% CI, 5.4–12.8) with 3 or more risk factors ($P<.0001$).[7] Other investigators found increased mortality from coronary artery disease to be associated with smoking (relative risk [RR]=5.0 [95% CI, 2.1–11.9]), hypercholesterolemia (RR=7.6 [95% CI, 3.0–19.5]) and hypertension (RR=6.7 [95% CI, 2.9–16.0]). (8)

While risk factor reduction seems logical for all patients who have asymptomatic ischemia, actual evidence of benefit is limited. In the MRFIT study, (9) high-risk men with asymptomatic ischemia were randomized to either usual care or a special intervention to reduce smoking, blood cholesterol, and diastolic blood pressure. The intervention group had lower cardiac mortality than men who received usual care (22 vs 53 per 1000, $P<.002$). (9) As observed in 2 large prospective cohort studies, one of which documented abnormal EST in 17%, males who improved their fitness had 23% (95% CI, 4–42) and 44% (95% CI, 5–59) lower mortality over 18 years of mean follow-up, respectively. (10,11) Smoking cessation is also important, associated with 41% lower mortality (95% CI, 20–57). (11)

Most of the evidence underlying the above recommendations derives from studies of men and hence may not apply directly to women. The American Heart Association's guidelines (12) for cardiovascular disease prevention in women do not consider EST results in risk assessment. They rely instead on the Framingham Risk Score to stratify women's 10-year risk of coronary events as low (<10%), intermediate (10%–20%), and high (>20%), and prioritize recommendations for risk factor reduction according to these levels. ❑

Table. Duke Treadmill Scores: 5-year all-cause mortality

ABNORMALITIES OBSERVED ON TREADMILL TESTING	
NONE	0.9%
DTS only	3.2%
HRR only	4.0%
CI only	4.0%
HRR & CI	8.2%
DTS & CI	9.2%
HRR & DTS	9.2%
CI, HRR, & DTS	18.0%

Example: Patients having abnormal Duke Treadmill score and Chronotropic Index but normal Heart rate recovery sustained 5-year, all-cause mortality of 9.2%. Those with abnormal DTS and HRR but normal CI coincidentally had the same 9.2% mortality. (6)
Duke Treadmill Test (DTS): Minutes in standard Bruce protocol –5 × (maximal ST deviation in mm) –4 × (0=no chest pain, 1=angina during EST, 2=EST stopped due to angina).
Heart Rate Recovery (HRR): abnormal if heart rate drops less than 12 bpm measured at least 2 minutes after stopping EST.
Chronotropic Index (CI): represents the ratio of heart rate reserve compared to metabolic reserve.
Normal is near 1.

FAST TRACK

Patients with intermediate- or high-risk scores need further testing, such as a stress echocardiograph or myocardial perfusion imaging

RECOMMENDATIONS FROM OTHERS

American College of Cardiology/American Heart Association (ACC/AHA) guidelines (1) favor medical treatment for low-risk patients with asymptomatic ischemia (annual cardiac mortality =1%—ie, DTS =5, or normal HRR or normal CI). The ACC/AHA recommend perfusion imaging

(or exercise echocardiography) for patients with asymptomatic ischemia who have intermediate or high-risk DTS. (1) Such imaging can refine prognosis, guide therapy with aspirin, beta blockers, lipid-lowering agents, and angiotensin-converting enzyme inhibitors, and possibly identify patients who might benefit from coronary angiography and revascularization (AHA/ACC Recommendation Class IIa–IIb, Level of Evidence B–C). ❑

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