

## Stress tests: How to make a calculated choice

*Spare your patients unnecessary stress testing by determining their pretest probability for CAD*

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### IN THIS ARTICLE

- How to determine pretest probability of CAD
- Calculating a Duke Treadmill Score. □

### PRACTICE RECOMMENDATION

- Estimate pretest probability of CAD in patients with chest pain on the basis of age, sex, pain characteristics, and cardiovascular risk factors (**B**).
- Low pretest probability patients should undergo an exercise treadmill test alone (**C**).
- Intermediate pretest probability patients, including those with complete right bundle branch block or less than 1 mm ST depression at rest should have an exercise treadmill test without imaging (**B**). Patients with an electronically paced ventricular rhythm (**C**) or left bundle-branch block (**B**) require myocardial perfusion imaging.
- In high pretest probability patients, coronary angiography is an appropriate initial strategy for CAD diagnosis (**C**).
- In women, the data are insufficient to justify routine stress imaging tests as the initial test for CAD (**C**). □

### STRENGTH OF RECOMMENDATION (SOR)

- A. Good quality patient-oriented evidence
- B. Inconsistent or limited-quality patient-oriented evidence

C. Consensus, usual practice, opinion, disease-oriented evidence, case series

Are you a wise “consumer” of stress tests? That is: Do you consider your patient’s CAD probability score before ordering an exercise treadmill test or pharmacologic stress myocardial imaging (PSMI)? Are you as well-versed as you’d like to be on the predictive value of things like the Duke Treadmill Score?

If your answer is No to either question, this review may help guide your use of stress tests, based on evidence. □

### WHAT IS THE PRETEST PROBABILITY OF CAD?

The decision to order an exercise stress test or a PSMI should be based on history, physical examination, and pretest probability for CAD. You can estimate the pretest probability for CAD in a chest pain patient based on the patient’s age, sex, and pain characteristics.<sup>1</sup>

Determine whether symptoms are typical, atypical, or nonanginal, based on whether the chest pain is substernal, brought on by exertion, or relieved by rest or nitroglycerin. (2)

To recap:

- Typical angina requires all 3 pain characteristics
- Atypical angina, only 2
- Nonanginal chest pain, 1. (2)

Use this information (along with the patient’s age) to determine whether he has a high,

intermediate, low, or very low likelihood of CAD (TABLE 1). From the low, to the intermediate, to the high pretest probability levels, the positive predictive value increases progressively (21%, 62%, and 92%) and the negative predictive value decreases progressively (94%, 72%, and 28%). (3) (These values are based on a review of symptomatic patients who had angiography following stress testing.)

Your patients' score dictates whether testing is required, and if so what kind.

**Very low pretest probability** patients should not have an exercise test, since they have a high risk of false-positive results. Evaluate and treat them for noncardiac causes of chest pain and begin primary prevention of CAD.

**Low pretest probability** patients should undergo exercise treadmill testing alone since negative results carry a high negative predictive value in both men and women, but positive test results may be false and can be evaluated by more studies.(3)

**Intermediate pretest probability** patients, including those with complete right bundle branch block or less than 1 mm ST depression at rest should have an exercise treadmill test without imaging modality. (3-5) However, intermediate pretest probability patients with baseline ECG

abnormalities such as electronically paced ventricular rhythm or left bundle-branch block will require myocardial perfusion imaging. (5)

**High pretest probability** patients should have coronary angiography as an initial strategy for diagnosis of CAD. (3) □

## HISTORY, EXAM, AND ECG DETERMINE TEST SUITABILITY

Can your patient take an exercise stress test, or will he need a pharmacologic stress test instead? (See "A guide to sensitivity, specificity, and likelihood ratios for stress tests.") Can he pedal a bicycle, walk, or exercise for 6 minutes? On physical examination, take note of his gait, mobility, and limb strength.

### FAST TRACK

*Intermediate pretest probability patients with left bundle branch block require myocardial perfusion imaging*

What medications is the patient taking? Digoxin may cause false ST changes, beta-blockers may prevent attaining maximum heart rate, and antihypertensive agents and vasodilators may alter the blood pressure response, producing a false negative result. Nitrates attenuate angina and the

Table 1

How to determine pretest probability of coronary artery disease STEP 1		STEP 2		STEP 3					
Ask 3 questions:		Total the number of "yes" answers to identify symptom pattern:		Find the cell in the matrix (below) where age, gender, and symptom pattern converge:					
<ul style="list-style-type: none"> <li>• Is chest pain substernal?</li> <li>• Is chest pain brought on by exertion?</li> <li>• Is chest pain relieved within 10 minutes by rest or nitroglycerin?</li> </ul>	0 of 3 = Asymptomatic		High probability		>90%				
	1 of 3 = Nonanginal chest pain		Intermediate		10%–90%				
	2 of 3 = Atypical angina		Low		<10%				
	3 of 3 = Typical angina		Very low		<5%				
AGE (YRS)	SYMPTOMS								
	ASYMPTOMATIC		NONANGINAL CHEST PAIN		ATYPICAL ANGINA		TYPICAL ANGINA		
	MEN	WOMEN	MEN	WOMEN	MEN	WOMEN	MEN	WOMEN	
35–45	Very low	Very low	Interme-diate	Very low	Interme-diate	Interme-diate	Interme-diate	Interme-diate	
45–55	Low	Very low	Interme-diate	Low	Interme-diate	Interme-diate	High	Interme-diate	
55–65	Interme-diate	Low	Interme-diate	Interme-diate	Interme-diate	Interme-diate	High	Interme-diate	
65–75	Interme-diate	Interme-diate	Interme-diate	Interme-diate	Interme-diate	Interme-diate	High	High	

Adapted from Diamond GA. (2)

associated ST depression of ischemia. (6) In addition, metabolic abnormalities and cocaine or alcohol use may affect heart rate, metabolic oxygen demand and the ability to perform the exercise treadmill testing.

On examination, document murmurs, rhythm abnormalities, vascular bruits, and abnormal pulses. Limit laboratory studies to recent cardiac damage screening if indicated. Screen with a resting ECG for arrhythmias, conduction abnormalities or preexisting cardiac damage. ST-segment (=1 mm) and T-wave changes such as inversions secondary to strain or old injury or conduction abnormalities such as bundle branch blocks and prolonged QT interval may obscure exercise treadmill testing findings. Consider spirometry for patients with asthma or chronic lung disease. □

## A GUIDE TO SENSITIVITY, SPECIFICITY, AND LIKELIHOOD RATIOS FOR STRESS TESTS

### Exercise treadmill testing

Sensitivity varies from 45% to 67% and specificity 72% to 90% with operator and patient variables. (6) An abnormal test in a man at a heart rate of 85% of predicted maximum for age has a sensitivity of about 65% and a specificity of 85% for CAD. In women, one meta-analysis demonstrated a sensitivity of only 61% and a specificity of only 70%. (8)

### PSMI

Pharmacologic stress myocardial imaging is similar to exercise treadmill testing. Dipyridamole and adenosine PSMI with thallium Tl 201 or technetium Tc 99m have a similar sensitivity of 90%, and specificity of 70% for detection of CAD. (6)

### Echocardiography

Overall sensitivity for exercise echocardiography was about 85% and for dobutamine stress echocardiography 82%. Dobutamine has a higher sensitivity than vasodilator echocardiography. (6)

### Likelihood ratios (LR) for exercise treadmill testing and PSMI

Based on a review of coronary artery disease with chest pain as the symptom and a reference standard of a coronary angiogram with >70% narrowing of one or more arteries, or >50% left main, the LR varies for sex and for each different

study. The positive LR (LR+) for exercise treadmill testing is 3.00 for men and 2.00 for women. The negative LR (LR-) for exercise treadmill testing is 0.650 for men and 0.560 for women. LR+ for exercise treadmill testing with thallium imaging is 5.9 (generally), but 2.20 for women; LR- is 0.200 and is 0.340 for women. Dipyridamole PSMI, LR+ is 3.30 and LR- is 0.180. (16) □

## THE DECISIVE FACTORS

Absolute contraindications to exercise treadmill testing include recent MI; significant aortic stenosis, (7) and weight exceeding equipment capacity. Relative contraindications to exercise treadmill testing (which can be superseded if the benefits of exercise outweigh the risks) include: hypertension (systolic >200 mm Hg/diastolic >110 mm Hg), (5) left main coronary stenosis and stenotic valvular disease. (For more on "Contraindications to exercise testing," see TABLE 2.) □

## THE ROLE OF IMAGING: IMPORTANT, YES – ROUTINE, NO

An important element of stress testing is, of course, the imaging method(s) that will be used. The options include myocardial perfusion imaging with thallium Tl 201 or technetium Tc 99m, and echocardiography.

### FAST TRACK

*The Bruce exercise treadmill testing protocol may not be appropriate for the elderly; a ramp method may be better*

Indications for myocardial perfusion imaging with exercise treadmill testing are a high pretest probability for CAD, an abnormal baseline ECG such as left bundle branch block, previous myocardial damage or coronary revascularization, or a previous equivocal or unexpected exercise ECG result. In women with an intermediate pretest probability for CAD, the sensitivity and specificity of an exercise treadmill testing is less than in men, which suggests that nuclear imaging would improve this test. (8) There is, however, insufficient data to justify initial routine stress imaging tests in women. (1)

Of the 2 agents used for myocardial perfusion imaging, technetium Tc 99m has more favorable imaging characteristics. (9) It has a shorter half-life (6 hours) than thallium Tl 201 (73 hours), and larger doses of technetium Tc99m may be used, permitting the assessment of ventricular function. (10)

Echocardiography may also be done with either exercise treadmill testing or PSMI to

Table 2

Contraindications to exercise testing
<b>ABSOLUTE</b>
<ul style="list-style-type: none"> <li>• Acute myocardial infarction (within 2 days)</li> <li>• High-risk unstable angina</li> <li>• Uncontrolled cardiac arrhythmias causing symptoms or hemodynamic compromise</li> <li>• Symptomatic severe aortic stenosis</li> <li>• Uncontrolled symptomatic heart failure</li> <li>• Acute pulmonary embolus or pulmonary infarction</li> <li>• Acute myocarditis or pericarditis</li> <li>• Acute aortic dissection</li> </ul>
<b>RELATIVE CONTRAINDICATIONS (CAN BE SUPERSEDED IF THE BENEFITS OF EXERCISE OUTWEIGH THE RISKS)</b>
<ul style="list-style-type: none"> <li>• Left main coronary stenosis</li> <li>• Moderate stenotic valvular heart disease</li> <li>• Electrolyte abnormalities</li> <li>• Severe arterial hypertension (in the absence of definitive evidence, the committee suggests systolic blood pressure of &gt;200 mm Hg or diastolic blood pressure of &gt;110 mm Hg)</li> <li>• Hypertrophic cardiomyopathy and other forms of outflow tract obstruction</li> <li>• Mental or physical impairment leading to inability to exercise adequately</li> <li>• High-degree atrioventricular block</li> </ul>
Source: Gibbons RJ, Balady GJ, Bricker JT, et al. ACC/AHA 2002 guideline update for exercise testing: A report of the American College of Cardiology/American Heart Association Task Force on practice guidelines (Committee on Exercise Testing). 2002. Available at: <a href="http://www.acc.org/qualityandscience/clinical/guidelines/exercise/exercise_clean.pdf">www.acc.org/qualityandscience/clinical/guidelines/exercise/exercise_clean.pdf</a> Accessed: March 6.

evaluate relative myocardial perfusion. While radionuclide technique assesses relative myocardial perfusion, echocardiography also evaluates global and regional function. Indications for echocardiography are similar to myocardial perfusion imaging but also include the need for prognostic information after MI, and to assess physiologic significance of a lesion or to determine the success of an intervention. □

## TIME FOR THE TEST: SELECTING THE PROTOCOL

While the Bruce exercise treadmill testing protocol is the most commonly used (82% of tests) (11) in healthy adults, it may not be appropriate for women or the elderly as most protocols were developed for the evaluation of men. (12) A ramp method with gradual increase in grade each minute is preferred by some clinicians when patients are unable to perform a standard Bruce protocol. Another option, the Modified Bruce protocol, which is more gradual than the standard Bruce protocol; it has two 3-minute warm-up stages. (12)

The 3 PSMI protocols include adenosine, dipyridamole, and dobutamine. Each has a different administration routine, (9) though ECG, blood pressure and pulse are taken every minute for all 3.

- **Adenosine** is infused with a pump over 6 minutes and technetium Tc99m is injected 3 minutes into the infusion.
- **Dipyridamole** is infused over 4 minutes and technetium Tc99m is injected 2 to no more than 5 minutes after the infusion. Theophylline is injected, after dipyridamole if necessary, no earlier than 1 minute after technetium Tc99m is administered to avoid interference with the uptake.
- **Dobutamine** is titrated with a dose increase every 3 minutes. Tc99m is injected after the first minute at the highest concentration. (Typically dobutamine is used with echocardiography). (6) □

## WHICH PHARMACOLOGIC STRESS TEST IS BEST FOR WHICH PATIENT?

### Adenosine

A potent vasodilator, this endogenous nucleoside is rapidly cleared (half-life, <10 seconds) along with its side effects of flushing, headache, and nausea.

### Dipyridamole

This coronary vasodilator inhibits the uptake of adenosine. The same side effects as adenosine – flushing, headache, nausea – may last longer with

dipyridamole (half-life, 13 hours) but they are more common with adenosine and are relieved by administering theophylline.

All methylxanthines may interfere with either dipyridamole or adenosine and should be held for 24 to 48 hours prior to examination.

- Avoid both adenosine and dipyridamole in patients with asthma, severe COPD ( $FEV_1 < 30\%$ ), second- or third-degree heart block, hypotension, or those who are on oral dipyridamole.

### Dobutamine

This synthetic catecholamine increases heart rate, systolic blood pressure, and myocardial contractility, thereby provoking ischemia. Dobutamine (half-life 2 minutes) is not affected by methylxanthines.

- It is preferred in patients who are unable to use adenosine or dipyridamole.
- Caution is needed in patients with systolic BP less than 100 mm Hg, hypertension, ventricular ectopy, and glaucoma.
- Side effects can be reversed with beta-blockers. □

## IDEAL ENDPOINTS AND THE REALITIES THAT MAY CREEP IN

The ideal endpoint in an exercise treadmill testing is 100% of the age-predicted maximum heart rate ( $220 - \text{age}$ ). Eighty-five percent of maximum heart rate is the minimum for an acceptable test.

### Absolute contraindications

Absolute indicators for stopping an exercise treadmill test are either a 10 mm Hg systolic drop in blood pressure from standing baseline, moderate to severe angina symptoms, feelings of syncope, skin color changes suggestive of hypoxia or hypotension, ischemic ST changes, or the patient's desire to stop.

### Relative contraindications

Relative indicators to stop include fatigue, shortness of breath, leg pain, increased arrhythmias – particularly PVCs that increase with the exercise level – and blood pressure = 250 systolic or 115 diastolic. (6)

Ideally, PSMI evaluations are terminated according to the prescribed length of infusions. They will also be terminated if a patient develops wheezing, severe or increasing chest pain or hypotension, neurological symptoms, ST-segment elevation abnormalities, or arrhythmias.

To reverse the side effects of adenosine or dipyridamole, aminophylline IV will be administered (1–2 mg/kg slowly, up to 250 mg). □

## HEART OF THE MATTER: WHAT A REPORT SHOULD COVER

Assuming you have ordered the stress test (and not done it yourself), a complete report should include

- ST changes
- symptoms during testing
- reason for ending the test
- estimation of exercise capacity
- blood pressure response
- the presence and frequency of arrhythmias or ectopy.

**Abnormal.** ST segment change is the most important ECG finding in a positive test; it is defined as  $>1$  mm horizontal or down sloping depression or elevation, at least 60 to 80 milliseconds after the end of the QRS complex and should prompt further workup to confirm CAD. (5) An abnormal ECG during a PSMI test indicates an elevated risk of multivessel CAD and should prompt further evaluation regardless of normal myocardial perfusion imaging. (13) □

## THE CALCULATIONS BEHIND THE SCORES

### Duke Treadmill Score

Duke Treadmill Score (DTS) = exercise time – ( $5 \times$  ST deviation) – ( $4 \times$  exercise angina), with 0 = no angina during exercise, 1 = nonlimiting angina, and 2 = exercise-limiting angina.

The score typically ranges from  $-25$  to  $+15$ . (4)

- **Low risk:**  $> +5$
- **Moderate risk:**  $-10$  to  $+4$
- **High risk:**  $< -11$

### Elderly Alternative Treadmill Score (for patients over 65 years of age)

This score has 2 variables in common with the Duke Treadmill Score (exercise duration or the MET equivalent and millimeters of ST changes). It also has 2 different variables (drop in exercise systolic blood pressure below resting value and history of congestive heart failure [CHF] or use of digoxin [Dig]). (17,18)

The score is calculated as follows:  $5 \times (\text{CHF/Dig [yes=1; no=0]}) + \text{exercise-induced ST depression in millimeters} + \text{change in systolic blood pressure score} - \text{METs}$

Systolic blood pressure score:

- 0 for an increase >40 mm Hg
- 1 for an increase of 31–40 mm Hg
- 2 for an increase of 21–30 mm Hg
- 3 for an increase of 11–20 mm Hg
- 4 for an increase of 0–10 mm Hg
- 5 for a reduction below standing systolic pre-exercise blood pressure.

A score of < -2 is low risk, -2 to 2 is moderate risk, and >2 is high risk.

**FAST TRACK**

*The Duke Treadmill Score which is predictive of 5-year survival, can ensure that high-risk patients receive further evaluation*

**Equivocal.** Reports that come back as equivocal will have ECG changes nondiagnostic of ischemia such as alterations in P- or T-wave morphology and nondiagnostic changes in AV conduction, particularly if changes revert to baseline during the rest period. Unifocal PACs or PVCs (<5/min) are not specific indicators for CAD and the development of bundle branch blocks are nondiagnostic findings. Equivocal results need additional testing such as myocardial perfusion imaging or angiography to document ischemia if the pretest probability is high.

**Incomplete or failure.** If your patient’s test involves equipment failure or if he (or the operator) was unable to complete the test, you should get a report to that effect. Depending on the nature of the failure, you may need to repeat the test, consider PSMI, or make a cardiology referral. □

**DUKE TREADMILL SCORE**

**A helpful calculation following treadmill testing**

If your patient had a positive or negative exercise treadmill test, consider calculating his Duke Treadmill Score (DTS), which is predictive of 5-year survival and significant severe CAD for patients who are younger than 75 years. (4,14)

DTS helps you to exclude low-risk patients from further invasive testing and ensure high-risk patients receive further evaluation and appropriate treatment. DTS appears to be more useful in women with an intermediate pretest score but not with a low pretest score. (15)

The DTS score typically ranges from -25 to +15. (5) Patients at low risk will have a score of > +5), moderate risk will have scores ranging from -10 to +4, and those at high risk will have a score of =-11. (4) □

**FAST TRACK**

*A modified Duke Treadmill Score is for patients over 65 who may have a limited exercise capacity*

A modified DTS is used for patients older than 65 years who may have a limited exercise capacity, controlled asymptomatic congestive heart failure, or be on digoxin, which may affect their ability to perform a maximal exercise treadmill test. (5) The values for the Elderly Alternative Treadmill Score are as follows: low risk (< -2); moderate risk (-2 to 2); and high risk (>2). (See “The calculations behind the scores.”)

**BOTTOM LINE**

DTS scores, Elderly Alternative Treadmill Scores, and pre-stress test CAD probability scores are all extremely useful. Integrating them into your practice can ensure that patients get the prompt care they may need, while sparing them unnecessary tests along the way. □

**Disclosure**

No potential conflict of interest relevant to this article was reported.

Figure 1. Template for dictating noninvasive cardiac tests

**Template for dictating noninvasive cardiac tests**

**Details:** Patient name, date of birth, date of procedure

**Title:** (Stress treadmill EKG) (dipyridole/Perisartine) (adenosine/tobutamine) (selenium Tc 99m) (Cardiolite) (Echo)

**History:** Patient is a ( ) year-old (male/female) presenting for (type of test) evaluation of (symptoms)

**Pretest probability:** Very Low; Low; Intermediate; High (If Very Low, why are you doing the test?)

**Medications** are (list meds - if on beta-blocker, comment if it was held).  
(Can comment on tobacco use and/or significant family history of CAD.)

**Examination** shows heart to be (regular or irregular? murmur?). Resting blood pressures are ( ) supine and ( ) standing.

**Resting EKG:** Resting EKG shows: Rhythm ( ), Rate ( ), PR ( ), QRSd ( ), QT ( ), QTc ( ), Axis ( ), R-wave progression (N/A/Abn), T-wave, ST elevation/ depression.

**Stress (Treadmill) EKG:** Patient was exercised for a total of ( ) minutes according to a (Bruce?) protocol with testing terminated due to (reached Max HR? Chest pain? Fatigue? Other?). Patient achieved a maximum HR of ( ) which represents ( ) % of the age-predicted\* maximum. Maximum METS reached ( ). Maximum blood pressure was ( ) and Double Product\*\* was ( ). During exercise testing patient experienced (list any symptoms or whether patient was free of symptoms). EKG tracings during testing showed (list any ischemic change [≥1 mm horizontal or down sloping ST depression or elevation ≥60-80 milliseconds after QRS complex] or arrhythmias, or absence of these). (If Cardiolite, indicate the time it was injected ( ) minutes/seconds.)

**OR**

**Adenosine/Cardiolite:** Adenosine ( ) mg was injected over 6 minutes according to protocol. Maximum blood pressure was ( ). During exercise testing patient experienced (list any symptoms or whether patient was free of symptoms). EKG tracings (during testing) showed (list any ischemic change or arrhythmias, or absence of these). Cardiolite was injected at ( ) minutes per protocol.

**Recovery:** During recovery patient (experienced chest pain, was asymptomatic?). Heart rate at the end of recovery was ( ) and blood pressure at the end of recovery was ( ).

**IMPRESSION**

1) Test is (Negative for ischemia? Positive for ischemia? Non-diagnostic - why?)

2) **Duke Treadmill Score:** Low Risk (with a score of ≥ +5); Moderate Risk (with scores ranging from -10 to +4); High Risk (with a score of ≤ -11)

3) **Elderly Alternative Treadmill Score:** Low Risk (≥ -2); Moderate Risk (-2 to 2); High Risk (>2)

4) (Comment on exercise tolerance if treadmill) or (Comment on pharmacologic tolerance - side effects)

5) (Comment if test was suboptimal due to failure to reach target HR, if unable to do finish treadmill)

6) (Comment if Cardiolite report is pending - "Cardiolite portion of test will be dictated as a separate report")

**HR ( )**, need to measure for QTc calculation = QT/HR (square root of HR)

\*Note: Target HR = 85% of age-predicted maximum  
Age-predicted maximum HR = 220 - age  
So, target HR = (220 - age) x .85

METS metabolic equivalent (resting oxygen consumption of about 3.5 mL/kg/min); calculated by treadmill or (Active & sedentary men; male cardiac patients = 14.76 + 1.379 (7) + 0.461 (7) - 5.012 (7)) or (Active & sedentary women = 4.38 (7) + 3.92), where T-time is: subtraction. Internet MET calculator available at: www.ama.net/Calculators/Treadmill.html.

\*\*Double Product = Max systolic BP x max HR

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