

Investigating Outpatient CAD: Which Test for Which Patient?

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The differential diagnosis of chest pain and subsequent risk stratification can be difficult. While a good clinical history is essential, further investigation is often required to:

- establish the diagnosis,
- assess prognosis and
- guide treatment.

With a variety of diagnostic tests available, the diagnostic strategy must weigh:

- the initial estimate of likelihood of coronary artery disease (CAD) (pretest probability),
- the tests' limited accuracy,
- costs,
- local availability and expertise,
- the effects on health outcomes of alternative investigations, as well as
- any special considerations for each patient.

A few simple tests can go a long way in ruling CAD in or out.

Initial assessment

A detailed clinical history is required from any patient presenting with a history of chest pain. Typical cardiac chest pain is retrosternal pain/pressure/tightness, with possible radiation to the neck, jaw or arms; precipitated by exertion; relieved by rest or nitroglycerin; and there may be associated dyspnea, diaphoresis, or nausea.

Conventional CAD risk factors are found in 80% to 90% of patients who develop CAD.^{1,2} The absence of CAD risk factors at the age of 50

Mindy's case

Mindy, 32, is healthy and active, but presents with substernal chest pain on exertion.

Side note

The pretest probability of a healthy, young female without cardiovascular risk factors is very low. Despite having typical chest pain, there is no need for further investigation. Reassure Mindy that the pain is unlikely due to coronary artery disease (CAD) and consider other causes.

Questions

1. What should I do if Mindy repeatedly returns with typical symptoms?
2. How should I approach Mindy if her father died of early CAD?

Answers

1. Some patients may have critical disease despite their low Framingham Risk Score (FRS); therefore, in these cases, further testing may be justified. This should only be the exception, though.
2. The true 10-year risk in patients with a family history of early CAD is double the calculated 10-year risk (FRS). Therefore, if this puts Mindy in the intermediate-risk category, further investigation would be recommended.

For another case, look to page 96.

is associated with a very low lifetime risk of CAD and markedly longer survival.³ Investigators from Duke University demonstrated that age, male gender and chest pain symptoms are the most powerful predictors of CAD.⁴

Table 1

The Duke treadmill score^{*,}****The Duke treadmill score¹**

(Time [min] of Bruce protocol) - (5) x (ST depression [mm]) - (4) x (the angina index)

Score	Risk group	Annual mortality
≥ 5	Low	0.25%
-10 to +4	Intermediate	1.25%
≤ -11	High	5.25%

Please note that a moderately-positive test only slightly increases mortality to that of the population average of about 1%.

* Mark DB, Hlatky MA, Harrell FE Jr, et al: Exercise treadmill score for predicting prognosis in coronary artery disease. *Ann Intern Med* 1987; 106(6):793-800.** Mark DB, Shaw L, Harrell FE Jr, et al: Prognostic value of a treadmill score in outpatients with suspected coronary artery disease. *N Engl J Med* 1991; 325(12):849-53.

Patients complaining of chest pain require a full risk factor assessment. The following have to be taken into consideration:

- diabetes mellitus,
- cigarette smoking (a pack or more a day),
- dyslipidemia,
- hypertension,
- obesity,
- Metabolic syndrome,
- chronic renal disease and
- a family history of premature CAD in a first degree relative (male < 55 years, female < 65 years).

Evidence of vascular disease (carotid bruits, erectile dysfunction and vascular claudication) suggests these patients have atherosclerosis and they should be considered high risk. The

ankle-brachial index and carotid dopplers are simple tests that can determine if vascular disease is present.

Estimating pretest probability

The use of a risk assessment scoring system is essential in patients with more than one risk factor. The Framingham Risk Score (FRS) estimates the 10-year risk of cardiac death and non-fatal MI (*i.e.*, based on age, gender, total-cholesterol [C] and HDL-C, smoking and systolic BP) and is recommended for the initial assessment of most patients.⁵ It is now conveniently available on the internet at www.nhlbi.nih.gov/guidelines/cholesterol.

In patients with a family history of early CAD, the calculated 10-year risk should be multiplied by a factor of two.^{6,7} All patients with diabetes mellitus and Metabolic syndrome have a very high long-term risk of CAD, thus early intervention may be warranted irrespective of calculated short-term risk.



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Stress testing

Non-invasive diagnostic stress tests vary in:

- diagnostic discrimination,
- prognostic accuracy,
- relative cost and
- interobserver variability.

High-risk patients

In patients with a very high pretest probability of CAD (FRS > 20% and typical chest pain), a positive stress test is highly predictive of CAD, but a negative test does not rule out CAD. While a noninvasive test adds little diagnostic information in this group, exercise stress testing is often performed before angiography, as it may influence the mode of revascularization (percutaneous coronary intervention vs. coronary artery bypass surgery).

Low-risk patients

In patients with a very low pretest probability of CAD (FRS < 10% and atypical chest pain), diagnostic stress tests contribute little additional information. A negative result is highly predictive of the absence of CAD, while a positive stress test most likely represents a false-positive. False-positive results often lead to unnecessary angiography, thus further investigation is of no benefit in patients with very low pretest probability.

Intermediate-risk patients

Patients with an intermediate pretest probability of CAD (FRS 10% to 20% and chest pain) are most likely to benefit from noninvasive testing. A positive stress test result increases the likelihood of disease warranting further investigations, while a negative stress test and good

Mike's case

Mike, 58, is a relatively active, non-diabetic, ex-smoker, with hypertension, a borderline lipid profile and some exertional chest pain.

Mike is an example of an intermediate-risk patient who would warrant further investigation, including full risk-factor assessment, as well as an exercise stress test. A positive result would suggest that Mike requires further investigation and should be referred to a cardiologist for consideration of angiography. A negative test, on the other hand, would be reassuring.

Questions

1. How should I approach a patient like Mike who presents to my office with a history of increasing anginal symptoms, but is not currently having chest pain?
2. How do some of the newer investigations play in (*i.e.*, homocysteine and C-reactive protein levels or calcium scores)?

Answers

1. A patient with unstable angina should be sent directly to the ED for further work-up.
2. At this point, we do not know enough about what to do with the abnormal results of these investigations. They are not included in the clinical risk assessment scores, therefore at this point, we do not suggest routinely using these tests.

exercise tolerance (≥ 8 METs) decreases the likelihood of disease (and moves the patient down to a lower-risk category) obviating the need for further testing.⁸

Exercise stress testing

The exercise stress test is simple, reproducible and inexpensive. Physical exercise is the preferred form of stress as it provides the most

information with regard to symptoms, functional capacity and hemodynamic response during activity (Table 1).⁹ Failure to achieve 85% of a patient's age-predicted maximum heart rate is inadequate to rule out CAD; thus patients unable to exercise to a sufficient degree should undergo pharmacologic stress imaging.

Exercise stress testing has a decreased specificity in:

- valvular disease,
- hyperventilation,
- hypoxia,
- hypokalemia,
- anemia,
- supraventricular tachycardias and
- hyperglycemia.

The presence of certain ECG abnormalities can interfere with the interpretation of the exercise stress test and necessitates stress testing with imaging, including:

- left bundle branch block,
- ventricular paced rhythm,
- Wolff-Parkinson-White syndrome and similar conduction abnormalities and
- ST-segment deviation > 1 mm at rest (including patients with left ventricular [LV] hypertrophy or on digitalis).

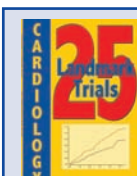
The most frequent contraindications to an exercise stress test in general practice include:

- severe aortic stenosis,
- hypertrophic obstructive cardiomyopathy,
- uncontrolled hypertension,
- uncontrolled congestive heart failure and
- uncontrolled arrhythmias (*i.e.*, atrial fibrillation).

Exercise ECG effectively identifies men at low and high clinical risk; however, the diagnostic value in women is limited by a lower

Take-home message

- The diagnostic approach varies with the pretest probability of CAD (Figure 1). It is strongly recommended to use a specific clinical assessment tool to calculate pretest probability prior to testing. Patients with a normal resting ECG should undergo standard exercise ECG testing. With abnormal resting ECG an exercise imaging test is required. Patients who cannot exercise require pharmacologic stress testing
- Patients with an intermediate pretest probability of CAD are most likely to benefit from noninvasive testing, as a positive test result increases the likelihood of disease, while a negative test usually obviates further investigation
- Patients with a high pretest probability of CAD do not require noninvasive testing for diagnosis, though it is often helpful in terms of prognosis and management
- Patients with a low pretest probability of CAD generally do not require further testing



Dr. Gyenes is also the author of a recently published reference book entitled *25 Landmark Trials in Cardiology*. The book details pivotal trials that have had a significant impact in the practice of cardiology, with editorial comments to help put each trial into perspective. The book is written with attention to important clinical subtleties in order to ensure that it is relevant to a broad range of health professionals. For more information on purchasing *25 Landmark Trials in Cardiology* please contact Dr. Gabor Gyenes at ggyenes@cha.ab.ca.

specificity of ST-segment changes compared with men. The optimal strategy for diagnosing CAD in women remains to be defined. For details, please see Shanks and Cujec's paper.¹⁰

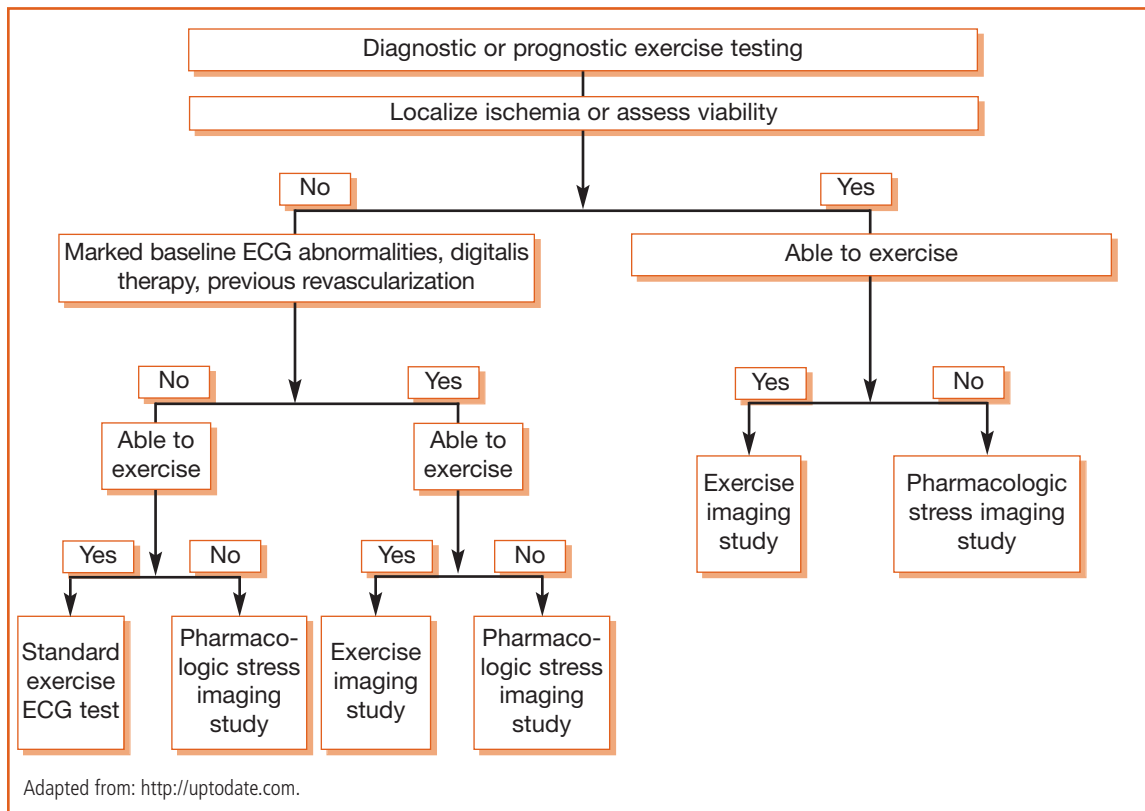


Figure 1. Choice of exercise testing modality in different clinical settings.

Noninvasive stress imaging

A number of alternative noninvasive tests are available:

- Echocardiography (ECHO) using either exercise or pharmacologic (dobutamine) stress
- Myocardial perfusion imaging using either exercise or pharmacologic stress (dobutamine or dipyridamole)

Both ECHO and perfusion imaging contribute important prognostic information including, the size and location of an area of ischemia, LV function and ejection fraction. **Dx**

References

1. Greenland P, Knoll MD, Stamler J, et al: Major risk factors as antecedents of fatal and non-fatal coronary heart disease events. *JAMA* 2003; 290(7):891-7.
2. Khot UN, Khot MB, Bajzer CT, et al: Prevalence of conventional risk factors in patients with coronary heart disease. *JAMA* 2003; 290(7):898-904.
3. Lloyd-Jones DM, Leip EP, Larson MG, et al: Prediction of lifetime risk for cardiovascular disease by risk factor burden at 50 years of age. *Circulation* 2006; 113(6):791-8.
4. Pryor DB, Shaw L, McCants CB, et al: Value of the history and physical in identifying patients at increased risk for coronary artery disease. *Ann Intern Med* 1993; 118(2):81-90.
5. Grundy SM, Pasternak R, Greenland P, et al: Assessment of cardiovascular risk by use of multiple-risk-factor assessment equations: A statement for healthcare professionals from the American Heart Association and the American College of Cardiology. *Circulation* 1999; 100(13):1481-92.
6. Michos ED, Nasir K, Rumberger JA, et al: Relation of family history of premature coronary heart disease and metabolic risk factors to risk of coronary arterial calcium in asymptomatic subjects. *Am J Cardiol* 2005; 95(5):655-7.
7. Murabito JM, Pencina MJ, Nam BH, et al: Sibling cardiovascular disease as a risk factor for cardiovascular disease in middle-aged adults. *JAMA* 2005; 294(24):3117-23.
8. Greenland P, Gaziano JM: Clinical Practice. Selecting asymptomatic patients for coronary computed tomography or electrocardiographic exercise testing. *N Engl J Med* 2003; 349(5):465-73.
9. Garber AM, Solomon NA: Cost-effectiveness of alternative test strategies for the diagnosis of coronary artery disease. *Ann Intern Med* 1999; 130(9):719-28.
10. Shanks M, Cujec B: Women & Heart Disease: Non-invasive testing in the diagnosis of CAD. *Perspectives in Cardiology* 2006; 22(9):23-8.