Non-Invasive Stress Testing in Patients With Suspected Coronary Artery Disease

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Barbara's case

Barbara is a 55-year-old post-menopausal woman who presents with a 3-week history of intermittent retrosternal chest pain occurring with exertion and occasionally at rest, but not during sleep, lasting seconds to minutes at a time. Traditional coronary risks and past health are remarkable for smoking (25 packs per year) and recently diagnosed impaired glucose tolerance (IGT), being managed with lifestyle modification.

Physical exam is normal. Resting 12-lead ECG shows non-specific T-wave inversions in the pre-cordial leads (V1-4). Exercise ECG is clinically negative but electrically non-diagnostic given baseline abnormalities.

How should Barbara's chest pain be evaluated further?

For the correct answer, see page 37.

Several modalities of cardiac stress testing are used in the community for coronary artery disease (CAD) screening. Exercise ECG is commonly used given its low cost and availability. Cardiac imaging techniques such as myocardial perfusion imaging (MPI) or stress echocardiography (SE) substantially improve accuracy and help guide management. The decision of which imaging modality to use is often dictated by the availability and clinical expertise at a given centre.[1,2]

Exercise ECG

Exercise ECG is a well-established and inexpensive approach in investigating myocardial ischemia and functional capacity. It is often performed using the Bruce treadmill protocol, where patients are subjected to increasing speed and incline every three minutes until they reach a minimum of 85% of their age predicted target heart rate. The test can be terminated early if there is a drop in BP, increasing symptoms such as chest pain, respiratory distress, ventricular tachycardia, or patient request (see American College of Cardiology/American Heart Association guidelines for full list).[2] The safety profile is very good with the incidence of acute MI or death being about one in 2,500 cases.[1] The sensitivity and specificity in detecting significant CAD are in the range of 45% to 65% and 60% to 75% respectively, depending on the study (work-up bias), extent of CAD, baseline ECG changes, female gender (higher false positive rate) and associated symptoms.[2-4] The Duke treadmill score, which integrates exercise duration, symptoms and ECG changes, augments the prognostic value of the exercise ECG.[5] Nonetheless, non-invasive imaging modalities are often required for improved diagnostic accuracy and prognostic purposes.

Stress ECHO utilizes two-dimensional images acquired with the patient at rest and immediately post stress.

Table 1
Exercise ECG, SE and MPI

Parameters	MPI	SE	ECG
Sensitivity	87%[4]	85%[4]	67%(45%*)[4]
Specificity	64%[4]	77%[4]	72%[2]
NPV (MACE)[7]	98.8% (36 months)	98.4% (33 months)	
Test duration	4-6 hours	< 1 hour	< 30 minutes
Cost (relative)	++++	++	+
Radiation	Yes	No	No
IV access	Yes	No	No
Additional information beyond ischemia	No	Yes	No
Baseline LV function	Yes	Yes	No

MPI: Myocardial perfusion imaging
SE: Stress echocardiography
NPV: Negative predictive value
MACE: Major adverse cardiac events
LV: Left ventricle
+: Relative cost
*No work-up bias

Exercise and pharmacological stress testing with cardiac imaging

Stress testing can be performed with exercise (treadmill/bicycle) or pharmacologic methods using ECHO or perfusion imaging. Both imaging modalities have been shown to improve sensitivity, specificity and provide valuable information pertaining to the site and extent of myocardial ischemia—not possible with exercise ECG.

The usual stress response is augmented contractility of all wall segments with normal resting left ventricular (LV) function. Fixed wall motion abnormalities represent previous areas of infarct, while stress- induced areas of asymmetrical hypokinesis signify areas of myocardial ischemia.

Perfusion imaging uses a radioisotope (thallium or technetium-based) which is injected intravenously at rest and again during stress, utilizing a gamma camera for image acquisition. The normal response to stress is homogenous uptake of the radioisotope. Image defects apparent only with stress signify areas of reversible ischemia while radioisotope defects present during rest as well represent previous areas of infarct.

FAQ

What are some factors that would preclude exercise ECG?

Resting ECG findings such as conduction abnormalities (bundle branch block, paced ventricular rhythm, Wolff-Parkinson-White), repolarization abnormalities with ST/T changes, or physical inability to exercise are some indications for the use of other non-invasive modalities.[2]

FAQ

What does a normal SE or MPI mean for my patients?

It confers a good prognosis, with absence from major adverse cardiac events > 97% at 3 years.[7]

In patients who are not able to exercise due to physical disability or poor functional capacity, pharmacological chronotropic and inotropic stress with dobutamine, or vasodilator stress with dipyridamole/adenosine is an alternative. Nevertheless, exercise is still the preferable form of stress as it provides information regarding symptoms, hemodynamic response and functional capacity.

Comparison of exercise MPI and exercise ECHO

SE and MPI have comparable diagnostic accuracy and prognostic value in CAD screening. Fleischmann, *et al* using a meta-analysis of 44 studies found similar sensitivities for the detection of CAD. SE and MPI had a sensitivity of 85% and 87% and a specificity of 77% and 64%, respectively.[7] Metz, *et al* in a meta-analysis demonstrated a negative predictive value for MI and cardiac death of > 98% over 33 to 36 months for both MPI and SE.[6] The positive predictive value increases in relation to resting LV function, site and extent of myocardial ischemia.

In addition to LV function and myocardial ischemia, SE provides information regarding LV size, valvular pathology and pulmonary pressures. SE is performed with no ionizing radiation, at a lower cost and with less procedural time than MPI (Table 1).[8]

More on Barbara's case

Barbara is describing atypical chest pain of 3 weeks duration. Given her age, post-menopausal status, IGT and smoking history, further investigation is warranted. The selection of stress ECG was not optimal given her baseline ECG abnormalities, which are common in middle-aged women, rendering the test potentially non-diagnostic. In Barbara's case, a non-invasive cardiac imaging modality would have been the test of choice.

SE and MPI both provide excellent and comparable diagnostic and prognostic information. Either modality can be used depending on availability and testing centre's expertise with each procedure. It is important to take into account the cost and discuss the procedure with the patient in terms of comfort, time and radiation exposure.

FAQ

What is the relative cost of the three non-invasive exercise modalities?

The cost of SE and MPI, when compared to exercise ECG testing, is about 3.8 and 9.0 times as high, respectively.[9]

FAQ

What are the effective doses of radiation for the various cardiac diagnostic tests?

The effective radiation doses are as follows:

- invasive cardiac catherization (7 Millisievert [mSv]),
- cardiac CT (19 mSv),
- technetium-based MPI scan (10 mSv),
- thalium MPI scan (17 mSv) and
- SE (no radiation—0 mSV)

The 1 year worldwide background radiation is 2.4 mSv.[10]

Take-home message

- A number of non-invasive strategies exist for the evaluation of suspected coronary artery disease
- Exercise (treadmill/bicycle) is the preferred form of stress testing as it provides information regarding symptoms, hemodynamic response and functional capacity
- An exercise ECG is often the first test performed given its low cost and availability. Stress imaging should be considered first-line in patients with abnormal resting ECG and in those with known CAD
- The choice of imaging modalities (SE vs. MPI) is often dictated by the availability and expertise at a given centre, taking into account factors such as cost, time and radiation exposure
- A normal study with a non-invasive imaging modality confers a good prognosis with absence from major adverse cardiac events of 99% and 97%, at 1 and 3 years, respectively

References

1. Lee TH, Boucher CA: Noninvasive Tests in Patients with Stable Coronary Artery Disease. N Engl J Med 2001; 344(24):1840-5.
2. Gibbons RJ, Balady GJ, Bricker JT, et al: ACC/AHA 2002 Guideline Update for Exercise Testing (Full Text). American College of Cardiology. www.acc.org. Accessed: December 15, 2009.
3. Froelicher VF, Fearon WF, Ferguson CM, et al: Lessons Learned From Studies Of The Standard Exercise ECG Test. Chest 1999: 116(5):1442-51.
4. Froelicher VF, Lehmann KG, Thomas R, et al: The Electrocardiographic Exercise Test In A Population With Reduced Workup Bias: Diagnostic Performance, Computerized Interpretation And Multivariable Prediction. Ann Intern Med 1998; 128(12 Pt 1):965-74.
5. Mark DB, Shaw L, Harrell FE Jr, et al: Prognostic Value Of A Treadmill Exercise Score In Outpatients With Suspected Coronary Artery Disease. N Engl J Med 1991; 325(12):849-53.
6. Metz LD, Beattie M, Hom R, et al: The Prognostic Value of Normal Exercise Myocardial Perfusion Imaging and Exercise Echocardiography. A Meta-Analysis. J Am Coll Cardiol 2007; 49(2):227-37.
7. Fleischmann KE, Hunink MG, Kuntz KM, et al: Exercise Echocardiography Or Exercise SPECT Imaging? A Meta-Analysis Of Diagnostic Test Performance. JAMA 1998; 280(10):913-20.
8. Gershlick AH, de Belder M, Chambers J, et al: Role Of Non-Invasive Imaging In The Management Of Coronary Artery Disease: An Assessment Of Likely Change Over The Next 10 Years. A Report from the British Cardiovascular Society Working Group. Heart 2007; 93(4):423-31.
9. Ministry of Health and Long-term Care: Schedule of Benefits for Physician Services under the Health Insurance Act: October 2009. www.health.gov.on.ca/english/ providers/ program/ohip/sob/sob_mn.html. Accessed: October 2009.
10. Einstein AJ: Radiation Risk From Coronary Artery Disease Imaging: How Do Different Diagnostic Tests Compare? Heart 2008; 94(12):1519-21.