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

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.

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.
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.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>MPI</th>
<th>SE</th>
<th>ECG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>87%(^4)</td>
<td>85%(^4)</td>
<td>67%(45%(^*)(^4)</td>
</tr>
<tr>
<td>Specificity</td>
<td>64%(^4)</td>
<td>77%(^4)</td>
<td>72%(^2)</td>
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<tr>
<td>NPV (MACE(^7))</td>
<td>98.8% (36 months)</td>
<td>98.4% (33 months)</td>
<td></td>
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<tr>
<td>Test duration</td>
<td>4-6 hours</td>
<td>&lt; 1 hour</td>
<td>&lt; 30 minutes</td>
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<tr>
<td>Cost (relative)</td>
<td>+++++</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Radiation</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
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<tr>
<td>IV access</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
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<tr>
<td>Additional information beyond ischemia</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Baseline LV function</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

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
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. 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. 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).
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.

**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.

**FAQ**

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

The effective radiation doses are as follows:
- invasive cardiac catheterization (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.

**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**