

COVER STORY



How best to evaluate symptoms suggestive of coronary disease?

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Mr Smith, a man with no previous cardiac history, presents to you with episodic chest discomfort. He is middle aged and has several coronary risk factors. How do you proceed?

Mr Smith has not presented with suspected myocardial infarction or unstable (rest, crescendo or recent onset) angina, where referral for urgent coronary angiography would be indicated. Neither is he asymptomatic, where the role of cardiac testing is controversial.

Rather, he has symptoms which may be cardiac in origin. The next step is to establish whether he has significant coronary disease and indications to commence treatment to prevent major vascular events.

A careful history, examination, ECG and appropriate blood tests are required – delineation of cardiac risk factors; detection of hypertension, sleep apnoea, or other vascular disease; elucidation of possible precipitating arrhythmia or valvular disease; detection of anaemia, thyrotoxicosis or diabetes, and measurement of renal function. Then what?

Investigations to establish the presence and extent of coronary atherosclerosis can be roughly divided into anatomical and “functional”.

ANATOMIC IMAGING

Invasive coronary angiography has long been the anatomical gold standard. Direct measurement of pressure gradients within coronary arteries and calculation of “functional flow reserve” can now provide information on the functional significance of narrowings identified.

Angiography requires (usually) day case hospitalisation. Small risks (well under 1 per cent) include vascular damage, embolism (e.g. stroke), contrast allergy and death (< 0.1 per cent). Older age, renal insufficiency, uncontrolled diabetes mellitus, bleeding propensity and morbid obesity can increase these risks. Cardiac factors such as the extent of coronary artery disease, congestive heart failure, low ejection fraction, recent stroke or myocardial infarction can increase cardiac and vascular complications but would not be expected with a presentation such as Mr Smith’s. However, the small risks, costs (procedural and hospital) and inconvenience mean that invasive angiography is not warranted initially in this case.

CT coronary angiography (CTCA) is a rapidly advancing technology, with new scanners providing high resolution images with very low radiation exposure (as low as 1mSv with the latest equipment) and none of the risks of invasive angiography except contrast reaction. CTCA provides very good evaluation of the severity and extent of

atherosclerosis, and also provides a coronary calcium score (I believe that in 2015 there is no real place for stand-alone coronary calcium scoring without CT angiography).

There is considerable promise that sophisticated computer analysis, using what is currently expensive, proprietary software, will provide functional flow as well as anatomic information.

CTCA also provides the opportunity to assess the pulmonary vessels and lung parenchyma. Many findings are incidental, but hiatus hernia, bronchiectasis, atelectasis and pulmonary embolic disease may provide an alternate explanation for the symptom being investigated.

CTCA is partially covered by Medicare only if referred by a specialist, with a gap of around \$300. Radiology practices tend to charge a discounted rate of around \$600 for direct GP referrals.

FUNCTIONAL TESTING

Functional tests compare myocardial perfusion at rest with that following stress designed to induce myocardial ischaemia or demonstrate differences in coronary perfusion. This can be achieved by a variety of means – physical exercise; an agent such as dobutamine, which mimics exercise; vasodilators such as dipyridamole, which increase blood flow in normal arteries more than in stenosed vessels. These tests do not assess atherosclerosis.

Exercise electrocardiography without cardiac imaging or “stress testing” is a simple, safe, cheap and widely available test best undertaken with treadmill exercise, with incrementing speed and treadmill slope e.g the “Bruce Protocol”. Obviously the patient has to be able to exercise, and the ECG should be interpretable in terms of ST segment change (difficult or impossible with, for example, left bundle branch block or resting ST abnormality such as with left ventricular hypertrophy).

The induction of ST segment depression, particularly if this is horizontal or downsloping, is the most reliable indicator of ischaemia. The test may allow better evaluation of the patient’s symptoms, assessment of physical conditioning and evaluation of rhythm and blood pressure before and after exertion.

Bayesian theory tells us that the sensitivity and specificity of the test depends on the population being evaluated. Thus, for example, in a woman, a positive test is significantly more likely to be a false positive than in a man.

In the case of Mr Smith, a good exercise tolerance (greater than 10 minutes) without inducing symptoms or



COVER STORY

ECG changes is associated with an excellent prognosis. Multivessel or left main coronary disease where coronary revascularisation will improve outcomes is unlikely to be missed. The gap after Medicare rebate is approximately \$150.

Combining the information gained from a stress test with imaging increases the sensitivity and specificity of the assessment.

Nuclear myocardial perfusion imaging provides images of coronary blood flow distribution using computerised tomography to assess myocardial uptake of technetium-labelled synthetic compounds, sestamibi or tetrofosmin. These provide better quality images at a lower radiation dose than the previously used radioactive-isotope of thallium, but still in the range of 10-20 mSv. Images at rest are compared with those after stress and/or vasodilators.

This test also assesses left ventricular global systolic function. The rest and stress scans are several hours apart which is less convenient than other functional tests.

The Medicare reimbursement for this test is good and gaps to patients vary from zero to \$440 across the metropolitan area.

Stress echocardiography allows diagnosis and localisation of reversible ischaemic areas in the left ventricle with high sensitivity and specificity. It can also be used to assess other parameters of interest including outflow tract gradients and pulmonary pressures with exercise. The baseline study (though not all providers include a full baseline study when stress echocardiography is requested) provides important anatomic information, including left ventricular size, wall thickness, regional wall motion abnormality indicating previous infarction, overall function, valve structure and function, and estimation of pulmonary artery pressure. Images are more likely to be technically inadequate where the patient is significantly obese or has significant obstructive pulmonary disease. Stress echocardiogram is a manpower- and equipment-intensive test with a static Medicare rebate for some years. Gaps are around \$300.

Cardiac MRI can be used for stress imaging, without the imaging limitations of echocardiography and with zero radiation exposure. It has a very high sensitivity and specificity but has had poor uptake in Australia due to the lack of a Medicare item number and its high relative cost.

HOW TO CHOOSE WHICH TEST?

The Prospective Multicentre Imaging Study for Evaluation of Chest Pain (PROMISE) published last month helps answer this question.

In this study, 10,003 symptomatic (mostly chest pain, some exertional dyspnoea), low to intermediate risk men over 54 or women over 65 with suspected coronary disease were randomly assigned to either CTCA or to functional stress testing with exercise electrocardiography (10 per cent), stress echocardiography (22 per cent), or nuclear myocardial perfusion imaging (68 per cent). The estimated pretest

likelihood of obstructive coronary artery disease was over 50 per cent. Approximately 11 per cent of tests in each group were reported as positive.

The tests performed drove subsequent management decisions. The patients were followed for a median of just over two years, with a composite primary end point of death, myocardial infarction, hospitalisation for unstable angina, or major procedural complication.

Event rates were low and similar in the two groups – 3.3 per cent in the CTCA group and 3.0 per cent in the functional-testing group with death or non-fatal myocardial infarction occurring in less than 1 per cent in both groups.

Radiation exposure in the CTCA group was higher. However the CT scanners used during the period of enrolment for this study would be considered entry-level now, and some WA cardiac specialty imaging centres currently use technology with a radiation dose around one tenth of the doses quoted in PROMISE.

The bottom line is that the outcomes in this study over a relatively short two-year follow-up were very good whichever investigative strategy was chosen. One wonders whether with lifestyle modification, treatment of hypertension, diabetes and hyperlipidaemia and aspirin, similar overall results might have been obtained without testing!

SO WHICH TEST DO I DO IN MR SMITH?

At a minimum, until a diagnosis is reached, he should be prescribed aspirin (or if contraindicated, clopidogrel), unless an alternative diagnosis with a risk of bleeding such as oesophageal ulceration is suspected or there is a contraindication to antiplatelet therapy. He should also be given a Nitrolingual spray which can be useful both diagnostically and therapeutically.

PROMISE tells us that the avenue taken for further investigation is not critical and can depend on other considerations – severe obesity or musculoskeletal conditions limiting exercise capability; factors affecting ultrasound imaging such as severe obesity or chronic obstructive pulmonary disease; cardiovascular issues such as hypertension or a murmur where additional useful structural heart information will be obtained with echocardiography; geography, time constraints and financial factors.

Demonstrating or ruling out atherosclerosis with CTCA would strongly influence the use of a statin and may be a good reason for this investigation if atherosclerosis or a strong indication for statin therapy is not already present.

Conflict of interest. I am fully conflicted! I or my superannuation fund own shares in hospitals providing coronary angiographic services and companies involved in all functional and anatomic coronary modalities described in this article and I perform invasive coronary angiography. The prices and gaps quoted in this article are rough guide only with discounts for concession cardholders almost universal. ■

References available on request.