Diagnosing myocardial ischaemia

ANNA S. HERREY

Anna Herrey emphasises the importance of recognising symptoms of myocardial ischaemia early, and discusses investigations and treatment options.

Coronary artery disease (CAD) is the most common cause of death in the UK. One in five men in the UK die of CAD. It is therefore important to recognise symptoms of myocardial ischaemia early. Myocardial ischaemia may cause angina (stable and unstable), cardiac rhythm disturbances and breathlessness as a consequence of ischaemic left ventricular dysfunction. Sometimes, however, myocardial ischaemia can be silent and patients remain asymptomatic – in these patients a careful risk assessment may be the key to identifying myocardial ischaemia.

RECOGNISING MYOCARDIAL ISCHAEMIA

Myocardial ischaemia describes a functional state during which myocardial oxygen demand exceeds the supply, usually because there is a significant narrowing in one or more coronary arteries. As a result, flow in the coronary arteries is reduced; it may be sufficient at rest, but not during exertion or at times of increased workload for the heart muscle. Factors increasing myocardial oxygen demand such as increase in heart rate or force of contraction therefore can provoke myocardial ischaemia.

Stable angina describes chest tightness or pain, sometimes radiating to the left arm, the jaw, or the neck (angina pectoris), brought on by physical exertion. Patients may also experience breathlessness on effort – dyspnoea is often referred to as ‘angina equivalent’. In stable myocardial ischaemia, symptoms typically resolve with rest. If symptoms persist or occur at rest, or occur with increasing frequency over a period of time (‘crescendo’), this is known as unstable angina and may herald an acute coronary syndrome.

The term acute coronary syndrome (ACS) is used to describe unstable angina, non-ST-elevation myocardial infarction (NSTEMI) and myocardial infarction with ST-elevation (STEMI), all of which require the urgent attention of a cardiologist. In addition to chest pain or breathlessness, patients with an ACS may suffer from...
nausea, vomiting and profuse sweating. Some patients report a feeling of ‘impending doom’.

Diabetic and/or elderly patients may present with atypical symptoms, such as breathlessness alone, nausea, epigastric pain or pain radiating to the right rather than the left arm. In approximately 25 per cent of patients, myocardial infarction is silent and is discovered only on ECG, imaging or bloods tests, or worse still, on autopsy.6 The mechanism of silent ischaemia is thought to be related to autonomic dysfunction, which is known to occur more frequently in patients with diabetes and the elderly.4,5 Recognising symptoms of myocardial ischaemia in these patients can be particularly challenging and the threshold for further investigation should be lower.

Cocaine can cause acute severe vasospasm, not just in atherosclerotic arteries, but also in perfectly normal coronaries, and is not infrequently the cause of myocardial infarction, and is not infrequently the cause of potentially life-threatening arrhythmia.6 Asking about illicit drug use therefore is an important part of the history.

DIAGNOSTIC TESTS

Following a comprehensive clinical history and examination, usually the first diagnostic test is a resting 12-lead ECG. While this will rarely show acute ischaemic changes such as dynamic ST depression or T-wave inversion, left bundle branch block or Q waves may point towards existing coronary disease, even if the patient is unaware, and will hence add valuable information for risk stratification.

The ischaemic cascade illustrates how different stages of myocardial ischaemia over time affect the sensitivity of the tests we use to detect it (Figure 1).

Perfusion abnormalities occur very early in the course of myocardial ischaemia. This explains why myocardial perfusion is such a sensitive test for diagnosing myocardial ischaemia. Next, diastolic function, ie the heart muscle’s ability to relax, becomes impaired. Relaxation for the heart muscle is an active, energy-consuming process. As ischaemia is ongoing, systolic function becomes abnormal – the patient will develop wall motion abnormalities on imaging. Fairly late in the ischaemic process, the resting ECG will show ischaemic abnormalities. Later still, the patient will develop chest pain.

The Table 1. Percentage of people estimated to have coronary artery disease according to typicality of symptoms, age, sex and risk factors

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Non-anginal chest pain</th>
<th>Typical angina</th>
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<tbody>
<tr>
<td></td>
<td>Men Low High</td>
<td>Women Low High</td>
</tr>
<tr>
<td>35</td>
<td>3</td>
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<td>45</td>
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<td>65</td>
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For men older than 70 with atypical or typical symptoms, assume an estimate >90%. For women older than 70, assume an estimate of 61–90% EXCEPT women at high risk AND with typical symptoms where a risk of >90% should be assumed.

High risk = diabetes, smoking and hyperlipidaemia (total cholesterol >6.47mmol/l); low risk = none of these three.

The shaded area represents people with symptoms of non-anginal chest pain, who would not be routinely investigated for stable angina.

If the patient’s chest pain has all three components, it is classified as typical angina; if two of three are present, the patient has atypical angina. If only one feature is present, the pain can be classified as non-anginal chest pain, in which case no further investigation is recommended (Table 1, shaded area), unless there is high clinical suspicion.

Patients can be divided into risk groups by age, gender and character of pain (Table 1).7 The pre-test probability of coronary disease dictates the mode of further investigation:

- low risk (10–29 per cent risk): CT coronary calcium scoring
- medium risk (30–60 per cent): functional cardiac imaging
- high risk (61–90 per cent): invasive coronary angiography.

Advanced imaging tests can be divided into anatomical and functional tests. Technically, myocardial ischaemia cannot be detected by anatomical tests because these image the coronary arteries (rather than the functional state of the myocardium), either non-invasively with CT or by invasive coronary angiography.
Coronary calcium scoring

Coronary calcium scoring by CT has an excellent negative predictive value of 99 per cent, which is why it is recommended for ‘low-risk’ patients, i.e., those with a low pre-test probability of having obstructive coronary disease (Figure 2).

CT coronary angiography

CT coronary angiography should be added on if coronary calcium is present and the calcium score is between 1 and 400 (Figure 3). With a score of >400, the amount of calcium will cause image degradation and coronary stenoses can no longer be accurately assessed; patients should have invasive coronary angiography instead.

While the actual image acquisition takes less than a minute, additional preparation is required. The patient’s heart rate should ideally be around 60, and those not already on a beta-blocker will often be given intravenous beta-blocker on the table, plus sublingual nitrate to dilate the coronaries, thereby facilitating better contrast opacification. Iodine-based contrast is used. Patients with bronchoconstriction, significant renal impairment or nitrate intolerance may therefore be suitable for calcium scoring, but not for CT coronary angiography. In these patients, functional testing represents an alternative if the coronary calcium score is not zero and clinical suspicion persists.

Invasive coronary angiography

Invasive coronary angiography is appropriate in patients with a high clinical suspicion of having obstructive coronary disease. This is undertaken via either a radial or a femoral artery. The advantage of this technique is the ability to proceed to angioplasty if necessary. Complications include rhythm disturbances, myocardial infarction, cerebrovascular events and vascular damage. The iodine-based contrast used for coronary angiography is nephrotoxic and can worsen pre-existing kidney disease.

Functional tests or ‘stress tests’, on the other hand, demonstrate the effect of demand–supply mismatch on the heart muscle, rather than coronary anatomy.

Treadmill testing

Although no longer recommended by NICE for assessment of chest pain, in selected cases a treadmill stress test can still be useful, for example in patients with known coronary disease when assessment of functional capacity is required.

Stress echocardiography

Stress echo is a highly sensitive and specific modality able to detect myocardial wall motion abnormalities caused by myocardial ischaemia. The best stressor is physiological exercise; however, some patients may be unable to exercise. For those patients, pharmacological stress can be used. Most centres in the UK use dobutamine; few use dipyridamole. Specific echo contrast is available to improve image quality, particularly during stress, but also in patients who do not have perfect acoustic windows. Dobutamine can cause fast heart rhythm disturbances, most seriously ventricular tachycardia.

Cardiovascular magnetic resonance

Stress cardiovascular magnetic resonance (CMR) in the UK most commonly refers to vasodilator stress with adenosine, a potent coronary vasodilator with a very short half-life. Myocardial perfusion is compared during stress and at rest using first-pass perfusion of a gadolinium-based contrast agent. The adenosine (or dipyridamole or regadenoson) produces hyperaemia and fast contrast uptake in normal myocardium and hypoperfusion with little contrast uptake in myocardium subtended by a significantly narrowed coronary artery (Figure 4). This test is more sensitive, but less specific than stress echocardiography. Adenosine can cause bronchospasm and transient bradycardic rhythm disturbances and is therefore contraindicated for patients with severe asthma and higher-grade atrioventricular block.

If vasodilator stress CMR is unsuitable, dobutamine stress is a viable alternative. It is particularly useful in patients in whom dobutamine stress echo is impossible, for example in a patient with poor acoustic windows caused by long-standing airways disease. The sensitivity and specificity of dobutamine stress CMR are similar to those of dobutamine stress echo, with slightly higher sensitivity because of better endocardial definition with CMR.

Patients with non-magnetic resonance conditional pacemakers and those with implantable defibrillators cannot have a stress CMR, and general contraindications for magnetic resonance imaging apply.

Myocardial perfusion scintigraphy

This technique uses a radionuclide tracer such as 99Tc-sestamibi or 99Tc-tetrofosmin (less commonly 201Tl-thallium) to assess
myocardial blood flow. Typically combined with adenosine (dipyridamole, regadenoson or even dobutamine) stress and often simultaneous handgrip or bicycle exercise, blood flow during stress and at rest are compared, similar to perfusion CMR and with similar sensitivity and specificity, but inferior negative predictive value than CMR. Average radiation exposure is considerable at 6–9 mSv, even with state-of-the-art equipment.

**TREATMENT OF MYOCARDIAL ISCHAEMIA**

Treatment is directed at improving blood flow to the heart muscle. The current European Society of Cardiology (ESC) guidelines for management of stable angina advise treatment tailored to the patient’s event risk. Those with low event risk (<1 per cent mortality per year) should receive optimum medical therapy; patients with an intermediate risk may be tried on medical therapy, while invasive coronary angiography should be considered in patients with relevant comorbidities such as renal disease or diabetes, or if the patient wishes. High-risk patients with an expected mortality of >3 per cent per year should be offered invasive coronary angiography ± coronary intervention ± optimum medical therapy. Table 2 explains how results of further diagnostic imaging will inform options for treatment.

**Medical therapy**

Optimum medical therapy can be divided into anti-ischaemic medications and preventive medications (Box 1).

Myocardial oxygen demand increases with a rise in heart rate or contractility. Beta-blockers are negatively chronotropic (ie reduce the heart rate) and negatively inotropic (ie reduce myocardial contractility), thereby limiting myocardial oxygen demand. Calcium channel blockers (CCBs) are arterial vasodilators acting on both coronary and other arteries, thereby reducing afterload and hence myocardial workload, as well as improving coronary flow. The dihydropyridine CCBs do not have a rate-limiting effect and can sometimes cause unwanted reflex tachycardia, while

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<th>Exercise stress ECG</th>
<th>High risk</th>
<th>Intermediate risk</th>
<th>Low risk</th>
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<tbody>
<tr>
<td></td>
<td>CV mortality &gt;3% per year</td>
<td>CV mortality 1–3% per year</td>
<td>CV mortality &lt;1% per year</td>
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<tr>
<th>Ischaemia imaging</th>
<th>High risk</th>
<th>Intermediate risk</th>
<th>Low risk</th>
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<td>Area of ischaemia &gt;10% (&gt;10% for SPECT; limited quantitative data for CMR – probably ≥2/16 segments with new perfusion defects or ≥3 dobutamine-induced dysfunctional segments; ≥3 segments of left ventricle by stress echo)</td>
<td>Area of ischaemia 1–10% or any ischaemia less than high risk by CMR or stress echo No ischaemia</td>
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<tr>
<th>Coronary CTA</th>
<th>High risk</th>
<th>Intermediate risk</th>
<th>Low risk</th>
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<td></td>
<td>Significant lesions of high-risk category (three-vessel disease with proximal stenoses, left main and proximal anterior descending coronary artery disease) Significant lesion(s) in large and proximal coronary artery(ies) but not high-risk category Normal coronary artery or plaques only</td>
<td></td>
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| CMR, cardiac magnetic resonance; CTA, computed tomography angiography; CV, cardiovascular; SPECT, single photon emission computed tomography. |

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Table 2. Definitions of risk for various test modalities in patients with confirmed myocardial ischaemia
Non-dihydropyridines such as diltiazem are negatively inotropic and chronotropic, ie reduce myocardial contractility and heart rate.

Nitrates are coronary vasodilators, but mainly act as venous pooling agents, thereby reducing filling pressures for the left heart. Nicorandil has similar properties to nitrates, producing coronary vasodilation. Ivabradine is a negatively chronotropic agent. By slowing the heart rate down, it reduces myocardial oxygen consumption, similar to beta-blockers, but via a different mechanism of action. Ranolazine exerts its antianginal properties by promoting calcium homeostasis in the cardiomyocytes. It does not have a heart-rate-reducing effect and is therefore useful in patients who have a slow heart rate even before treatment.

Many of these drugs work synergistically, and varying combinations of these produce a greater reduction in ischaemia than would monotherapy. Similarly, unwanted side-effects such as reflex tachycardia seen with CCBs or nitrates may be offset by beta-blockade.

Revascularisation
Revascularisation is achieved by either coronary artery bypass surgery or minimally invasive surgery, ie by coronary angioplasty via either the femoral or the radial artery.

Implications for non-cardiac surgery
The ESC is currently re-writing its guidelines on preoperative cardiac risk assessment and perioperative cardiac management in non-cardiac surgery. It has issued a statement that routine perioperative beta-blockade is no longer advisable and an individual risk assessment should be undertaken prior to non-cardiac surgery.9

SUMMARY
Coronary disease is the most common cause of death in UK men. A detailed history is a key first step to diagnosing myocardial ischaemia. NICE guidance is available to guide further investigation of patients with suspected myocardial ischaemia, and new guidelines from the ESC can help plan the appropriate treatment.

Acknowledgements
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REFERENCES