Nuclear cardiology in clinical practice

Mark A Appleby, Dudley J Pennell

This article is an overview of nuclear cardiology for the busy clinician. We discuss the use of myocardial perfusion scans, radionuclide ventriculography, positron emission tomography scans and the interpretation of nuclear scan reports.

Nuclear cardiology is well established as an important tool in the management of cardiology patients (Zaret and Wackers, 1993a,b). The techniques are widely used in the USA and Europe, but less so in the UK, where nuclear cardiology was performed in 0.9 per 1000 per year in 1994 (Pennell et al, 1998). This needs to treble to meet the European average activity which is the British Cardiac Society target (Pennell et al, 1998). The most widely used nuclear technique is myocardial perfusion imaging.

MYOCARDIAL PERFUSION IMAGING

Thallium scans

Injection of radioactive thallium into the blood enables myocardial perfusion to be imaged because the heart avidly takes up the tracer according to regional blood flow (*Figure 1*). Thallium is taken up by 2 mechanisms, namely the Na+/K+ ATPase and diffusion along the electrochemical gradient. When thallium is injected during exercise, ischaemic regions show defects in activity. However, the distribution of thallium between myocardium and the blood is dynamic and after a period of rest, repeat imaging can be performed which shows the distribution of thallium as if a resting injection had been performed. In the setting of coronary artery disease, improvement in tracer activity in an area of stress abnormality indicates the presence of reversible ischaemia (*Figure 2*). Fixed defects indicate infarction, with the severity of the defect being a guide to the severity of muscle loss. Although ischaemia has traditionally been assessed using exercise tests, the number of false negatives and false positives is high relative to those found with thallium scans. Large studies show that mean performance for exercise tests is a sensitivity of 80% and a specificity of 70%, which compares poorly with a 93% sensitivity and 88% specificity for thallium scans (Kotler and Diamond, 1990). Thallium scans are also powerful predictors of prognosis in coronary disease. A normal scan is associated with a very low coronary event rate of 0.9% per year (Brown, 1991). The likelihood of future cardiac events increase exponentially as the size and severity of the stress defects increase (Ladenheim et al, 1986; Machecourt et al, 1994).

Technetium scans

Tracers labelled with technetium (Cardiolite, DuPont, MIBI or Myoview, Amersham International, tetrofosmin) are also available, and in general, these yield higher image quality than those using thallium (Sridara et al, 1993). These

Dr Mark A Appleby is Cardiology Specialist Registrar in the Yorkshire Heart Centre, Leeds LS1 3EX and **Dr Dudley J Pennell** is Senior Lecturer and Honorary Consultant in the Royal Brompton Hospital, London

Correspondence to: Dr DJ Pennell

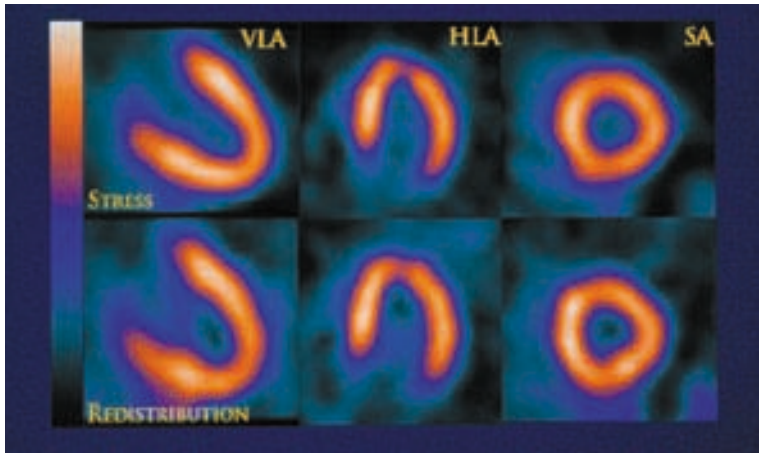

Figure 1. Normal myocardial perfusion imaging. There is homogenous tracer activity throughout the myocardium both at stress and rest. This indicates a low likelihood of significant coronary artery disease and a very low likelihood of future cardiac events. The VLA (vertical long axis), HLA (horizontal long axis) and SA (short axis) correspond approximately to a parasternal long axis, apical four chamber and parasternal short axis at echocardiographic views.

agents show little or no redistribution, which is useful in studies of myocardial salvage post-infarction. Two injections are required, the first usually during exercise and the second at rest, and these are commonly performed on the same day.

Pharmacological stress

Approximately one-third of patients are unable to exercise or perform poorly, which limits the use of exercise as a cardiac stress technique. Pharmacological agents may be used as an alternative, increasing the diagnostic rate. Adenosine, dipyridamole or dobutamine may be used (Pennell, 1994). Adenosine or dipyridamole (contraindicated in asthma) are vasodilators which increase coronary flow in normal vessels relative to those with stenosis, causing heterogeneous tracer uptake. Dobutamine stimulates beta-receptors, increasing myocardial oxygen demand, which simulates exercise. The increased diagnostic rate using pharmacological agents is set against loss of information about exercise duration and symptoms, but in practice, this is not usually problematical.

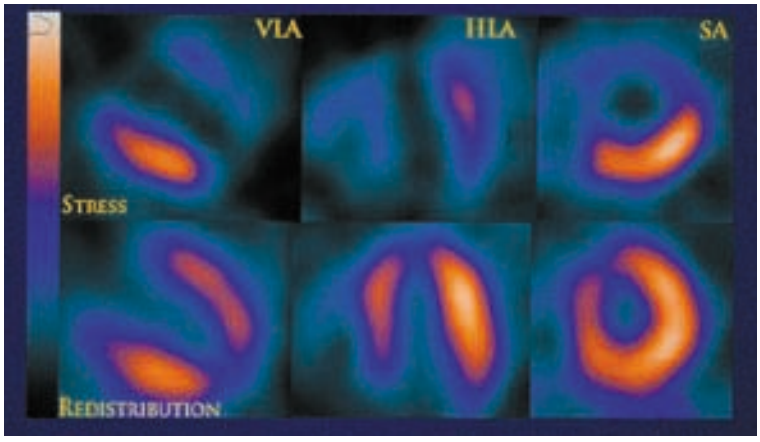

Figure 2. Thallium myocardial perfusion imaging of patient with left main stem stenosis. There is severe reversible myocardial ischaemia of the anterior wall septum, apex and lateral wall indicating a high likelihood of future cardiac events. HLA= horizontal long axis; SA= short axis; VLA= vertical long axis.

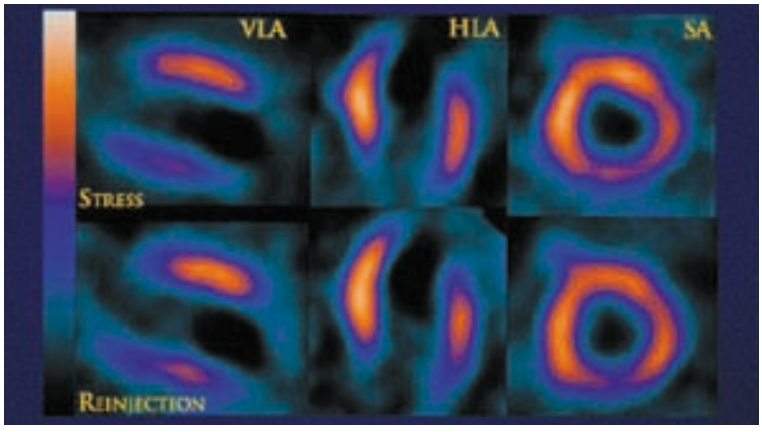

Figure 3. Thallium myocardial perfusion imaging in a patient with transmural anteroapical infarction. The stress images show absent tracer activity in the apical anterior wall and apex. There is mild non-transmural extension into the inferior and lateral walls. There is no significant change with the reinjection of thallium at rest. The anteroapical wall would be expected to be akinetic and not recover with revascularization. HLA= horizontal long axis; SA= short axis; VLA= vertical long axis.

Interpretation of nuclear scan reports

Myocardial perfusion tomograms are displayed in three perpendicular planes along the long axis of the left ventricle (*Figure 1*) (American College of Cardiology et al, 1992). Raw data are converted into colour scales to enhance interpretation of images. In the GE-colour scale shown in this review, normal areas are shown as white to orange and abnormal areas are shown as blue-black. The heart is divided into the anterior wall, lateral wall, inferior wall, septum and apex, and commonly each is subdivided into apical or basal sections, resulting in a total of 9 possible segments. Ischaemia affecting one segment is described as mild ischaemia, two or three segments as moderate, and four or more segments as severe.

Certain observations may be regarded as normal variants. Inferior attenuation (loss of counts as a result of tissue absorption) results from an increased distance from the camera. Breast tissue may result in anterior attenuation. The apex appears thinner because of technical resolution issues. Reduced activity at the base of the septum is seen as a result of the membranous section.

Fixed defects in perfusion scans occur after infarction (*Figure 3*) while reversible defects result from ischaemia. Ischaemia is usually caused by coronary artery stenosis, but this is not always true, as some other physiological conditions such as syndrome X and hypertrophic cardiomyopathy are associated with ischaemia in the absence of coronary disease. When the question of viability and hibernation arises, a reinjection of thallium at rest is often given to ensure that underestimation of the residual muscle mass does not occur. This would cause an area to be labelled as infarction when it might be hibernating.

The area of affected myocardium varies according to the coronary artery anatomy, but the left anterior descending artery nearly always supplies the anterior wall, septum and usually the apex. The circumflex artery supplies the lateral wall. The inferior wall may be supplied by the right coronary artery or the circumflex artery according to dominance.

Stunned and hibernating myocardium

Hibernating myocardium is a state of chronically impaired contraction in which viable myocardium is present (*Figure 4*) (Burn and

Caplin, 1995). It is not fully understood, but the poor contraction in hibernating myocardium is recoverable following successful revascularization of the heart using coronary angioplasty or bypass surgery (Rahimtoola, 1995). Stunning of the heart follows ischaemia, typically after coronary occlusion. Repeated stunning or long-term reduced blood supply to the heart leads to loss of heart muscle proteins, and both may be implicated in the genesis of hibernation. Thallium scans identify areas of preserved viability where contraction is impaired. Positron emission tomography (PET) using 18F-FDG (fluorodeoxyglucose) is useful for identifying hibernating myocardium in cases difficult to diagnose using a perfusion scan (Maddahi et al, 1994).

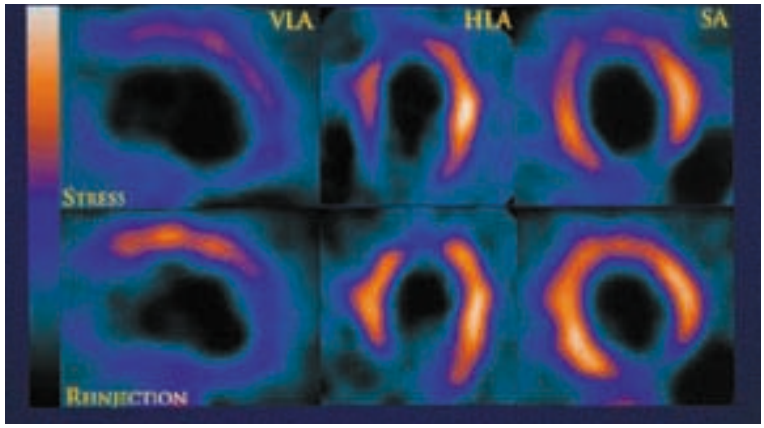

Figure 4. Thallium myocardial perfusion imaging after anteroapical infarction. There is reduced tracer activity in the anterior wall, apex and septum with extension into the inferior wall. After reinjection of thallium, improvement is seen in the anterior wall and septum, but not in the apex and inferior wall. The anterior wall was akinetic on echocardiography, but shows good thallium uptake and reversible ischaemia. It is therefore hibernating. The inferior wall showed marked hypokinesis appropriate to the moderately severe non-transmural infarction which would not indicate any likelihood for recovery. The patient underwent revascularization surgery with good recovery of contractile function in the anterior wall. HLA= horizontal long axis; SA= short axis; VLA= vertical long axis.

Radionuclide ventriculography

Echocardiography is usually adequate for the assessment of left ventricular function. Radionuclide ventriculography (RNV or multiple gated acquisition; MUGA scan) is reserved for those patients in whom echocardiographic images are difficult to acquire or when good reproducibility is required such as in adriamycin cardiotoxicity. Technetium is injected to label red blood cells. The number of counts in the heart in systole and diastole allows evaluation of the ejection fraction (*Figure 5*). Normal left ventricular function corre-

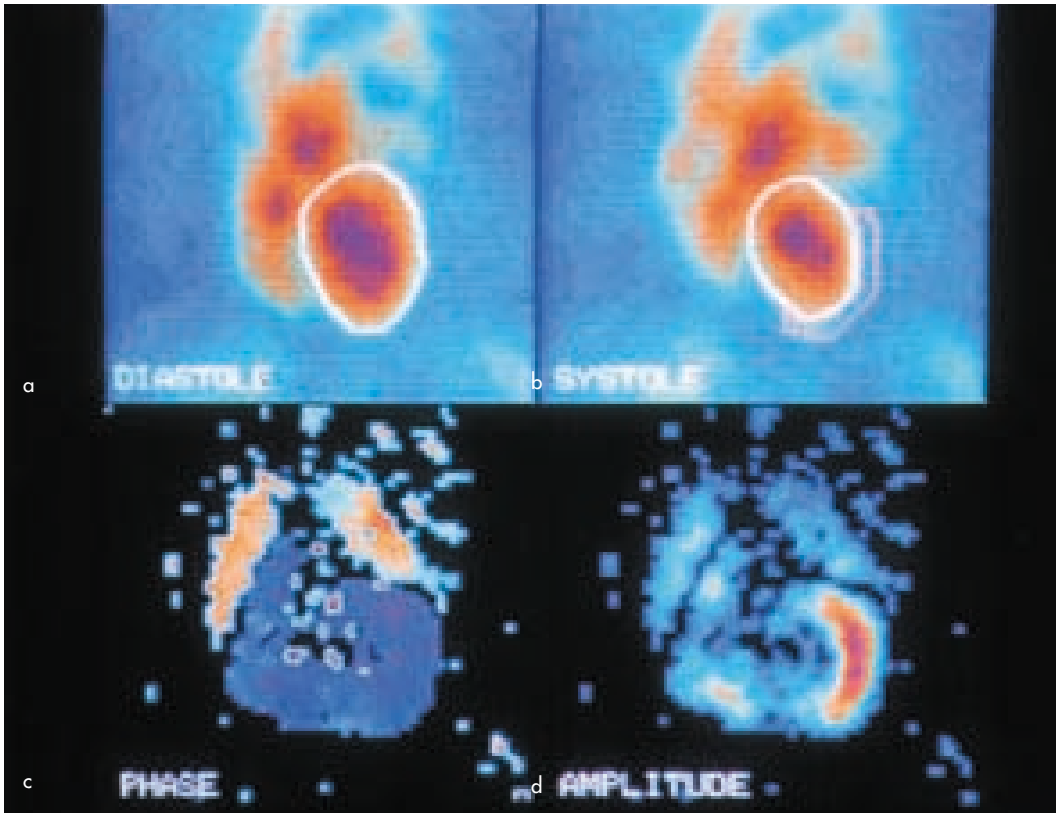

Figure 5. Radionuclide ventriculography study. a and b. End-diastolic and end-systolic frames in the left anterior oblique view. The left ventricle is circled by a white line. Ejection fraction is calculated by comparing counts in end-diastole and end-systole. c. Phase image, showing the timing of peak contraction, is normal. Atria and ventricles are clearly separated. d. Amplitude image, showing akinetic septal wall motion, but satisfactory lateral wall motion.

sponds to an ejection fraction of 50–70%. The ejection fraction is strongly correlated with mortality, particularly when below 30%.

Other nuclear scans

A number of other radioactive tracers are available. Radioactively labelled antimyosin antibodies or pyrophosphate may be used to identify necrotic myocardium (Johnson et al, 1989). The number of agents and techniques used is likely to continue to rise as recognition of the additional data gained with nuclear scans increases. **HM**

American College of Cardiology, American Heart Association, Society of Nuclear Medicine Policy Statement (1992) Standardization of cardiac tomographic imaging. *Circulation* **86:** 338–9

Brown KA (1991) Prognostic value of thallium-201 myocardial perfusion imaging. A diagnostic tool comes of age. *Circulation* **83:** 363–81

Burn S, Caplin J (1995) Myocardial hibernation. *Br J Hosp Med* **53:** 395–402

Johnson L, Seldin D, Becher L et al (1989) Antimyosin imaging in acute transmural myocardial infarction: results of a multicentre clinical trial (abstract). *J Am Coll Cardiol* **13:** 27–35

Kotler T, Diamond G (1990) Exercise thallium-201 scintigraphy in the diagnosis and prognosis of coronary artery disease. *Arch Intern Med* **113:** 684–702

Ladenheim ML, Pollock BH, Rozanski A et al (1986) Extent and severity of myocardial hypoperfusion as predictors of prognosis in patients with suspected coronary artery disease. *J Am Coll Cardiol* **7:** 464–71

Machecourt J, Longere P, Fagret D et al (1994) Prognostic value of thallium-201 single photon emission computed tomographic myocardial imaging according to extent of myocardial defect. Study of 1926 patients with follow up at 33 months. *J Am Coll Cardiol* **23:** 1096–106

Maddahi J, Schelbert H, Brunken R, DiCarli M (1994) Role of thallium-201 and PET imaging in evaluation of myocardial viability and management of patients with coronary artery disease and LV dysfunction. *J Nucl Med* **35:** 707–15

Pennell D (1994) Pharmacological cardiac stress: when and how? *Nuc Med Commun* **15:** 578–85

Pennell D, Caplin J, Tweddel A, Prvulovich E (1998) Nuclear Cardiology in the UK: British Nuclear Cardiology Society Survey 1994. *Nucl Med Commun* **19:** 305–13

Rahimtoola S (1995) The hibernating myocardium. *Am Heart J* **117:** 211–13

Sridara B, Bratt S, Rigo P et al (1993) Comparison of myocardial perfusion imaging with technetium-99m-tetrofosmin *vs* thallium-201 in coronary artery disease. *Am J Cardiol* **72:** 1015–19

Zaret B, Wackers F (1993a) Nuclear cardiology. Review article I. *N Engl J Med* **329:** 775–83

Zaret B, Wackers F (1993a) Nuclear cardiology. Review Article II. *N Engl J Med* **329:** 855–63

KEY POINTS

- The number of nuclear cardiology investigations continues to rise in the UK and needs to treble to meet British Cardiac Society targets.
- Thallium and technetium scans assess the presence of reversible myocardial ischaemia suitable for revascularization procedures.
- A normal myocardial perfusion scan is associated with a very low coronary event rate, and usually indicates that invasive investigation is not warranted. The risks increase rapidly as the severity and extent of ischaemia increases.
- Thallium scanning is useful for identifying hibernating myocardium, but in difficult cases positron emission tomography may be required.
- Radionuclide ventriculography assessment of ventricular function is used for those patients in whom echocardiographic images are difficult to acquire, or when accuracy or reproducibility is an important issue.