Nuclear imaging

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Abstract
Nuclear cardiology is a well established and commonly performed technique which provides physiological information regarding myocardial perfusion and function. Three techniques are described; myocardial perfusion scintigraphy (MPS), radionuclide ventriculography (RNV) and positron emission tomography (PET). MPS is useful in patients unable to complete an exercise test or those likely to produce a false positive result; in particular women, diabetics and those with left bundle branch block. The technique has also been validated in patients undergoing non-cardiac surgery, before and after coronary revascularization and in the assessment of myocardial viability. MPS relies on the changes in cellular uptake of radioactive tracers at rest and during myocardial stress. Matched defects represent sites of infarction whereas mismatch between normal perfusion at rest and reduced perfusion during stress indicates ischaemia. Cardiac risk is proportional to the size of the perfusion defect. RNV relies on blood pool labelling to assess regional ventricular function with excellent reproducibility. Cardiac PET scanning is more commonly used for the assessment of myocardial viability; however, newly available perfusion tracers make it a realistic technique for the assessment of coronary artery disease.

Keywords cardiovascular disorders; coronary artery disease; gamma camera; hibernating myocardium; left ventricular function; myocardial perfusion scintigraphy; nuclear cardiology; positron emission tomography; radionuclide ventriculography; SPECT

What's new?

- The recent introduction of cadmium zinc telluride (CZT) gamma cameras has revolutionized the acquisition time and image quality of myocardial perfusion scintigraphy studies. Typical imaging times are now only 2–3 min.
- SPECT/CT and PET/CT hybrid imaging allows the addition of cardiac anatomy to perfusion and function; essentially a complete one-stop assessment for patients with suspected coronary artery disease.
- Rubidium-82 imaging allows myocardial perfusion to be assessed on a PET camera without the need for a cyclotron.
- Specific A2a receptor agonists promise coronary vasodilatation without bronchospasm.
- MIBG imaging can assist in the prediction of adverse cardiac events in patients with left ventricular systolic dysfunction.

Nuclear imaging comprises myocardial perfusion scintigraphy (MPS), radionuclide ventriculography (RNV), and positron emission tomography (PET). All of these procedures involve the use of radioactive isotopes that are injected intravenously and detected using specific cameras. MPS is the most commonly used and is discussed in some detail within this article.

Myocardial perfusion scintigraphy (MPS)

Indications

MPS is a widely available investigation for the assessment of coronary artery disease (CAD) and is recommended by the UK National Institute for Health and Clinical Excellence[1] (NICE) as a first line diagnostic investigation for the assessment of CAD in patients for whom a standard exercise test is either impossible or unhelpful. These include patients with limited mobility, groups in whom the exercise test has poor specificity (e.g. women and diabetics) and those where interpretation is hampered by pre-existent abnormalities of the ECG (e.g. left bundle branch block). In addition, low risk patients may be referred if diagnostic uncertainty persists after clinical and exercise test assessment. MPS is also recommended in patients with established CAD, to assess residual ischaemia after myocardial infarction and to guide the planning of revascularization procedures in patients with multivessel disease. The American Heart Association guidelines support MPS as a validated tool in patients for whom electrocardiographic stress testing is sub-optimal.[2] Similarly the European Society of Cardiology guidelines supports MPS as a validated, cost-effective tool for the early detection and risk stratification of obstructive coronary artery disease.[3]

Other uses include risk stratification in heart failure (including viability assessment) and before elective non-cardiac surgery, and as an early 'at the door' investigation for triage of emergency attendees with chest pain.

Technique

MPS consists of two parts; the rest scan and the stress scan. Different protocols exist depending on the tracer used and local preference. Stress may be achieved physiologically (treadmill or bicycle exercise) or with pharmacological coronary vasodilators (adenosine and dipyridamole) or inotropes (dobutamine).

Adenosine acts on the A2a receptor to cause coronary artery vasodilatation and dipyridamole increases endogenous adenosine levels by inhibiting its breakdown and increasing uptake. Both agents can cause bronchospasm and should be used with caution in patients with reversible airways disease. Adenosine also causes significant bradycardia and should be withheld in patients with underlying second/third degree heart block. Theophylline preparations and caffeine antagonize the effect of adenosine and should be withheld for 12 h before scanning. Dobutamine is an alternative agent if neither of these vasodilators is suitable – it acts as a beta agonist to increase the heart rate and causes vasodilatation indirectly via an increase in

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myocardial oxygen demand. Relative contraindications to its use include recent myocardial infarction or unstable coronary disease.

At peak stress, a radioactive tracer (^{201}Thallium, ^{99m}Technetium Sestamibi or ^{99m}Technetium Tetrofosmin) is injected into the peripheral circulation. The technetium-based agents bind to myocytes and single photon emission CT (SPECT) imaging follows after 30 min. One - or two-day protocols are required. ^{201}Thallium redistributes rapidly and stress imaging may be undertaken 5–10 min after isotope injection.

Acquisition

Standard MPS scanning uses a gamma camera and ECG-gated SPECT to image uptake of radiopharmaceutical tracer into the myocardium at rest and during stress (Figure 1). The use of gating to match underlying cardiac rhythm has significantly reduced artefact and improved the accuracy of MPS.

Reporting

Tracer uptake and left ventricular dilatation are compared during rest and stress acquisitions. Abnormalities of uptake are reported to describe the number, location, inducibility, extent and severity of the perfusion defect – the total ischaemic burden. Some centres use the validated summed stress score to predict prognostic risk.[4] A normal scan predicts an annual rate of adverse cardiac events less than 1%, even in patients with medium-to-high risk pre-test probabilities.[5] In low-to-medium pre-test probabilities, this annual event rate remains low (around 0.6%) for up to 5 years of follow-up.[6]

The risk of a cardiac event can also be estimated from an abnormal scan (Figure 2). In broad terms, an abnormal MPS predicts a 7% annual risk of a significant cardiac event.[6] In patients with suspected CAD, this annual risk rises by 7% for every 1% increase in inducible perfusion defects and by 3% for every 1% increase in resting myocardial ischaemia.[7] Gated scanning allows accurate and reproducible estimation of left ventricular ejection fraction (LVEF) – an additional indicator of risk. An LVEF < 45% or end systolic volumes >70 ml indicate poorer outcomes in the presence of any inducible perfusion defect.[8]

Studies using MPS following myocardial infarction suggest an increase risk of a further event if >10% of reversible ischaemia is demonstrated.[9] The nuclear sub-study of COURAGE[10] demonstrated that a >5% ischaemia reduction was associated with a reduction in adverse events, supporting the use of MPS to target and monitor patients treated with either revascularization or intensive medical therapy.

Figure 1 Typical modern sodium iodide gamma camera designed for dedicated cardiac work. The sodium iodide crystal heads are perpendicular to each other and rotate around the patients' heart in 32 steps. Collimators in front of the heads only allow perpendicular photons through to the crystals. The resulting scintillation is amplified by photomultiplier tubes and converted to an electrical signal which is gated to the patients ECG. Transaxial slices are created which are reconstructed to standard orthogonal planes and displayed on the computer workstation. Fixed planar imaging (non-rotating camera heads) is no longer used for MPS work; SPECT (single photon emission CT) is preferred especially as this allows functional assessment.

Radioactivity and safety

The radioactivity burden is dependent on the tracer and protocol used. A typical dose required for a 1-day Technetium study involves 1000–1500 Mbq (equivalent to exposure in the region of 8–12 mSv). This is higher than a diagnostic coronary angiogram (2–8 mSv) but similar to a coronary CT scan. The dose associated with background environmental radiation exposure in the UK is 2.6 mSv p.a. The overall 10-year increased risk of a malignancy associated with radiation is approximately 1:2000 per 10 mSv exposure, superimposed upon the 1:3 background risk of developing cancer in the general population.

The risk of a serious complication, death, myocardial infarction or sustained ventricular tachycardia is 1.2 in 10,000 for adenosine and physiological stress tests.[11,12] A higher complication rate of 335 adverse reactions was noted in a large meta-analysis of 26,438 dobutamine stress echocardiographic studies.[13]

Comparison with non-nuclear techniques

A meta-analysis of MPS using all tracers and types of stress reported a sensitivity of 87% and specificity of 73% for the detection of angiographically significant (>70%) coronary artery stenoses.[14] This compares with a sensitivity of 78% and specificity of 70% for exercise ECG testing[15] and 76% sensitivity and 88% specificity in smaller studies of stress echocardiography.[16]

Cost

MPS is a cost-effective strategy for investigation of CAD in selected groups; those who have or are likely to have an equivocal exercise stress test[17] and those with an intermediate pre-test probability of CAD to avoid unnecessary further investigation.[18]

MIBG

Iodine-123-metaiodobenzylguanidine (MIBG) imaging is used to identify patients with known LV dysfunction at high risk of sudden cardiac death. Reduced uptake of the radioactive iodine tracer is linked with LV sympathetic denervation and a poor prognosis.

Radionuclide ventriculography (RNV)

Mainly superseded by echocardiography, radionuclide ventriculography (RNV) measures LVEF using blood pool labelling