Current and future applications of cardiac nuclear medicine

RAD Magazine, 41, 483, 24

Dr M A Loudon
Specialist registrar in cardiology

Dr N Sabharwal
Consultant in cardiology
Oxford University Hospitals NHS Trust

Introduction

Cardiac nuclear medicine refers to three techniques:
1. Radionuclide ventriculography (RNV, also known as MUGA)
2. Myocardial perfusion scintigraphy (MPS)
3. Positron emission tomography (PET)

Radionuclide ventriculography has been largely superseded by echocardiography. Occasionally it is helpful in determining ventricular function when echocardiographic views are limited and there is a contraindication to magnetic resonance imaging (MRI).

MPS is by far the most commonly used imaging modality to assess myocardial ischaemia. It provides robust data on perfusion, viability and function. It is being challenged by techniques such as stress echocardiography, cardiac MRI (CMR) and cardiac computed tomography (CT).

Cardiac PET remains highly specialised and is primarily used as the gold standard for assessment of myocardial viability. The last few years have seen an exciting, expanding role for the detection and management of endocardial infection, cardiac sarcoidosis, and in complex heart failure.

Current clinical use and recent developments

Myocardial perfusion scintigraphy

The first radiopharmaceutical isotope tracer was 201thallium. Thallium redistributes freely between the blood pool and myocytes and has a half-life of 73 hours. As it decays, it emits photons which are detected by the sodium iodide crystals within the gamma camera. 99mtechnetium compounds, bound to either sestamibi or tetrofosmin, are popular. They have the advantage a shorter half-life (six hours), so rest and stress scans can be on the same day and there is no need for an on-site cyclotron as the tracer can be prepared in advance and reconstituted on site. Technetium compounds are retained by intact myocytes and the decay detected by the gamma camera in the same way as 201thallium. Recent years have seen erratic supplies of technetium and resurged in the use of thallium. Thallium is probably the better SPECT tracer for the assessment of myocardial viability.

A typical 99mTc MPS scan exposes the patient to 6-14mSv of ionising radiation (2.6mSv being a typical annual background exposure, with an annual limit of 20mSv for staff). New solid state scanners are reducing acquisition time and radiation exposure. Cadmium zinc telluride (CZT) has revolutionised image quality and scanning times, down to as low as two minutes. Colleagues in Zurich are pioneering low dose ultrafast techniques such that a 90-minute stress/rest acquisition at 2mSv is possible.

Ideally, physiological stress using a bicycle or treadmill is used, with the isotope tracer of choice injected at peak stress, as determined by heart rate and workload. Physiological stress also provides useful data on the blood pressure and heart rate response to exercise and is the technique of choice. If the patient is not able to exercise, then pharmacological stress is used instead.

Adenosine based compounds are the most frequently used pharmacological stress agents. Adenosine causes coronary vasodilatation. In a diseased coronary vessel, maximal flow dilatation cannot occur and areas of ischaemia will become hypo-perfused. Adenosine based agents were traditionally unsuitable for those with asthma due to bronchoconstriction and those with any high degree heart block. Newer more specific A2a agonists, such as Regadenoson, have reduced these risks and are now in routine clinical use. This particular agent is a non-weight adjusted bolus given over 10 seconds with a good safety record. It can be delivered during or after dynamic exercise ensuring adequate stress is achieved irrespective of workload. Our use of the treadmill has therefore increased as we have the reassurance of these selective A2a agonists in the background. Inotropic agents such as dobutamine are now rarely used at our institution.

MPS has a major role in those with undifferentiated chest pain. It is also useful in the assessment of viability in heart failure and in the assessment of ischaemia in those with known coronary artery disease. It provides excellent prognostic data with a normal scan equating to an annual cardiovascular adverse event rate of less than 1% per annum. If present, the amount of ischaemia is also prognostically important. Greater than 10% ischaemic burden confers an annual risk of an adverse cardiovascular event of nearly 5%. A fall in ejection fraction on stress, known as transient ischaemic dilation, is an additional adverse sign. Multi-centre studies are underway looking at the effect of ischaemic burden on revascularisation strategies. MPS is currently the only technique that allows accurate quantification of ischaemic burden.

Worldwide, MPS remains the “workhorse” of many departments, offering a high throughput, high quality service for the investigation of chest pain. However, other modalities have certainly improved and are competing for the role that MPS currently occupies. Large studies such as MR-IMPACT2 and CE-MARC have tested MPS versus CMR in the assessment of patients with chest pain. These studies have confirmed that CMR perfusion is a promising technique that has a good sensitivity and specificity when it comes to diagnosing CAD. While both studies have received criticism there is no role for complacency within nuclear cardiology services. The challenge for nuclear cardiology is to provide a high quality MPS service. The strength of MPS is the wealth of prognostic evidence and the ability to quantify ischaemic burden.

miBГ

123I-miBГ is a tracer whose uptake reflects the distribution of the sympathetic nervous supply to the heart and mediastinum. In heart failure, there is over-activation of the sympathetic nervous system due to a reduction in uptake of pre-synaptic norepinephrine. 123I-miBГ is an analogue of epinephrine and can be detected by standard gamma camera planar imaging. From this the sympathetic innervation of the myocardium and the heart to mediastinal miBГ ratio is calculated. This has strong prognostic significance in both
ischaemic and non-ischaemic heart failure, irrespective of LV ejection fraction and biomarker levels. Figure 1 shows a planar mIBG scan confirming poor cardiac uptake relative to the mediastinum. This is a high risk scan.

**DPD**

$^{99m}$Technetium $^{1}$diphosphono $^{2}$propanodicaboxylic acid ($^{99m}$Tc-DPD) is an established bone scan tracer with a novel role in identifying cardiac amyloid. Cardiac amyloid is a condition with abnormal protein deposition in the heart, carrying a poor prognosis. Existing investigations are not specific in differentiating amyloid from other infiltrative disease or in the type of amyloid protein itself (there are three important varieties). DPD scintigraphy shows promise in the diagnosis and severity of certain types of cardiac amyloid, showing cardiac, soft tissue and major organ involvement. Figure 2 shows cardiac uptake in a patient with TTR cardiac amyloid, note the reduced bone signal.

**Positron emission tomography**

Positron emission tomography (PET) has seen a significant expansion over the last few years but remains an expensive and highly specialised investigation. Several tracer compounds are used in PET, the most common being $^{18}$F-deoxyglucose (FDG), which is used to detect changes in glucose metabolism. There are several cardiac conditions in which this is useful. These include myocardial viability, which is usually combined with an assessment of myocardial perfusion. Viability in PET is determined by comparing uptake of perfusion tracer with glucose metabolism. This assessment of viability is more sensitive as it detects “hibernating” myocardium, i.e. hypoperfused but metabolically active myocardium. It may also be combined with anatomical information from coronary CT angiography – so called hybrid imaging.

Other uses for PET include detection of intra cardiac infections, as areas of active infection are highly metabolically active. This can be especially useful in looking for complications of infective endocarditis, such as root abscess, particularly around prosthetic valves. It is also helpful in suspected device infection (such as pacemakers or ICDs). PET has a role in monitoring cardiac and extra cardiac sarcoid, although its role in diagnosis is not yet established. This is an area of active research.

$^{18}$F-sodium fluoride (NaF) has been studied and shown to be useful in discriminating culprit plaque in acute coronary syndromes. It has also proved its worth as a research agent in the study of calcific heart valve disease.

**PET perfusion**

For myocardial perfusion PET has several options. $^{82}$Rb is popular outside the UK. It requires an on-site generator but will allow for a full stress/rest vasodilator PET study within 30 minutes. The generator is replaced every four to six weeks. This test can easily be combined with CT coronary angiography to provide complete functional and anatomical information.

If an on-site cyclotron is available then perfusion can be performed with NH$_3$. Oxygen labelled water also allows for absolute flow quantitation.

Flurpiridaz $^{18}$F tracer is a promising perfusion tracer, which is currently in clinical trials. Recent trials have shown improved diagnostic performance for PET with greatly enhanced image quality when used as a perfusion tracer. Figure 3 shows an example of enhanced image quality using flurpiridaz $^{18}$F, compared with the same patient undergoing a $^{99m}$TC study. Alternatives such as NH$_3$ require an on-site cyclotron which limits their availability. Any $^{18}$F based perfusion tracer would therefore have a significant advantage. Clearly all the cardiac PET applications require time and expertise on PET scanners that presently have a significant amount of mainly FDG-based oncology work.

**Conclusion**

Cardiac nuclear medicine is re-emerging as both a competing and a complementary technique to other imaging modalities. Decreasing scan time and radiation, together with enhanced image quality, should ensure the ongoing utility of MPS. Hybrid imaging with cardiac CT angiography is a very exciting development.

Cardiac PET is emerging as an exciting field with an ever expanding role as new isotopes emerge. Hybrid techniques with MRI (PETMR) are developing and cardiac imaging is likely to benefit significantly.
Figure 3

$^{18}$F-flurpiridaz PET perfusion scan compared to a $^{99m}$Tc-sestamibi scan in the same patient. The signal to noise ratio is improved with increased diagnostic accuracy with the PET tracer.