Nuclear cardiology

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Nuclear cardiology has undergone great changes since its inception 20 years ago. Imaging methods have improved, there are new radiotracers, and the applications of nuclear cardiology techniques have significantly expanded. The two most common nuclear cardiology tests are myocardial perfusion imaging (MPI) and radionuclide ventriculography. This article focuses primarily on MPI, which comprises more than 70% of studies, and its role in patient management (Table 1).

Myocardial perfusion imaging

Principles

Myocardial perfusion studies are performed using a radiotracer that distributes in the patient’s heart in proportion to regional flow. Typically, two sets of images are acquired reflecting perfusion at peak stress and at rest. Radiotracers distribute uniformly in normally perfused myocardium (Fig 1). In areas supplied by functionally significant coronary stenoses there is a stress defect that improves on rest imaging (reversible defect) (Fig 2). Stress defects that fail to improve on rest imaging (fixed defects) generally represent infarcted areas (Fig 3).

Stress techniques

The choice of stress technique lies between maximal dynamic exercise and pharmacological stress. Dynamic exercise is physiological, it provides hemodynamic data with important prognostic value and remains the stress technique of choice for the majority. For patients unable to exercise maximally or in whom exercise electrocardiographic (ExECG) data are either already available or would be unhelpful (Table 2), pharmacological stress using one of the vasodilator agents (adenosine or dipyridamole) or a catecholamine (dobutamine or arbutamine) is recommended. Adenosine is preferred for pharmacological stress in most cases; the technique is fast, safe and requires little patient cooperation. Dobutamine should be used if asthma is present or if there is sino-atrial disease without a pacemaker. MPI coupled with pharmacological stress has comparable diagnostic value to that observed with dynamic exercise.

Radiopharmaceuticals

The choice of radiotracers currently lies between thallium-201 (201TI) and two technetium-99m (99mTc)-labelled compounds, 99mTc-MIBI (Cardiolite) and 99mTc-tetrofosmin (Myoview). The main difference between the 201TI and the

![Fig 1. Normal myocardial perfusion after stress.](image1)

![Fig 2. Myocardial perfusion images in a patient with chest pain.](image2)

Table 1. Uses of myocardial perfusion imaging in chronic coronary artery disease. (Reproduced from Ref 2 by permission of Elsevier Science).

| Indication                                      | Class |
|------------------------------------------------|-------|
| Detection of ischaemia in symptomatic or selected asymptomatic patients | I     |
| Risk stratification before non-cardiac surgery | I     |
| Identification of 'culprit' lesion prior to PTCA | I     |
| Restenosis after PTCA in symptomatic patients | I     |
| Ischaemia in symptomatic patients after CABG    | I     |
| Pre-revascularisation assessment of viability or ischaemia | I     |

Class I status is defined as 'usually appropriate and considered useful'
CABG = coronary artery bypass grafting
PTCA = percutaneous transluminal coronary angioplasty
that the latter exhibit minimal redistribution from their initial pattern of uptake. Thus, two separate injections have to be given to compare perfusion at rest and under stress. The available data do not indicate superiority of one tracer over another, although the higher energy (140 keV) 99mTc agents may be preferable in obese or large-breasted patients in whom the low energy photons (60–80 keV) of 201TI would be severely attenuated. The high count rate and stable myocardial distribution of the 99mTc agents also permit left ventricular (LV) function to be determined as an adjunct to perfusion imaging.

**Patient preparation**

Patients should have only a light meal before MPI. Those undergoing pharmacological stress with adenosine or dipyridamole should avoid caffeine, a competitive inhibitor of adenosine, for at least 12 hours. An exaggerated response to vasodilator stress may occur in patients taking oral dipyridamole, so this should also be stopped for 12 hours.

**Diagnosis of coronary disease**

MPI is an established non-invasive method for the detection of coronary artery disease (CAD). It is diagnostically superior to ExECG (sensitivity and specificity 80% and 92% vs 68% and 84%, respectively) because perfusion abnormalities occur at lower levels of ischaemia than either ST segment depression or anginal chest pain (Fig 4).

Fig 4. The ischaemia cascade. The graph represents the order of physiological events that occur with increasing levels of ischaemia (LV = left ventricle). (Adapted from Ref 7 by permission of Elsevier Science.)

MPI has the additional advantage of being able to localise ischaemia to a specific coronary distribution, within which larger and more severe defects usually correlate with proximal and more severe stenoses. Importantly, almost all patients with left main or multivessel CAD have abnormal scans with multiple thallium defects, and many also show lung uptake of thallium. Identification of these patient subsets is critical because their survival is improved by surgical intervention.

The requirements for expensive equipment together with the radiation burden to the patient mean, however, that MPI is usually employed for diagnosis when ExECG is either unhelpful or leaves doubt. This may occur when:

- the resting ECG is abnormal (left bundle branch block, repolarisation abnormalities or LV hypertrophy)
- equivocal ST segment changes occur with exercise
- abnormal ST segment changes are seen despite a low pre-test probability of CAD

Table 2. Indications for pharmacological stress.

- Restricted exercise tolerance
- Contraindication to exercise
- Left bundle branch block
• ExECG is normal despite a high pre-test probability of CAD
• only submaximal exercise has been achieved.

Very obese patients can exceed the weight-bearing capacity both of a treadmill and of a coronary angiographic imaging table. Diagnostic MPI can be performed successfully, but advance warning of patient size is essential for optimal quality.

**Prognosis**

*Patients with known or suspected coronary artery disease.* MPI has strong prognostic power for future cardiac events. A normal stress perfusion study predicts a favourable prognosis even where there is known CAD. The risk for future cardiac events in these patients is less than 1% per year, a rate approaching that of a normal age-matched population. Conversely, severe and extensive reversible defects predict an adverse prognosis. Where MPI indicates low risk, patients can usually be managed medically in the absence of intractable symptoms. Patients with a high risk pattern (Table 3), should be considered for coronary angiography and revascularisation.

The prognostic value of MPI is independent of the imaging technique, form of cardiac stress and radiotracer used, and it is incremental to that provided by clinical and ExECG data. Importantly, more expensive coronary angiographic data provide little or no significant additional prognostic value (Fig 5).

**Myocardial infarction.** The two major determinants of prognosis after infarction are LV ejection fraction and the presence and extent of stress-induced reversible ischaemia. ExECG is the most common test for prognosis after infarction, but the overall sensitivity of ST segment depression is low (average 27%) and the relative insensitivity reflects the difficulty in interpreting ST segment changes when the resting ECG is abnormal, coupled with the frequent use of submaximal ExECG. By contrast, MPI provides effective risk stratification irrespective of the resting ECG. It can be performed safely within 2–3 days of infarction using vasodilator stress, thus allowing the early discharge of patients identified as low risk.

Data in non-thrombolysed patients have consistently shown the superiority of MPI over both submaximal ExECG and coronary angiography for risk stratification. All three techniques can identify patients at high risk of reinfarction or sudden death but MPI most reliably identifies the very low risk patients (Fig 6). Initial concerns that MPI might have reduced prognostic value in thrombolysed patients appear unfounded. Recent data suggest that

**Table 3. Predictors of adverse prognosis.**

- Lung uptake of radiotracer with stress
- Left ventricular dilatation with stress
- Presence of redistribution
- Severe and extensive perfusion defect

![Fig 5. Incremental prognostic value of tests performed in hierarchical order.](image)

In 316 patients followed for 28 months, myocardial perfusion imaging (MPI) combined with clinical and exercise electrocardiographic (ExECG) data provided significantly more prognostic information than clinical alone, clinical plus ExECG or clinical plus ExECG and coronary angiography (angi). Addition of angi to MPI added little further information (NS = not significant). (Adapted from Ref 17 by permission of Elsevier Science).

Pre-operative evaluation. It is well known that patients undergoing non-cardiac vascular surgery often have associated CAD that may be clinically unapparent. The peri-operative mortality and morbidity in these patients are usually due to the underlying CAD which can be evaluated using MPI. Patients with normal perfusion studies and/or without reversible defects have a very low risk of peri-operative cardiac complications. Conversely, those with reversible perfusion defects are at increased risk. However, the positive predictive value of an abnormal scan in this population is only 15–30%, so clinical variables (eg previous infarct, history of diabetes mellitus, angina or heart failure) should be combined with the results of MPI to optimise risk stratification. Low-risk patients can safely proceed to surgery, while those at high risk should be considered for coronary angiography before surgery.
After coronary angiography

In a substantial proportion of patients, MPI is performed after coronary angiography to assess the haemodynamic significance of coronary stenoses. In patients with severe symptoms but a modest (25–75%) or imperfectly visualised angiographic abnormality, MPI can help determine whether revascularisation is warranted. In symptomatic patients with multivessel disease unsuitable for coronary artery bypass grafting, MPI can identify the most functionally severe stenosis and guide culprit lesion angioplasty.

Post-intervention evaluation

The main problem with percutaneous transluminal coronary angioplasty (PTCA) is the high restenosis rate in the following six months (30–50%). For patients with typical angina following PTCA, coronary angiography is generally indicated. However, MPI may be more appropriate if symptoms are suspicious but atypical. A normal perfusion study will usually obviate the need for repeat coronary angiography. ExECG is an alternative method to detect restenosis in patients with single vessel disease and a normal resting ECG, but has limited predictive value when there is multivessel disease or an abnormal resting ECG.

It is important to perform post-PTCA MPI at the correct time. An abnormal scan very early after PTCA is poorly specific for restenosis as coronary flow reserve and perfusion abnormalities can take several weeks to resolve. MPI is best withheld for at least four weeks after PTCA. A baseline study pre-PTCA is also essential for comparison.

Detection of viable myocardium

In a subset of patients with CAD and symptomatic LV dysfunction, LV performance is reduced because of chronically ischaemic but viable myocardium. The detection of viable myocardium is clinically relevant because LV function in such patients may improve after revascularisation. Thallium rest/redistribution and stress/redistribution/reinjection imaging are both nearly as effective as positron emission tomography in differentiating irreversibly infarcted from viable myocardium.

Radionuclide ventriculography

Radionuclide ventriculography (Fig 8) is performed using red blood cells labelled with 99mTc-pertechnetate and provides accurate and reproducible information regarding LV function. The widespread availability of echocardiography means

Fig 7. Kaplan-Meier curves depicting freedom from cardiac events in patients after myocardial infarction on the basis of myocardial perfusion imaging (MPI) data. Extent of reversible ischaemia has strong prognostic power in thrombolysed and non-thrombolysed patients alike. (QISCH = extent of ischaemia; LV = left ventricle; Rx = therapy).

Fig 6. Comparison of prognostic power of submaximal exercise electrocardiography, thallium myocardial perfusion imaging (TI-MPI) and coronary angiography for risk stratification after uncomplicated myocardial infarction. The separation of the thallium curves is statistically superior to the other two techniques, and TI-MPI best identifies low-risk patients (MTD = multiple thallium defects; ITD = single thallium defect; Rd = redistribution; LU = lung uptake).
that the use of radionuclide ventriculography is limited to cardiac patients for whom an adequate echocardiographic window cannot be achieved and for serial monitoring of patients in cardiac failure and those undergoing cardiotoxic chemotherapy.

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Radionuclide imaging in cancer management

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Imaging, both anatomical and metabolic, has a major role in the optimal management of patients with cancer at different stages in the course of the disease. Complete surgical excision gives the patient the best chance of a curative treatment for most cancers, but many patients are found to be inoperable at surgery or relapse soon after major surgery has been performed. This usually indicates that primary ‘curative’ surgery was inappropriate.

The important question at initial diagnosis is usually ‘is the tumour localised or is it disseminated?’; in most cases, the answer will determine whether a tumour is resectable and potentially curable or has disseminated to such an extent that primary surgery is inappropriate or chemotherapy and/or radiotherapy is a necessary adjunct before or after surgery. Metabolic radionuclide imaging is increasingly shown to be cost-effective by reducing the frequency of unnecessary surgery with the high associated health care and clinical costs. Though surgery remains of prime importance, chemotherapy and radiotherapy are increasingly used as alternatives for the primary treatment of cancer as well as adjuvants to surgery. Neo-adjuvant chemotherapy is an attempt to downstage an inoperable tumour to one that can be treated surgically with a hope of curative resection. Metabolic imaging is also used to predict and measure an early response to chemotherapy or radiotherapy in order to monitor and tailor treatment regimens. In some cases, metabolic imaging provides sufficient accurate information by itself, while at others it is complementary to anatomical imaging with computed tomography (CT) or magnetic resonance imaging (MRI).

The approach to tumour staging is similar in different cancers:

- **T stage**: the primary lesion which usually relates the size of the tumour, and is largely determined by anatomical imaging methods.
- **N stage**: spread to regional lymph nodes.
- **M stage**: metastatic spread to other parts of the body.

### Key Points

The role of imaging in cancer management is:

- To distinguish benign from malignant masses
- To stage the disease (local, nodes and metastases)
- To detect recurrence of tumour
- To direct biopsy
- To select or plan therapy
- To monitor and predict therapeutic response