CH1-CHEST

Myocardial Perfusion Scintigraphy With Exercise And Pharmacological Stress

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Introduction

Cardiac studies including myocardial perfusion scintigraphy was begun in the Singapore General Hospital, Nuclear Medicine Department in 1983. From a few patients per year using planar imaging, we have in 1994 studied 1500 patients for myocardial perfusion, using mainly SPECT (Single-photon emission computerised tomography) and radionuclides such as Thallium-201, Technetium-99m sestamibi and Tc-99m tetrofosmin. Patients have been stressed using treadmill exercise or pharmacological agents; we have used dipyridamole, and dobutamine for pharmcological stress but have no experience with intravenous adenosine. Since we do not possess a PET (positron emission tomography) camera, we have no experience in Singapore with the use of PET tracers such as Fluorine-18 fluorodeoxyglucose (FDG) or Carbon-11 labelled fatty acids, though these are metabolic tracers rather than perfusion radiopharmaceuticals. Similarly, though we use Tc-99m pyrophosphate for localising clinically doubtful infarcts, we have not had access to Indium-111 labelled antimyosin antibody to enable infarct-avid imaging. However multigated angiography (MUGA) scans using technetium-labelled red blood cells (RBC) for ventricular function have been performed at rest and with exercise over the last 12 years, in the Department.

Radionuclides

Ideal perfusion tracer:

- distribute in myocardium in proportion to blood flow over the range of values in health and disease.
- extracted efficiently from blood by myocardium on its first pass through the heart.
- remain in the myocardium for the period of data acquisition.
- rapid elimination from the body, post acquisition, to allow repeat studies.
- high photon flux with energy 100-200 keV.
- low radiation dose to patient.
- easily available and cheap.

Thallium-201

Thallium-201 has been used for myocardial perfusion scintigraphy for more than fifteen years. It is a potassium analogue with physical half-life (T½) of 73 hours and main gamma emission of 69-80 keV. Entry into myocardium is about 4% of injected dose, and Thallium-201 enters into the cardiac myocyte largely by active transport using the Na-K ATPAse dependent exchange mechanism. The distribution in the myocardium is proportional to blood flow over a wide range of values. After i.v. injection at stress, there is progressive redistribution. Hence imaging must begin within 5 -10 minutes of injection and repeat imaging is done at 4 hours; in infarcted myocardium there is a lack of redistribution, while in ischaemic (hibernating) myocardium there is redistribution. Thallium-201 imaging with exercise or pharmacological stress is good for assessment of myocardial viability. In many centres a re-injection of a small dose (1.5mCi) is done to confirm viability of myocardium. The radiation burden of Thallium-201 is high and hence the increased tendency to use technetium-99m labelled radiopharmaceuticals.

Technetium-Labelled Isonitriles

Sestamibi (2-methoxy-isobutyl-isonitrile) has the best myocardium to background ratio. The radiation dose to the patient is low, while the image resolution is better due to good count statistics. The tracer diffuses passively through the capillary membrane, and after crossing the myocyte cell membrane along the electropotential gradient, it localises in the mitochondria at high concentration. There is rapid blood clearance of sestamibi and no significant redistribution. Due to the good count-density it is possible to do first-pass radionuclide ventriculography, as well as to gate the acquisition using 'R' wave of the ECG, and hence regional wall motion and wall thickening of LV can be studied.

Separate injections of tracer need to be given for

stress and rest studies; thus one can study patients using a two-day protocol or a same day protocol either doing rest-stress or stress-rest imaging. It is also possible to do dual isotope SPECT combining Thallium and sestamibi using different energy windows. There are quantitative programmes (e.g. C-equal) to estimate size of perfusion defects and extent of reperfusion if any. Sestamibi has an added advantage that it can be used in the acute infarction situation, since imaging can be delayed post-injection. We have assessed the value of sestamibi imaging in acute infarctions treated with rTPA and are presently evaluating sestamibi imaging for acute infarction pre and post emergency PTCA.

Technetium-99M Diphosphine Complexes (Tetrofosmin)

- similar to sestamibi.

Technetium-99M teboroxime

- boronic acid adducts with Technetium-99m dioxime.
- lipophilic and passive diffusion into myocyte.
- rapid washout.

Pet Perfusion Tracers

Rubidium-82 and Nitrogen-13 Ammonia are PET tracers that allow blood flow to the myocardium to be studied. The images are of better resolution and it is possible to do attenuation correction. Other PET tracers such as Fluorine-18 fluorodeoxyglucose (FDG) and Carbon-11 labelled fatty acids have been used to study myocardial metabolism. FDG in particular is useful to identify viable myocardium using FDG/flow mismatch.

Treadmill Exercise

We use a modified Bruce protocol that starts with a speed of 1.7 mph a gradient of 10 degrees increasing every 3 minutes by 0.8 mph and by 2° in gradient. Some centres employ a supine bicycle exercise protocol. The complication rates from exercise tests is about 0.01%. Exercise is to be avoided in patients with active inflammation/ infection of the heart, or when unstable cardiac conditions are present (e.g. unstable angina, left main stem disease, heart failure serve valve disease, severe pulmonary or systemic hypertension), or when severe arrythmias are likely to be provoked. The exercise test for myocardial perfusion scanning aims at achieving the greatest amounts of stress within the limits of safety. False negative results will occur in some patients with coronary artery disease due to submaximal stress.

Pharmacological Stress

Dipyridamole and Adenosine

This is done for patients who are unable to do bicycle or treadmill exercise due, example for, to severe bone/joint lower limb disease, leg claudication, physical handicap, or unwillingness to exercise.

Most of our experience is with the use of dipyridamole a vasodilator like adenosine; adenosine mediates the cellular action of dipyridamole and can be given directly intravenously. Both these drugs produce mild increase in heart-rate and mild to moderate fall in blood pressure. Dipyridamole is given i.v. at a rate of 0.56 mg/kg over a 4 minute period followed 4 minutes later by the Thallium or Technetium-99m sestamibi. The hyperemic response produced by the vasodilator, reduces the flow reserve in arteries with fixed stenosis and thus a relative 'steal' in blood flow may induce ischemia. Side-effects are flushes, headaches, chest-pain, diziness and epigastric discomfort with nausea. These side-effects are readily reversed by intravenous aminophylline. Patients with evidence of Asthma should not be tested with dipyridamole while caffeine and methylxanthines should be avoided for 12-24 hours as these interfere with the coronary vasodilation of dipyridamole and adenosine.

Dobutamine

Dobutamine is a beta-agonist which increases myocardial oxygen demand though combined inotrophic and chronotrophic actions; it also provokes myocardial ischemia by dilating the distal coronary vessels, leading to increased coronary flow and a fall in perfusion pressure distal to coronary stenoses. The drug is given as an infusion and the dose given is 10 μg/kg/min and increased in 10 μg/kg/min step every 3 minutes up to a maximum dose-rate of 40 μg/kg/min. Symptoms include flushes, nausea, headache and light-headadress. Side-effects are supraventricular tachycardia, atrial fibrillation and premature ventricular and atrial beats. Hypotension may occur; dobutamine is safe in Asthma.

Both dobutamine and dipyridamole have given excellent results with Thallium-201 and Tc-99m sestamibi myocardial perfusion imaging, similar to exercise stress.

Artifacts

1. breast attenuation.
2. diaphragmatic attenuation.
3. overlying abdominal visceral activity.
4. apical variation.
5. myocardial 'hot' spots.
6. LBBB (left bundle branch block).
7. myocardial hypertrophy.

In summary myocardial perfusion scintigraphy using exercise/pharmacological stress has a higher sensitivity for detecting coronary artery disease (CAD) (80%) and a higher specificity (92%) for excluding CAD compared to the exercise ECG, using the angiographic gold standard of 50% stenosis as comparison. It is also possible to indicate the extent of disease and the severity is further confirmed by noting increased pulmonary uptake of tracer or transient ischemic dilation of the left ventricle.