Clinical review

Recent developments in non-invasive cardiology

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Tremendous advances have been made in non-invasive cardiology, such as improved visualisation of the anatomy and function of the heart and better physiological markers of cardiac function and heart disease. These advances provide better diagnostic information and guide therapy and risk stratification. All the techniques give information over and above that derived from the clinical history and examination, but should be interpreted in the context of the clinical background. In this review, we discuss important developments in non-invasive cardiology, focusing on areas that have recently come into clinical use.

Sources and selection criteria

We searched PubMed for recent trials and systematic reviews on non-invasive cardiac imaging published between 2000 and July 2004. We also consulted recent international guidelines to develop an overview of the evidence base in non-invasive cardiology.

Cardiovascular magnetic resonance imaging

Cardiovascular magnetic resonance imaging has improved the detection of heart disease. Accurate diagnosis provides the basis of treatment options and of monitoring response to treatment. It also gives important prognostic information that can be difficult to glean from the history and examination alone. Conventional procedures such as echocardiography often produce suboptimal images due to poor echo windows with limited spatial resolution. In particular, the apex of the left ventricle is difficult to visualise, resulting in missed diagnoses such as apical hypertrophic cardiomyopathy.¹ X ray angiography is invasive and associated with morbidity and mortality as well as exposure to ionising radiation. Cardiovascular magnetic resonance yields high resolution, high contrast images by mapping the radio signals absorbed and emitted by hydrogen nuclei in a powerful magnetic field. No x rays are involved. The contrast agent gadolinium is sometimes used to increase the signal. Gadolinium is safe, even in patients with severe renal failure. Scans can be oriented in any plane of the body and are not limited by acoustic windows. Because of its three dimensional nature, magnetic resonance imaging has become the ideal method for measuring ventricular mass and volume.² Some patients are not suitable for the procedure, such as those with cardiac pacemakers or defibrillators. Scanning should also be

Recent advances

Cardiovascular magnetic resonance imaging is the newest technique for non-invasive cardiology

It assesses cardiac function, mass, and volume and can detect myocardial infarction and fibrosis

Computed tomography is used to quantify coronary calcium, high scores being related to increased risk, but its use remains controversial

Myocardial perfusion scintigraphy single photon emission computed tomography is cost effective in investigating patients with suspected coronary disease

Ambulatory blood pressure monitoring is now a valuable technique for guiding practice in hypertension

The level of B natriuretic peptide increases with ventricular dysfunction, thus providing prognostic information

avoided in patients with metallic fragments near a vital structure, such as the retina, or with brain aneurysm clips. Patients with claustrophobia may be difficult to scan, although small doses of benzodiazepine can help. Pregnant women can be scanned, although preferably not in the first trimester.

Cardiovascular magnetic resonance imaging has a rapidly increasing role in cardiology (box 1) and is routinely used to assess anatomy, cardiovascular function, and blood flow. It is also valuable in angiography, where it has supplanted invasive techniques other than for assessing the coronary circulation.

Infarction and viability

Gadolinium accumulates in myocardial scar and fibrotic tissue and provides high resolution images, something that has never before been possible in vivo. Myocardial infarction can be detected with exquisite sensitivity, which has the potential to improve the management of chest pain syndromes (fig 1) and to predict

Additional figures and advances in echocardiography, cardiomyopathy, and non-invasive ambulatory blood pressure monitoring are on bmj.com

functional improvement after revascularisation.³ Emerging practical applications include adjudication when other techniques give equivocal results (for example, borderline abnormal results on electrocardiography, minor motion wall abnormalities on echocardiography), and the assessment of myocardial viability.⁴⁻⁵ These findings correlate well with positron emission tomography⁶ but without the drawbacks of poorer spatial resolution, cost, and radiation. Such studies should be considered when there is uncertainty about previous infarction or about the benefits of revascularisation.

Coronary angiography

The role of magnetic resonance imaging in the detection of coronary disease and characterisation of atheroma is still under investigation, but shows promise. Around 72% of patients have been accurately diagnosed as having any coronary artery disease and 87% as having left main vessel or three vessel disease.⁷ Uniquely, cardiovascular magnetic resonance can be used to examine the composition and size of carotid and coronary plaques and has the potential to identify plaques vulnerable to rupture.⁸ Cardiovascular magnetic resonance is now used to identify the course of anomalous coronary arteries, which are associated with sudden death, and for this application the technique is regarded as the ideal.⁹ It is not recommended for routine detection of coronary artery disease as its spatial resolution is inferior to that of coronary angiography.

Myocardial perfusion imaging

Perfusion cardiovascular magnetic resonance imaging is being developed. This involves fast imaging of the myocardium during the passage of a bolus of gadolinium. The procedure takes less than 20 minutes, involves no ionising radiation, and has much higher resolution than conventional techniques such as scintigraphy single photon emission computed tomography and positron emission tomography. In a study of

Fig 1 Gadolinium enhanced images of patient with lateral wall myocardial infarction. Four chamber view of heart (A), with bright signal in lateral wall of left ventricle (LV). Signal results from gadolinium late enhancement as result of accumulation of contrast agent in scar tissue. (B) Corresponding short axis cut through left ventricle

patients with angina but with normal coronary arteries (syndrome X), subendocardial perfusion gave abnormal results with cardiovascular magnetic resonance imaging but not with scintigraphy single photon emission.¹⁰ Perfusion imaging may lead to better diagnosis and treatment of patients with normal coronary angiograms (10-20% of coronary angiograms). Early work on perfusion cardiovascular magnetic resonance imaging in coronary disease seems promising.¹¹

X ray computed tomography in ischaemic heart disease

Computed tomography is another area being assessed for non-invasive assessment of the coronary circulation. It is highly sensitive to calcium, a marker of atherosclerosis.¹² Computed tomography generates an index of coronary calcification—the total coronary artery calcium score. This index is being used for the early detection of asymptomatic coronary atherosclerosis and, more recently, for risk stratification in established coronary disease. Computed tomography may also be used for coronary angiography. The results are similar to cardiovascular magnetic resonance imaging, but clinical application remains to be defined.

Fig 2 Computed tomography image of left and right coronary artery coming off aortic root

Box 1: Current clinical applications of cardiovascular magnetic resonance imaging

- General—measurement of cardiac volume and function; if echocardiography is unsatisfactory
- Great vessels—accurate sizing; detection of dissection, coarctation, stenosis; anomalous vessels
- Congenital heart disease—check for concordance of atrioventricular or ventriculoarterial connections; check for great vessels connections; assessment of conduits; assessment of complex anatomy
- Ischaemic heart disease—detection of regional wall motion abnormalities or infarction; assessment of viability
- Cardiomyopathy—identification of hypertrophic cardiomyopathy, dilated cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy; detection of fibrosis or scarring; risk stratification; quantification of iron overload in thalassemia
- Left ventricular mass—accurate assessment in hypertension; assessment of response to therapy
- Valvular disease—quantification of regurgitation
- Pericardium—assessment of thickening
- Cardiac masses—characterisation of tissue; assessment of extent of tumour

Fig 3 Nuclear perfusion scan showing noticeably impaired perfusion in all territories except for basal septum. Results also offer quantitative analysis of left ventricular volume and estimation of ejection fraction

Arterial calcification is an integral part of atherosclerosis, and the extent of calcium is related to the burden of atheroma (fig 2). The higher the calcium score the more likely is coronary stenosis, although the sites of the greatest calcium deposits are not usually the site of stenosis. Coronary calcium therefore cannot be used to locate stenosis when planning revascularisation. The number of vulnerable plaques, however, rises with increasing atheroma burden, and therefore the calcium score may be expected to predict cardiac events. A key limitation is that a lack of calcium does not exclude the presence of active atherosclerosis in an artery, as shown in hearts during autopsy when “soft” vulnerable plaques and severe coronary artery stenosis may be present even in the absence of calcium.¹³ Studies have shown an increased rate of cardiac events in asymptomatic patients with a high calcium score (>400; scores of 100-400 represent intermediate risk and those of 0-100 a low risk).¹⁴ This area remains controversial.¹⁵ Current guidelines recommend more work in this area and suggest that computed tomography is

Box 2: Key ongoing clinical trials

- UK natriuretic peptide study—pragmatic multicentre study of the diagnostic value of measuring plasma B type natriuretic peptide in patients with suspected heart failure in primary care
- Multiethnic study of atherosclerosis (MESA)—National Institutes of Health led 10 year multicentre study to evaluate electron beam computed tomography and other imaging techniques for the prediction of coronary heart disease risk in healthy people
- Risk factors, evaluation of coronary calcium and lifestyle (RECALL) study—population based, prospective cohort study of the relative risk associated with the extent of coronary atherosclerosis measured by EBCT-derived calcium scores for myocardial infarction and cardiac death in 4200 unselected people
- Beyond endorsed lipid lowering with EBCT scanning (BELLES)—study of the effect of 12 months’ treatment with lipid lowering drugs on total coronary calcium score

not yet suitable for widespread population screening.¹⁶ Computed tomography is being used in some screening programmes to reassure patients with low coronary calcium scores. The cost effectiveness of this approach is being evaluated. In patients with high scores, aggressive modification of risk factors and further investigations such as myocardial perfusion scintigraphy single photon emission computed tomography are appropriate.

Nuclear cardiology

A difficult challenge in clinical practice is evaluating the differential importance of coronary lesions in patients with multivessel disease. Single photon emission computed tomography (SPECT) is the current standard for assessing the haemodynamic effects of coronary stenoses. It relies on the difference in distribution of a radioactive tracer, such as thallium, at rest and after stress. In patients with myocardial ischaemia, uptake of tracer is reduced after stress and improves at rest. Single photon emission computed tomography is more specific and sensitive in the diagnosis of ischaemia than is exercise electrocardiography, and the extent and severity of the abnormality is strongly predictive of future cardiac events. This information can be used to direct revascularisation strategies such as angioplasty or bypass surgery. Single photon emission computed tomography is also useful in the non-invasive evaluation of patients, particularly women, with equivocal or suboptimal exercise test results.

Major advances have been recently implemented with single photon emission computed tomography. Firstly, image gating has allowed the simultaneous assessment of perfusion and wall motion by linking cardiac motion to each point in the cardiac cycle on the electrocardiogram. This improves specificity in areas affected by attenuation artefacts, while providing information on ventricular volumes and function.¹⁷ Secondly, cost effectiveness is now established, and strategies that include the technique early in the work-up of patients with suspected coronary disease have been shown to be beneficial in terms of clinical outcome and cost.¹⁸ Thirdly, recent work has established the technique’s benefit in avoiding unnecessary admissions to hospital in patients with acute coronary syndromes,¹⁹ and the acceptance that normal or near normal perfusion results usually obviate the need for invasive coronary angiography because of low hard annual event rates of <1% (fig 3). In contrast, patients with abnormal scans have a 12-fold greater annual event rate (7.4%).²⁰

B natriuretic peptide in heart failure

Diagnosis in patients with suspected heart failure can be difficult, particularly when echo access is limited. Follow up of patients to determine therapeutic response is also problematic. B natriuretic peptide is a neurohormone secreted primarily by myocytes in response to volume expansion and pressure overload, and it plays a key part in circulatory homeostasis.²¹ The plasma level of B natriuretic peptide is high (>100 pg/ml) in patients with ventricular dysfunction,²² and this enables the differentiation between

Additional educational resources

Review papers

Chronic heart failure: national guidelines for diagnosis and management in primary and secondary care. Developed by the National Collaborating Centre for Chronic Conditions at the Royal College of Physicians. 2003 www.rcplondon.ac.uk/pubs/books/CHF/heartfailure.pdf

Budoff MJ, Achenbach S, Duerinckx A. Clinical utility of computed tomography and magnetic resonance techniques for noninvasive coronary angiography. *J Am Coll Cardiol* 2003;42:1867-78

Underwood SR, Anagnostopoulos C, Cerqueira M, Ell PJ, Flint EJ, Harbinson M, et al. Myocardial perfusion scintigraphy: the evidence. *Eur J Nucl Med Mol Imaging* 2004;31:261-91

Websites

Society for Cardiovascular Magnetic Resonance (www.scmr.org)—background information for the use of cardiovascular magnetic resonance imaging

American Society for Echocardiography (asecho.org)—excellent website offering information on echocardiography to both healthcare professionals and the public

American Society of Nuclear Cardiology (www.asnc.org)—comprehensive and well designed website with links to further educational resources in the specialty of nuclear cardiology

Information for patients

British Heart Foundation (www.bhf.org.uk)—website designed for the public as well as for cardiologists interested in cardiovascular research

Cardiomyopathy Association (www.cardiomyopathy.org)—support group for patients with cardiomyopathy

American Heart Association (www.americanheart.org)—website providing a plethora of resources on common cardiac conditions and on managing risks associated with cardiac disease

pulmonary and cardiac causes of dyspnoea.²³ B natriuretic peptide is also a powerful marker of the severity heart failure and its prognosis (see fig C on bmj).²⁴ It has been used to monitor the efficacy of heart failure therapy²⁵ and to predict the success of β blocker treatment.²⁶ Simple assays are now available, at low cost. Work is underway to determine the value of B natriuretic peptide for heart failure in primary care and for emergency diagnosis.²⁷⁻²⁸ Recently published work has also demonstrated the cost-effectiveness of B natriuretic peptide screening in asymptomatic men over the age of 60.²⁹

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