Current Use and Emerging Trends of Cardiac Imaging with Computed Tomography and Magnetic Resonance Imaging

a report by

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Objectives of Cardiac Imaging

Chest pain is the most frequent cause of emergency department visits in the US, and adverse cardiac events (ACEs) (cardiac death, myocardial infarction, unstable angina, surgical or percutaneous coronary revascularisation) are the most prevalent cause of morbidity and mortality in the Western world. Therefore, establishing obstructive coronary artery disease (CAD) as the cause of chest pain and identifying subclinical coronary artery disease that is likely to progress to the symptomatic (angina) stage or to become the substrate of an ACE are important objectives of cardiac imaging.

Currently Available Imaging Modalities

Invasive, catheter-based coronary angiography using various modes of access to the vascular system is the standard for direct visualisation of obstructive CAD and has been in use since 1959. All non-invasive or minimally invasive stress imaging modalities such as echocardiography, single photon emission computed tomography (SPECT) or positron emission tomography (PET) rely on indirect signs such as reduced perfusion reserve or stress-induced regional myocardial dysfunction to diagnose obstructive CAD from the ischaemia that blood-flow-limiting (significant) coronary stenoses cause. These imaging modalities generally cannot diagnose subclinical CAD that has not yet progressed to significant stenoses (usually defined as more than 70% to 75% of the diameter of a reference segment). Also, none of the invasive or non-invasive imaging techniques can predict the risk of future ACEs reliably.

Technical improvements of computed tomography (CT) and magnetic resonance imaging (MRI) have allowed their clinical use for structural or functional imaging of the heart since the early 1990s. MRI and CT have distinct strengths and weaknesses in imaging of the cardiovascular system, and the choice between the modalities currently depends on the clinical question to be answered. Their ability to directly but minimally invasively image the coronary arterial tree has generated wide interest.

Currently, two different CT modalities are in use for cardiac imaging. Electron beam CT (EBCT) scanners use no mechanically rotating parts for image generation, allowing high temporal resolution. As the first CT technique suitable for cardiac imaging, EBCT is the standard, owing to validation studies beginning in 1984. However, EBCT is not widely available (approximately 200 scanners in the US) because of its limited value in scanning organs other than the cardiovascular system. Multislice CT (MSCT) uses mechanically rotating gantries, acquiring multiple (currently up to 16) images of high spatial resolution and low image noise simultaneously with every rotation. MSCT scanners have been available since 1999 and are widely used as body scanners (approximately 2,000 scanners in the US). The radiation dose received by the patient in cardiac MSCT studies is higher than that received in cardiac EBCT studies.

Cardiac Imaging with CT and MRI

Cardiac CT Imaging

Currently, the main uses of cardiac CT are for

coronary artery calcium (CAC) scanning and CT coronary angiography (CTCA). CAC scanning does not require administration of iodinated contrast medium and is performed either to establish obstructive CAD as the cause of chest pain in symptomatic patients or to estimate the prognosis for having a future ACE in asymptomatic patients (screening). CAC represents coronary atherosclerotic plaque and is quantified as Agatston or volume scores. It is controversial whether CAC scores derived from EBCT and MSCT scanners are equivalent.

**CAC Scanning**

**Diagnosis of Obstructive CAD**

Because of a biologic mechanism called ‘vascular remodelling’, not all coronary plaque results in significant stenoses. However, high CAC scores indicate high coronary plaque burden that is likely to have overwhelmed the vascular remodelling capacity and to have resulted in significant stenoses. This use of cardiac CT imaging for the diagnosis from CAC scores of obstructive CAD as the cause of chest pain is well validated and sensitive, but it requires use of age- and sex-specific threshold values of CAC scores to be acceptably specific. An Expert Consensus Document issued in 2000 by the American Heart Association (AHA) and the American College of Cardiology (ACC) did not endorse the use of CAC scanning for the diagnosis of obstructive coronary artery disease because of low specificity.

**Prognosis for Asymptomatic Patients**

The majority of ACEs occur not as a result of chronic, significant coronary stenoses, but as a result of the rupture of so-called vulnerable or unstable plaque that leads to acute coronary arterial thrombosis. Vulnerability or instability of plaque is a biologic feature, and no clinically used imaging modality can reliably identify coronary plaques prone to rupture. In particular, the histologic relationship between CAC and unstable plaque is not clear, but high CAC scores indicating high coronary plaque burden may indirectly imply the associated presence of unstable plaque. The use of CAC scanning for the screening of asymptomatic patients is controversial. Recent retrospective, non-randomised studies suggest that high CAC scores, or CAC scores exceeding the 75th percentile of the normal distribution of CAC for age and sex, are associated with an up to 22-fold increased risk of ACEs. The 2000 AHA/ACC Consensus Document deems appropriate selective use of CAC scoring in patients with intermediate risk on the basis of classic coronary risk factors.

**CTCA**

CTCA requires intravenous administration of iodinated contrast medium at a volume higher than needed for invasive, catheter-based coronary angiography. Image quality can be limited by the small calibre of distal coronary branches, blurring artifact due to cardiac motion and presence of coronary calcification. Some centres administer pharmacologic agents to reduce the heart rate before CTCA to maximise image quality. Typically, 80% to 90% of the major epicardial coronary arterial branches can be imaged in diagnostic quality (see Figure 1). Sensitivity and specificity exceeding 90% have been reported for identifying significant coronary stenoses with the newest generation of scanners for those coronary segments that could be imaged in diagnostic quality. CTCA is also useful to establish patency of previously placed coronary artery bypass grafts.
and to identify the proximal course of congenitally abnormal coronary arteries.13

**Cardiac MRI**

Cardiac MRI may be used for imaging cardiac anatomy and function and blood flow in the large vessels near the heart in patients with congenital heart disease or valvular heart disease. The main uses of MRI in patients with CAD are stress imaging and viability studies.

**Cardiac Stress MRI**

Cardiac MRI without stress and during stress induced by physical exertion or intravenous injection of dobutamine can be performed to diagnose significant coronary stenoses on the basis of stress-induced regional myocardial dysfunction. This use of MRI is similar to stress echocardiography. Dobutamine MRI is logistically difficult because it requires MRI-safe (i.e. non-ferromagnetic) equipment (infusion pump, exercise device). Dobutamine MRI may provide better image quality than echocardiography in certain patients (for example patients with lung disease), but cannot be performed in patients unable to tolerate lying in enclosed spaces. Sensitivity and specificity for identifying significant coronary stenoses comparable with or better than exercise echocardiography have been reported.14

**MRI Viability Imaging**

MRI of the myocardium late (15–20 minutes) after administration of an intravenous bolus of gadolinium contrast medium can aid decision-making on percutaneous or surgical coronary revascularisation of patients with global or regional left ventricular dysfunction. Gadolinium is an extracellular agent that is quickly washed in and washed out of structurally normal myocardium. However, gadolinium contrast enhancement is prolonged in irreversibly damaged (non-viable) myocardium (see Figure 2). Late myocardial enhancement predicts with high accuracy the lack of functional myocardial recovery after revascularisation. It identifies patients in whom revascularisation may not be indicated.15

**Future Directions of Cardiac Imaging with CT**

The most promising future directions of cardiac CT are serial quantification of CAC progression and plaque imaging.

**Serial Quantification of Coronary Calcium Progression**

Measuring the CAC score serially at intervals of one to two years may serve two purposes: assessment of the adequacy of risk factor control; and prognostication.

Primary modification of elevated cholesterol values decreases the incidence of clinical ACEs. Adequate
control of low-density lipoprotein cholesterol levels decreases the annual progression of CAC, indicating a slowing of the progression of coronary atherosclerosis. Therefore, progression of CAC at a high rate might suggest the need for more aggressive pharmacologic and non-pharmacologic risk factor modification. However, there is no data to prove that this use of CAC scanning to monitor the efficacy of risk factor control is clinically relevant (i.e. affects the incidence of ACEs). Nevertheless, the 2000 AHA/ACC Consensus Document considers this approach to be promising.

The rate of progression of CAC might be an indicator of the degree of activity of CAD in individual patients. Clinical studies currently investigate whether the relative progression of CAC over time is an indicator of the risk of having ACEs more powerful than the absolute quantity of CAC measured at a single time.

**Plaque Imaging with Cardiac CT**

CTCA with intravenous administration of contrast medium can demonstrate non-calcified atherosclerotic plaque. Some investigators argue that non-calcified plaque could be more likely to rupture and cause ACEs than plaque that is stabilised by calcification. Therefore, non-calcified plaque diagnosed by CTCA could be a predictor of the risk of having ACEs. From comparative studies with catheter-based, invasive intravascular ultrasonography, minimally invasive CTCA can classify non-calcified plaques into soft and intermediate (fibrotic) plaque. However, the relationship between soft or intermediate plaque imaged by CTCA and biologically unstable plaque that is prone to rupture is not established.

**Future Directions of Cardiac Imaging with MRI**

The two most promising future directions of cardiac MRI are myocardial perfusion measurement and plaque imaging.

**Myocardial Perfusion Measurement with Cardiac MRI**

Analysing the signal intensity in myocardial MRI images over time after administration of a bolus of gadolinium can allow qualitative and at least semiquantitative assessment of myocardial perfusion. The use of MRI for myocardial perfusion measurement requires pulse sequences with high temporal resolution and fitting of the measured signal intensity curve to complex mathematical models. Despite its complexity, MRI myocardial perfusion measurement at rest and during induced stress can indirectly demonstrate the presence of significant coronary stenoses. New contrast agents, pulse sequences and image acquisition and post-processing techniques are expected to improve the ability to measure myocardial perfusion by MRI. MRI myocardial perfusion measurement may complement CTCA for comprehensive minimally invasive evaluation of the heart by cross-sectional imaging.

**Plaque Imaging with Cardiac MRI**

The high contrast resolution of MRI allows differentiation among various plaque components by biophysical and biochemical features such as chemical composition and water content. The development of molecular MRI imaging may further

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facilitate identification of plaque constituents and biologic correlates at risk of rupture. Various contrast agents may accumulate passively in certain cell types or bind actively and specifically to certain cellular biomarkers. For example, ultrasmall superparamagnetic particles can identify the presence of macrophages in unstable plaque. Early work in a tumor model has been reported on imaging, using monoclonal antibody-conjugated contrast agents, cell surface proteins similar to those up-regulated in vascular wall segments prone to developing atherosclerosis. These and similar methods will be important to improve the understanding of the biologic activity in and the identification of coronary plaques prone to rupture.

Cost-effectiveness of New Cardiac Imaging Modalities

The future use of cardiac CT and MRI depends not only on their sensitivity and specificity in diagnosing obstructive CAD and their ability to predict ACEs, but also on their cost–benefit ratio. Little data is available on the cost-effectiveness of cardiac CT and MRI.

A few studies have suggested that, in patients with low to intermediate pretest probability of CAD, CAC scanning as the initial non-invasive test can be a more cost-effective pathway for identifying patients in need of invasive coronary angiography to identify significant coronary stenoses than traditional diagnostic pathways, especially those beginning with treadmill exercise testing. Similarly, absence of CAC on CT scanning may save costs by reliably identifying patients who do not need expensive invasive coronary angiography despite suggestive history and stress testing.

There is substantial interindividual variability in the extent of the vascular atherosclerosis that develops in the presence of classic risk factors, suggesting a genetic basis for the susceptibility to these risk factors. Among patients with risk factors for CAD, detection of subclinical CAD by CAC scanning may allow focusing aggressive primary risk factor modification with expensive pharmacologic agents on those patients who are at highest risk of developing advanced vascular disease.

Initial detection of subclinical CAD could potentially decrease the cost of cardiovascular morbidity and mortality to society by identifying patients in whom disabling ACEs can be prevented or postponed by risk factor modification. Serial CAC scanning might aid in this approach by monitoring the effect of lifestyle modification or pharmacologic intervention in delaying CAD progression. However, such potential unproven benefits must be weighed against the cost of broad population-based application of cardiac CT or MRI, especially if performed in combination with each other, as proposed by some authors.

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