CCS / CAR / CANM / CNCS / Can SCMR
Joint Position Statement on
Advanced Non-invasive Cardiac Imaging using
Positron Emission Tomography, Magnetic Resonance Imaging and
Multi-Detector Computed Tomographic Angiography
in the Diagnosis and Evaluation of Ischemic Heart Disease

Canadian Cardiovascular Society, Canadian Association of Radiologists
Canadian Association of Nuclear Medicine, Canadian Nuclear Cardiology Society, Canadian Society of Cardiac Magnetic Resonance

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Abstract

Background: In decades, advanced imaging modalities with excellent diagnostic capabilities, have emerged. The aim of this position statement was to systematically review existing literature to define Canadian recommendations for their clinical use.

Methods: A systematic literature review to 2005 was conducted for positron emission tomography (PET), multi-detector CT angiography (MD-CTA) and magnetic resonance imaging (MRI) in ischemic heart disease. Papers meeting criteria were reviewed for accuracy, prognosis data and study quality. Recommendations were presented to a primary and secondary panel of experts where consensus was achieved.

Results: Indications for PET include detection of CAD with perfusion imaging, and viability using FDG to define LV function recovery and/or prognosis after revascularization (Class I). Detection of CAD in patients, vessel segments and grafts using CT angiography is considered Class IIA at the time of the literature review. Dobutamine MRI is 'Class I' for CAD detection and, along with late gadolinium enhancement (LGE) MRI, Class I for viability detection to predict LV function recovery. Imaging must be performed in institutions and interpreted by physicians with adequate experience and training.

Conclusions: Cardiac imaging using advanced modalities (PET, MD-CTA, MRI) is useful for CAD detection, viability definition and in some cases prognosis. These modalities complement the more wide-spread SPECT and echocardiography. Given the rapid evolution of technology, initial guidelines for clinical use will require regular updates. Evaluation of their integration in clinical practice should be ongoing. Optimal use will require proper training. *A joint effort among specialties is recommended to achieve these goals.*

Overview

Cardiovascular disease is the leading cause of mortality and a major cause of morbidity for Canadians. Non-invasive methods for diagnosis and risk stratification remain the cornerstone of management of patients with heart disease. Over the past few decades, advanced imaging modalities have emerged with excellent diagnostic capabilities. However these techniques are costly and require specific advanced training. While several professional organizations and governments have established recommendations for advanced imaging technologies, (1-4) Canadian recommendations had not previously been developed. The aim of this position statement is, therefore, to systematically review the existing literature so as to recommend indications for the clinical use of these modalities, and to define areas requiring further research and investigation.

The Canadian Cardiovascular Society (CCS), Canadian Association of Radiologists (CAR), Canadian Association of Nuclear Medicine (CANM), Canadian Nuclear Cardiology Society (CNCS), and the Canadian Society of Magnetic Resonance (CanSCMR) had each identified advanced cardiac imaging as a priority for assessment. Primary and secondary panels of experts and practitioners were assembled. (Appendix 1) Given the scope and timelines, it was agreed that this position paper would focus on ischemic heart disease (IHD) (detection, prognosis and viability), with future position statements and/or guidelines focusing on ventricular function and non-ischemic heart disease.

Methods

Search Method for Identification of Studies

A systematic literature review was conducted for the three imaging modalities: positron emission tomography (PET), magnetic resonance imaging (MRI) and multi-detector CT angiography (MD-CTA). Searches for each modality were divided into four categories: Coronary artery disease (CAD) and/or ischemia detection and diagnosis; CAD prognostication; myocardial viability detection; and viability prognostication. A systematic search of the literature, using validated BMJ filters for diagnosis and prognosis, was used to identify the best evidence for use of PET, computed tomography (CT) and MRI. A total of 3,655 references were reviewed. Databases searched were Medline (1966 to June 2005); Embase (1980 to June 2005); and Cochrane, Issue 3 2005; as well as other evidence based medicine (EBM) sites such as that of the Agency for Healthcare Research and Quality (AHRQ). Where a published meta-analysis existed, searches were started from this point forward. MRI was limited to 2004–2005, due to a meta-analysis by Danias, P (1991–Jan 2004 covered) (5). Searches for viability 'detection' using PET were limited to 2001–June 2005 (systematic review by Bax J ; covered up to 2001) (6) and prognosis using viability PET were limited to 2001–June 2005 (meta-analysis by Allman. (7))

For each topic, further exclusions such as size of study and method of imaging were added in areas where there were a very large number of studies. This allowed for practical and accurate review of the best work. Other studies that may have been missed by the systematic review were identified through cross-referencing of identified articles and literature review after June 2005. Lists of titles and abstracts that met search inclusion criteria were provided to the subgroups and reviewed to confirm that they met inclusion criteria. Full manuscripts that met inclusion criteria were circulated to the subgroup teams for review. The imaging subgroups updated literature beyond the primary search strategy time period when key references were identified that met inclusion criteria.

All members of the subgroup reviewed the papers for their specific modality. Sensitivity and specificity tables were completed. The study quality of each paper reviewed was assessed by subgroup members using the quality information questionnaires from the University of Alberta Evidence Based Medicine (EBM) Working Group: http://www.med.ualberta .ca/ebm/diagworksheet.htm; and http://www.med.ualberta.ca/ebm/prognosisworksheet.htm.

Based on the data review, preliminary draft recommendations were prepared and presented to the primary and secondary panels using the standard scoring methods adapted from previous guidelines on imaging from the American College of Cardiology (ACC), The American Heart Association (AHA) and the American Society of Nuclear Cardiology (ASNC). (Appendix 2) Following this, the recommendations were consolidated by the primary panel and circulated to the secondary panel for review and feedback. These recommendations and the document were then finalized by the panels and submitted to the executives of the participating organizations for approval.

Positron Emission Tomography

Given the large number of studies using PET, additional restrictions on search material were applied. For CAD detection, studies were excluded if they involved tracers other than Rb-82 and N-13–ammonia, applied flow quantification as the only method for defining disease, or involved fewer than 20 patients. For prognosis, only studies that considered PET findings in the prediction of outcomes were considered.

Detection and prognosis of coronary disease: Myocardial perfusion imaging (MPI) using Rb-82 or N-13-ammonia PET is a widely accepted technique. (1,2) Images are acquired at rest and during pharmacological stress. PET MPI has often been considered the most accurate non-invasive means for detecting functionally significant coronary disease. (1,2, 8-10) It is considered to be at least as accurate as single photon emission computed tomography (SPECT) MPI.

Diagnosis: Standard relative MPI uses perfusion radiotracer uptake relative to the maximum uptake in the heart to detect regional reductions. These defects in tracer uptake are indicative of functionally significant CAD. This principle is the same for PET and SPECT imaging. One advantage of PET MPI is the use of accurate and reliable attenuation correction that improves specificity and probably also sensitivity. This feature may be particularly relevant in patients with obesity or a body habitus prone to attenuation artifact. PET also provides high spatial resolution among nuclear imaging techniques. (11) Gating of PET MPI (and ^{18}F-fluorodeoxyglucose (FDG)) provides additional clinical information with respect to regional wall motion and left ventricular (LV) function. (2,12,13)

The mean sensitivity and specificity of MPI PET for detection of CAD are 89% and 89% with ranges from 83–100% and 73–100% respectively. (Table 1). (8,9,13-24) Comparison studies support that PET is at least as accurate as SPECT (8,9,14,20,25,26) and that disparate results are due to greater sensitivity and specificity of PET. (8,9,17,20,26,27) A recent study by Bateman et al. demonstrates superior diagnostic accuracy and normalcy rates for gated PET MPI compared to those of gated SPECT MPI ($p = 0.02$). (13) Recent advances in PET including PET/CT are currently being evaluated in multicentre studies such as the SPARC study. (28) The accuracy of PET for CAD detection has not been compared to that of CT or MRI.

In general the studies reviewed were considered to be of good quality, although some early studies did not report all the information now needed to assess quality. Most studies provided prospective evaluation, did not direct the gold standard procedure, and studied relevant patient populations. One study minimized bias by using a matched cohort design and random selection from an electronic database. (13) Most studies report blinded evaluation, but such information was not reported in one study, so blinded evaluation could not be confirmed. (15)

PET MPI and prognosis: A normal PET MPI indicates an excellent prognosis. Hard cardiac event rates range from 0.09% to 0.9% depending on the population and definition of normal. (29-31) These rates are comparable to those for SPECT MPI. (32,33) Patients with PET MPI defects have a worse prognosis for death (4.3% per year) (29) or hard events (7.0% per year with moderate to severe defects). (31) Recent data also indicate the prognostic value of PET MPI in specific populations with obesity or those referred after non-diagnostic ^{99m}Tc-SPECT MPI. (31) The prognostic value of PET/CT is being evaluated in the SPARC study. (28)

Table 2 summarizes the published data on prognosis. A study by MacIntyre et al., which evaluated the clinical outcome in patients with a negative thallium-201 SPECT study and positive PET MPI (26) is not included. This study did not consider the prognostic value of PET per se, although it did support the added value of PET over thallium-201 SPECT. Studies considering other outcomes such as restenosis post-PCI and risk assessment prior

to vascular surgery were not included in prognosis studies listed but are discussed below in 'Other Considerations'.

Exercise PET: (15-17, 34-38) This is feasible and combines the advantages of attenuation correction with the functional capacity data from exercise. There are disadvantages, however: the supine bicycle exercise done is prone to motion artifacts, while the treadmill, which is outside the camera, does not allow absolute flow quantification. Small studies support the accuracy of the method and its utility compared to pharmacological MPI with PET. (15-17, 34-38)

Quantification of myocardial blood flow is used to measure flow at rest and during stress. ^{13}N-ammonia and ^{15}O-water are well validated in this regard. (2, 39-41) ^{82}Rb has also been applied but requires a correction for its lower extraction fraction. (42,43) The advantage of flow quantification is that it provides a very sensitive means to evaluate and monitor therapies. It allows detection of early vascular and endothelial changes affecting flow before overt disease has developed and has the potential to define the hemodynamic significance of a stenosis (44) or balanced reductions in flow and flow reserve in patients with multivessel disease. (2,42) In these circumstances or in conditions which may affect the coronary microvasculature such as Syndrome X (2,45), there may be added value in the application of flow quantification, but clinical studies to evaluate this potential added value have been small and limited. In routine PET MPI, flow quantification is *not* required. Clinical application must be defined on a case by case basis.

Other considerations: ^{82}Rb PET MPI and the measurement of relative flow reserve have been applied and studied for the detection of restenosis six months following angioplasty. In 45 patients, the sensitivity and specificity of relative flow reserve measurements were 93% and 74% respectively. (46)

^{64}Cu-PTSM has also been shown to accurately detect coronary artery disease with sensitivity of 91% and normalcy rate of 100% among a group of 45 subjects. (47)

^{82}Rb PET MPI has also been applied for the prediction of peri-operative and late cardiac events in patients undergoing vascular surgery. In a study of 78 patients, most with intermediate risk factors for peri-operative events (diabetes, stable angina, compensated heart failure, prior myocardial infarction (MI)) (83% had >1 Eagle criteria), reversible ischemia on PET MPI had a 45% positive predictive value for post-operative events (unstable angina, MI, cardiac death) and a normal scan had a 92% negative predictive value. These are comparable to previous SPECT studies with the positive predictive value (PPV) range of 14–50% and negative predictive value (NPV) range of 85–100%. (1,48)

Myocardial Perfusion Imaging (MPI) using PET for Diagnosis and/or Risk Stratification of CAD

Recommendations

The interpretation of Cardiac PET MPI should be carried out only by physicians and institutions with adequate training and experience.

Class I Indications

1. Pharmacological MPI using PET for the diagnosis of CAD* and/or risk stratification of patients who
    a. have non-diagnostic non-invasive imaging tests or where such a test does not agree with clinical diagnosis (Level B evidence).
    b. may be prone to artifact that could lead to an equivocal other test, such as obese patients (Level B evidence);
    c. are unable to exercise or have left bundle branch block (LBBB) or ventricular pacing (Level B evidence).

Class IIa Indications

1. Pharmacological MPI using PET for the diagnosis of CAD* and/or risk stratification of patients who are able to exercise (Level B evidence);

2. For diagnosis and risk stratification of patients being considered for high-risk non-cardiac surgery who have intermediate clinical risk predictors; or have mild clinical risk predictors with poor functional capacity (<4 METS) (Level B/C evidence).

* Diagnosis is intended for patients with intermediate pretest likelihood of disease.

Class IIb Indications

1. Exercise PET using MPI for the diagnosis of CAD and/or risk stratification (Level B evidence);

2. Quantification of myocardial flow to determine the hemodynamic significance of a given coronary stenosis or to diagnose balanced multivessel disease (Level B/C evidence);

3. Quantification of myocardial flow to define impaired microvascular function (eg. Syndrome X) (Level B/C evidence).

Class III (no benefit or harmful)

1. Contraindications to all pharmacological agents (dipyridamole, adenosine, dobutamine);

2. Unstable pattern of ischemic chest pain;
3. Contraindications to radiation exposure.

Myocardial viability diagnosis: In addition to the exclusions noted above, additional restrictions were applied to FDG viability imaging studies. Excluded were studies with sample size ≤20; mean ejection fraction (EF) ≥ 40%; early post MI (≤10 days); LV recovery evaluation ≤ 8 weeks, or lack of LV recovery or outcome evaluation.

FDG PET imaging has long been regarded as the best standard for detection of viable recoverable myocardium. (2,49) In a comprehensive review of all prior viability studies, Bax et al. identified that FDG PET was the most sensitive method for predicting wall motion recovery while dobutamine echo was the most specific. (6) Few studies compared FDG imaging and dobutamine echo in more severe LV dysfunction, but a key finding in the study by Pagano et al. was the superiority of FDG PET over dobutamine echo in a group of 30 patients with very severe LV dysfunction (EF=23 $\pm$ 7) (PPV;NPV for FDG PET: 66;96%, dobutamine echo: 68;55%). This was even greater in the worst functioning (akinetic) segments (PPV;NPV for FDG PET: 80;94%; dobutamine echo: 73;41 %). (50) Comparison studies with MRI are even more limited (51) and have not compared prediction of LV function recovery.

Qualitative FDG PET imaging is used in conjunction with perfusion imaging to define perfusion defects with metabolic activity (PET mismatch indicating recoverable hibernating myocardium) or without metabolic activity ('PET match' indicating non-recoverable scar tissue); (2,52) or regions with maintained perfusion and metabolism in dysfunctional segments (chronic repetitive stunning with potential for recovery). (53,54). LV volume is also an important consideration as marked remodeling may prevent recovery of function even in the presence of viability. (55)

Quantification of FDG uptake applies Patlak graphical analysis of dynamic time-activity FDG data to determine the rate of uptake. This can be used to estimate exogenous myocardial glucose utilization (MGU). Maintained MGU indicates the presence of viable recoverable myocardium.

Both methods provide accurate means for predicting recovery of function after revascularization. (2,6,56,57) Recent data also indicate that PET-defined scar tissue and hibernating myocardium can be combined with clinical parameters to predict LV function recovery. (52) This approach is currently being evaluated in a randomized controlled trial (RCT). (58) Gating of FDG PET provides additional clinical information with respect to regional wall motion and LV function. (2,12)

From the studies included in this review, the sensitivity and specificity of FDG PET for LV function recovery are 91% and 61% respectively (see Table 3) (6,54,59-65) with ranges from 80–100% and 44–92%. These studies support the earlier meta-analysis indicating that FDG PET has a high level of sensitivity. Lower specificity likely relates to incomplete revascularization or failure to account for prolonged LV function recovery. (11,50,53)

The studies included in this review were gerenally considered to be of good quality, although some did not report some information needed to fully assess quality. It was sometimes difficult to identify the raw data to determine sensitivity and specificity. Although this was possible in most cases, occasionally it was not possible at all. (63) Most studies provided prospective evaluation, but it was sometimes unclear if revascularization was directed by the FDG PET imaging. Several studies focused on the most relevant patient population, i.e. those with IHD and severe LV dysfunction. Most studies reported blinded evaluation or used objective quantification methods. There was also variability in methods: for viability determination (mismatch vs % uptake of FDG); in follow-up duration; and in regional versus global LV recovery and analysis method. Regardless of the variability, there was consistent evidence to support the value of FDG imaging and in particular, the higher sensitivity of FDG PET over that of other methods. Thus, FDG PET has the potential to more definitively rule out viable myocardium when this is needed to select patients for revascularization.

Myocardial viability and prognosis: Table 4 outlines recent FDG PET studies that deal with prognosis. (7,66-74) Outcome data have consistently demonstrated that FDG PET defines viable myocardium in patients with LV dysfunction, and that these patients are at high risk for cardiac events including death, if they do not undergo timely revascularization. (71-75) Recent data support that early intervention in patients with viable myocardium can improve survival rates. (75) There is one small published randomized controlled trial comparing FDG PET with ^{99m}Tc-methoxyisobutyl isonitrile (MIBI) SPECT. Trends but no significant differences in outcomes were identified. However, in this study two-thirds of patients had mild-moderate LV dysfunction and were not representative of the population most likely to benefit from defining viable myocardium. (76) Prolonged delays to revascularization (mean >110 days) and technical comparison issues were the other limitations of this particular study. Ongoing RCTs are evaluating the utility of FDG PET in directing therapy in patients with severe LV dysfunction and IHD. These studies will help to further define the role of viability imaging in this patient population.

Many techniques are valuable in defining viable myocardium in patients with mild or moderate LV dysfunction. However, in patients with severe LV dysfunction, knowing the extent of scar tissue and hibernating myocardium (which can be defined using FDG PET), is often important in decision making for revascularization. (2,57) Fusion imaging of FDG PET with MRI or CT may provide even greater accuracy for detecting viable tissue, through combining the advantages of each technique.

Myocardial FDG PET Viability Imaging

Recommendations

The interpretation of FDG PET viability imaging should be carried out only by physicians and institutions with adequate training and experience.

Class I Indications

1. To define myocardial viability in patients with
    a. ischemic heart disease and severe LV dysfunction, to identify extent of recoverable myocardium and prognosis in patients being considered for revascularization or cardiac transplantation (Level B evidence);

    b. moderate to large fixed perfusion defects or with equivocal results on another viability test (Level B evidence).

Class IIa Indication

1. Moderate systolic LV dysfunction and IHD to identify the extent of recoverable viable myocardium and prognosis in patients being considered for revascularization or cardiac transplantation (Level B evidence).

Class III (no benefit or harmful)

a. Contraindications to insulin;
b. Severe untreated hypokalemia;
c. Contraindications to radiation exposure.

Computed Tomography Angiography

Detection of coronary artery disease: With the recent advances in the spatial and temporal resolution of multi-detector computed tomography (MDCT) scanners, cardiac CT angiography is feasible and is increasing in accuracy. Computed tomographic angiography (CTA) has the benefits of being a non-invasive modality with the potential of providing anatomical information with a very short imaging sequence (5–25 seconds). By obviating the need for arterial access and cannulation of the coronary arteries, CTA may avoid many of the risks associated with conventional invasive coronary angiography.

Computed tomographic angiography has been used to assess native coronary arteries, arterial and saphenous vein bypass grafts, coronary stents and anomalous coronary arteries. (77-82) Numerous studies have evaluated the accuracy of 16-slice MDCT with invasive coronary angiography (Table 5) (79,83-99) and have demonstrated good accuracy in coronary segments that can be evaluated (> 1.5 mm in diameter). The overall sensitivity and specificity for defining angiographic disease for 16-slice MDCT are 87% and 96% respectively. For detection of disease in patients, the sensitivity and specificity for detecting disease are 91% and 95% for 16-slice MDCT. More recently, the few studies using 64-slice MDCT have also demonstrated very good accuracy with a larger number of segments that could be evaluated than is the case using 16-slice MDCT (Table 6). (94,100-102)

Patients referred for coronary angiography are generally suspected of having obstructive CAD on the basis of the results of previous non-invasive investigations. This unavoidable bias in patient selection may result in the overestimation of CTA specificity (i.e., the underestimation of the false positive rate of CTA studies). However, the use of normal reference segments and vessels to determine vessel specificity suggests that any overestimation of specificity is probably small. The negative predictive value of CTA has consistently been excellent. CTA may therefore be most beneficial in patients for whom the diagnosis of obstructive CAD needs to be ruled out.

Cardiac motion and coronary calcification are two important limiting factors in the use of CTA. Accordingly, certain patients should not routinely undergo CTA such as those with irregular cardiac rhythms (e.g. atrial fibrillation, frequent extrasystoles), severe coronary calcification, an inability to perform sufficient breath-holds, and contraindications to intravenous contrast agents or to radiation exposure.

A recent meta-analysis of MDCT and MRI confirms the utility of CTA and also suggests that CT angiography has a significantly higher diagnostic accuracy than MRI for detection of significant CAD. (82) At this time, there is no data supporting the use of CTA for determining patient prognosis. The use of this diagnostic technique is the focus of current studies such as the SPARC trial (28) and will continue to be a focus of future investigation.

Ionizing radiation exposure with CT remains a concern. The estimated effective radiation dose with 16-slice CTA ranges from 7-15 mSv. (93,103,104) However, given the shorter imaging time of 64-slice MDCT, improved digital acquisitions systems and x-ray tube modulation, the radiation exposure associated with 64-slice MDCT is expected to be the same or slightly lower (4.8-14 mSv), although this remains to be confirmed by an independent source. The radiation dose of CTA appears to be similar to slightly higher than other traditional non-invasive modalities. Clinicians must continue to strive to minimize patient exposure to ionizing radiation. Future technological developments must be made without additional increases in patient radiation exposure.

As advances in CT hardware and software are made, Cardiac CT has the potential to improve cardiac patient care. Research is underway to investigate its utility in acquiring functional data such as the assessment of regional wall motion, estimation of ejection fraction and perfusion imaging.

Calcium scoring (with MDCT) is used to identify calcified plaque, which may have prognostic value but is beyond the scope of this evaluation. CTA also shows promise in the assessment of atherosclerotic plaque but remains a research tool.

Future Directions: Cardiac CT has promise in several areas pertinent to the assessment of patients with suspected or documented CAD. Ongoing research evaluates the ability of CT to assess coronary artery atherosclerotic plaque, (105,106) coronary stents, LV function, (107-109) myocardial perfusion (110) and/or myocardial viability. (111)

At the time of this review, there were limited data on 64-slice CTA, and the panel anticipates that these recommendations will require amendments as CTA continues to evolve.

CAD Detection with CT Angiography

Recommendations

The interpretation of cardiac CT and CTA should be carried out only by physicians and institutions with adequate training and experience.

Class I Indication

1. Assessment of anomalous coronary arteries (Level C evidence).

Class IIa Indications

1. 16- or 64-slice MDCT for patient diagnosis of significant coronary artery disease (≥ 50% diameter stenosis)(Level B evidence);
2. 16- or 64-slice MDCT for identification of coronary artery segments with significant stenosis (≥ 50% diameter stenosis) in coronary segments ≥ 1.5 mm in diameter (Level B evidence);
3. 16- and 64-slice MDCT for the assessment of graft patency (Level B evidence).

Class IIb Indication

1. 64-slice MDCT for the assessment of all coronary segments including those with vessel diameters < 1.5 mm (Level B evidence).

Class III (no benefit or harmful)

1. Diagnosis of CAD in patients with
    a. irregular dysrhythmias (atrial fibrillation, frequent extrasystoles);
    b. severe coronary calcification;
    c. inability to perform sufficient breath-holds;

d. renal failure or other contraindications to intravenous contrast agents;
e. contraindications to radiation exposure.

Magnetic Resonance Imaging

Cardiovascular magnetic resonance (CMR) imaging provides a very broad set of tools for diagnosis and prognosis in patients with coronary artery disease. The assessment of cardiac function, morphology and mass with CMR using 3D methods with no geometric assumptions has been extensively validated. These quantitative measurements have excellent inter-study reproducibility.

Detection of coronary artery disease: Several cardiac magnetic resonance (CMR) approaches are used to detect CAD. These include the direct visualization of the coronary artery lumen; visualization of ischemic myocardial injury (infarction); and detection of the effects of induced ischemia on wall motion, perfusion and coronary blood flow.

Coronary magnetic resonance angiography: Magnetic resonance angiography (MRA) and quantification of vascular flow is a common approach used in almost all vessels in the body except the coronaries. It remains technically challenging to image the coronary arteries with the temporal and spatial resolution necessary to predict > 50% stenoses. This is due to the size, tortuosity and, most importantly, complex motion of the coronary arteries during the cardiac cycle. Published data do not provide information on the diagnostic performance of recently modified 3D navigator techniques. In reported studies, the negative predictive value for coronary magnetic resonance angiography (CMRA) to exclude multi-vessel proximal obstructive CAD reached 81% in a recent multi-centre trial (112) but current techniques have not yet been shown to reproducibly predict diameter stenoses even in broad categories or adequately examined distal vessels. Three techniques have been extensively studied at 1.5 Tesla field strength: 2D breath held, 3D breath held, and 3D navigator. (112-138) The majority of these studies are performed without any magnetic resonance contrast agents. In two recent meta-analyses of 999 patients in 28 MRA studies, the positive and negative predictive values for detection of > 50% stenosis in interpretable segments were 65% and 90% respectively (Table 7). (5,82) If uninterpretable segments are included these values fall to 37% and 85% respectively. More recent work has been performed at 3 Tesla and yielded a sensitivity of 82% and a specificity of 89%. (114) Overall CMRA has a good diagnostic performance in all vessels except the circumflex coronary artery, which is likely due to its proximity to the adjacent blood pools of the left atrium and ventricle, and lower signal from its location which is often furthest from the receiver coil. False positive rates remain high. A review of the studies suggests that the greatest value of CMRA is with a negative study in a patient with low pretest probability of CAD. (5) Currently there are no clinically approved

truly intravascular magnetic resonance contrast agents that could increase the signal-to-noise ratio to such a level to permit improved coronary imaging. However, research is ongoing.

Coronary bypass graft patency has also been examined with CMR using MRA and MR flow measurement techniques. (139-150) While the positive predictive value for the detection of a patent bypass graft has been reported to be as high as 95%, limitations such as metallic clip artifacts reduce the negative predictive value to the 44% range. (150)

The course of anomalous coronary arteries which can induce ischemia, especially if the artery passes between the aorta and pulmonary artery, can be clearly delineated by CMR when compared to x-ray angiography. (151-154)

Stress wall motion: Using CMR, stress is induced pharmacologically, as physical exercise is difficult to perform within the magnet bore and often induces motion artifacts. Dobutamine stress-induced wall motion abnormalities are easily appreciated using the high quality imaging of CMR. This technique is well established and trials have shown it to be as good as or better than dobutamine stress echo in the diagnosis of CAD. Data from eight studies involving a total of 893 patients show an average sensitivity and specificity of 90% and 84% respectively (Table 8). (155-162) Objective quantification with techniques such as tagging, in which nulled signal lines deformation changes are recorded, adds to the sensitivity of the technique.

Stress perfusion: Myocardial perfusion can also be measured during stress (either with dobutamine or dipyridamole) following a first pass of an intravenous bolus of gadolinium contrast (0.1 mmol/kg) injected at 5-7 mL/s. The signal increase, as gadolinium washes into the myocardium, can be quantified as perfusion maps. Hypoperfused myocardial segments are seen as dark regions of low signal during first pass of the contrast. These techniques have been extensively studied and validated in animal models. Validation in human studies has also been performed with good correlation to x-ray angiography, PET and SPECT. Data from 11 studies involving a total of 647 patients show an average sensitivity and specificity of 84% and 86% respectively (Table 9). (162-172) Recently the MR-Impact study of 241 patients showed that first pass perfusion CMR was superior to SPECT in detecting CAD. Impaired subendocardial perfusion has also been demonstrated in metabolic syndrome. Newer non-contrast techniques to examine tissue oxygen levels such as T2* dependent effects in BOLD imaging hold promise but further investigation is needed.

Myocardial viability: CMR employs two techniques to examine myocardial viability: Dobutamine stress MR (DSMR) to induce improvement of contractility of dysfunctional segments; and late gadolinium enhancement (LGE). DSMR has been shown to have similar or improved ability to predict contractile improvement post-

revascularization compared to that of dobutamine stress echo. Data from 14 studies involving a total of 569 patients demonstrate a sensitivity and specificity of 91% and 94% respectively (Table 10). (124,159,173-180)

LGE is a CMR technique to image non-viable/infarcted myocardium. The extravascular contrast agent gadolinium (0.1-0.2 mmol/kg) accumulates within infarcted tissue which has a larger extravascular space than does normal tissue. This accumulation leads to visualization of infarcted myocardium as areas with altered signal intensity in inversion recovery gradient echo sequences. This technique has been thoroughly validated in animals. LGE has been widely studied in humans. It shows good correlation with PET and superiority to SPECT in quantifying both viable and non-viable myocardium. Data from 13 studies involving a total of 357 patients reveal a sensitivity and specificity of 81% and 83% respectively for predicting recovery or lack of recovery of LV function (Table 11). (51,177,180-190) The transmurality of the infarct can also be determined, and this can be used to improve the ability of LGE to predict recovery after revascularization. In Kim et al. (181) for example, examination of severe hypokinetic, akinetic or dyskinetic segments with < 25% transmural LGE had a 79% chance of functional recovery after revascularization compared to a 6% chance of recovery if LGE showed > 50% transmurality. (181)

For both LGE MRI and dobutamine stress MRI for viability, the number of studies involving patients with more significant LV dysfunction (EF < 40%) is limited. Further studies continue to be needed in the patient population with severe LV dysfunction.

Currently, there are few studies evaluating the impact of DSMR and LGE CMR on cardiac outcomes, but several studies are currently underway. Outcome studies in patients with *severe* LV dysfunction are limited.

Evaluation of acute coronary syndromes: CMR has been used in the emergency room in the assessment of chest pain. CMR showed a sensitivity and specificity of 84% and 85% respectively for identifying patients with CAD. Multi-variate analysis including standard clinical tests (ECG, troponin, TIMI risk score) showed that CMR was the strongest predictor of CAD. CMR added diagnostic value over clinical parameters, including identification of enzyme-negative unstable angina. This promising data needs to be confirmed in other centres. CMR also identifies microvascular obstruction in acute MI. This is demonstrated early (1–2 minutes) after intravenous injection of gadolinium. At this timepoint, inversion recovery CMR shows areas within the MI with severely compromised perfusion as black, indicating areas with microvascular collapse. Microvascular obstruction detected by CMR has been linked to ventricular remodelling and adverse cardiovascular events. Finally, the transmural extent of late gadolinium-enhancement CMR predicts recovery of function following acute MI. CMR is effective in demonstrating the complications of acute MI, including ventricular aneurysm, pseudoaneurysms, ventricular septum perforation, and mitral regurgitation. Echocardiography may yield false

positive and false negative results when employed to look for LV thrombi in post-infarction patients. CMR is useful in this regard.

CAD Detection Using MRI

Recommendations

The interpretation of Cardiac MRI should be carried out only by physicians and institutions with adequate training and experience.

Class I Indications

1. Assessment of anomalous coronary arteries (Level C evidence);
2. Detection of coronary stenosis > 50%
    a. stress function with dobutamine (Level B evidence).

Class IIa Indication

1. Detection of coronary stenosis > 50%
    a. Stress First Pass Perfusion (Level B evidence).

Class IIb Indications

1. Detection of coronary stenosis > 50%
    a. Coronary MR angiography (Level B evidence);

2. Graft Patency
    a. Coronary MR angiography (Level C evidence).

Class III (no benefit or harmful)

1. contraindication to MRI;
2. contraindication to gadolinium contrast;
3. inability to perform sufficient breath-holds.

Myocardial Viability using MRI

Recommendations

The interpretation of Cardiac MRI should be carried out only by physicians and institutions with adequate training and experience.

Class I Indications

1. Assessment of myocardial viability in patients with LV dysfunction or akinetic segments for predicting recovery of ventricular function following revascularization

a. Late Gadolinium Enhancement (Level B evidence);

b. Dobutamine Stress Wall Motion (Level B evidence).

Class IIa Indications

1. Assessment of myocardial viability to determine prognosis following revascularization in patients with moderate/severe LV dysfunction

   a. late gadolinium enhancement (Level B/C evidence);

   b. dobutamine stress wall motion (Level B/C evidence).

Role of Echocardiography and SPECT Imaging (1,28,191-194)

Echocardiography remains an established imaging modality in patients with ischemic heart disease. The identification of segmental LV wall motion abnormalities, at rest or induced by exercise or pharmacologic (dobutamine or dipyridamole) stress, allows the detection of CAD and provides clinically useful prognostic data. dobutamine stress echocardiography has demonstrated utility in the detection of myocardial viability, and the prediction of recovery of function post-revascularization. Important advances in echocardiography have occurred over the past decade, with the aim of further improving the accuracy and reproducibility for CAD detection and prognostication. While a full discussion is beyond the scope of this current position statement, these advances have included, 1) real-time 3D echocardiography, enabling acquisition of 3D volume sets and off-line tomographic analysis, 2) techniques to quantify wall motion during stress echocardiography, including tissue Doppler, strain rate imaging and colour kinesis, and 3) the use of microbubble contrast agents for left ventricular opacification and myocardial perfusion. These ultrasound contrast agents are approved for use in Canada to improve LV endocardial border delineation, and have been demonstrated to increase the diagnostic accuracy and reproducibility of stress echocardiography, and reduce interobserver variability. Studies have now demonstrated the utility of contrast echocardiography to image myocardial perfusion at rest and during pharmacologic stress, allowing the simultaneous assessment of regional wall motion and perfusion, and potentially resulting in improved detection of CAD and myocardial viability.

Cardiac perfusion imaging using radioisotopes is a well-established technique that has been and continues to be the mainstay of noninvasive diagnosis and determination of prognosis for patients with coronary artery disease. It is a very robust technique that is widely available throughout the world. Myocardial perfusion imaging has excellent sensitivity and specificity for the detection of coronary artery disease. Over recent years, advances in radioisotopes, gating of images, and attenuation correction have significantly improved the sensitivity and specificity of the test. There is a vast literature (more than 50,000 patients) on the determination of prognosis for

patients in whom coronary artery disease is suspected. There are several advantages to using this technique. Standard protocols have been published, and acquisition of images is operator-independent. Large numbers of cardiologists, nuclear medicine physicians, and radiologists are able to interpret myocardial perfusion images. Training standards have been published in Canada and the United States. Appropriateness criteria have been published recently in the United States. Guidelines for the performance and use of radionuclide perfusion images have been published in the United States and are under development in Canada. Using tomographic imaging, left ventricular ejection fraction and volumes can be calculated, allowing simultaneous assessment of myocardial perfusion and function. Although perfusion imaging is usually performed in conjunction with stress testing (which adds prognostic value), it is possible to use pharmacological stress in patients who cannot exercise to their target heart rate. Myocardial perfusion images have the advantage of detecting physiology rather than anatomy. Many studies have shown the incremental value of physiological imaging over anatomical evaluation of coronary artery disease using coronary angiography. Myocardial perfusion imaging has also been very useful in special populations such as women and patients with diabetes.

The newest advances have been in instrumentation. Manufacturers have developed hybrid gamma cameras with CT. These hybrid devices have improved the specificity of perfusion imaging through the ability to do CT attenuation correction. However, newer cameras also have diagnostic CT scanners that can be used for calcium scoring and CT angiography, allowing an assessment of atherosclerosis rather than of just ischemia. Myocardial perfusion imaging will likely remain the standard for detection of coronary artery disease and for determining prognosis. The more advanced techniques discussed in this paper are very exciting developments. It will be important to develop pathways for the appropriate use of all the imaging techniques.

Due to their large clinical experience and ongoing advances in imaging technology, echocardiography and nuclear SPECT imaging will continue to play important first-line roles in the assessment of patients with CAD. As the advanced imaging techniques discussed in this position statement continue to develop, and as experience and long-term prognostic data grow, these newer modalities will likely play an ever-increasing role in the management of patients with ischemic heart disease. They serve as complementary tests when results of initial imaging tests are equivocal or non-diagnostic, and in some cases, first-line tests at sites with established expertise. Given that certain newer imaging modalities hold great promise for the non-invasive evaluation of the coronary tree, an approach combining a *functional* assessment of wall motion and perfusion, using nuclear SPECT, PET, echocardiographic or MRI techniques, with an *anatomical* assessment, with cardiac CT angiography or MRI, holds a certain appeal in the evaluation of patients with ischemic heart disease. New algorithms for patient evaluation will continue to evolve but will continue to involve SPECT and echocardiography.

Radiation Exposure

Table 12 lists the radiation exposure from common non-invasive radionuclide or x-ray based cardiac procedures. CT angiography appears comparable to other standard non-invasive imaging methods. (103, 194-197)

Cost Considerations:

Economic evaluation is an important consideration in the development of new technologies. In any cost-effectiveness analysis, it is important to determine the population under consideration, the intervention, the comparator or comparators, the perspective of the study, the outcomes and the costs involved. Analysis and modelling of the underlying processes involved also generally require some knowledge of factors (or covariates) that determine the costs and outcomes of the intervention.

For PET MPI imaging, cost data have been conflicting. In one study that compared PET to treadmill, SPECT MPI and coronary angiography, PET had the most favourable incremental cost-effectiveness ratio. (198) In another study that compared PET MPI, stress echocardiography, SPECT MPI, and coronary angiography, PET had the worst cost-effectiveness ratio. (199) However, these studies apply theoretical models that depend very much on the studies selected and clinical care assumptions. They do not consider evaluation in real patient populations, nor the impact of recent data on diagnostic accuracy or prognosis. They are also not valid in Canada where costs may be considerably lower in certain settings in which efficient practice considerations have been implemented. Despite these limitations, an evaluation regarding the 'selection of patients for angiography' suggested that PET and SPECT MPI are both cost-effective approaches in patients with intermediate pre-test likelihood of CAD. (200)

One study evaluated the incremental cost of FDG PET viability imaging in patients with ischemic heart disease and LV dysfunction. (201) Compared were coronary artery bypass grafting (CABG) for all patients, PET to select those with hibernating myocardium for grafting, and medical therapy for all patients. A health care perspective was used. Costs and outcomes were considered for one year from the time of initial treatment. The study concluded that FDG PET viability imaging was cost-effective in the selection of patients with LV dysfunction referred for CABG.

To our knowledge, no published studies have evaluated the incremental cost-effectiveness of MRI or CT angiography in patients with coronary artery disease. For new technologies such as CT angiography and fusion or hybrid imaging, there will need to be careful prospective consideration of costs in real patient populations.

Concluding Remarks

The recommendations in this position statement are based on the literature to 2005 and selected works published in early 2006. The best available evidence is combined with clinical expertise and opinion to determine the recommendations noted above.

The recommendations demand that any imaging technique be performed and interpreted in institutions and by physicians who have adequate experience and training.

It is anticipated that the availability of all these advanced imaging techniques will increase in Canada. This document serves as an initial guideline for clinical use. Given the rapid evolution of technologies and emerging literature, such recommendations will require regular updates; by the time this position statement is published, some of the recommendations may be outdated. Therefore, this position statement should be used as a guide and taken in the context of time and available data.

Future research and evaluation studies of diagnostic imaging would be helped by consistently reporting details of the patient population, methods of recruitment and blinded analysis. The gold standard method used for comparison should not be influenced by the test being evaluated. Studies should consider applicability and potential impact to patient management and outcome. Studies should consider criteria that have been developed and that are being applied to evaluate quality of data and evidence.

Imaging laboratories and facilities should engage in collection of patient registry data to allow characterization and improvement in appropriate utilization of these technologies for which access is currently limited.

Standardized reports appropriate for the specific technology should be developed and utilized across facilities. This combined with network integration of images may reduce the need for repeat testing.

Continued research will always be required to better characterize the utility, diagnostic and prognostic value of these tests. This will assist in the development of evidence-based patient care pathways and algorithms for an increasingly complex array of tests that are now available.

Finally, with the rapid emergence of these technologies, training guidelines are also needed. Imaging specialties and clinical specialties must further integrate their practices. This need must be transmitted to trainees who will become the experts to perform and interpret these tests in the future. A joint effort among specialties is recommended to achieve this goal.

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Table 1: PET CAD DIAGNOSIS

Author	Year	Number	Stress	Tracer	Reference CAG	Sensitivity +ve test	Sensitivity Pt. w. CAD	Sensitivity %	Specificity -ve test	Specificity Pt. w.o. CAD	Specificity %
Schelbert HR	1982	45	dipyridamole	$^{13}NH_3$	>50%	31	32	97%	13	13	100%
Tamaki N	1985	25	exercise	$^{13}NH_3$	N/R	18	19	95%	6	6	100%
Yonekura Y	1987	50	exercise	$^{13}NH_3$	>75%	37	38	97%	12	12	100%
Tamaki N	1988	51	exercise	$^{13}NH_3$	>50%	47	48	98%	3	3	100%
Gould L (@)	1986	50	dipyridamole	$^{82}Rb/^{13}NH_3$	QCA SFR < 3	21	22	95%	9	9	100%
Demer L (@)	1989	193	dipyridamole	$^{82}Rb/^{13}NH_3$	QCA SFR < 4	126	152	83%	39	41	95%
Go RT	1990	202	dipyridamole	82Rb	>50%	142	152	93%	39	50	78%
Stewart RE	1991	81	dipyridamole	^{82}Rb	QCA >50%*	50	60	83%	18	21	86%
Marwick T	1992	74	dipyridamole	^{82}Rb	>50%	63	70	90%	4	4	100%
Grover McKay	1992	31	dipyridamole	^{82}Rb	>50%	16	16	100%	11	15	73%
Laubenbacher	1993	34	dipyridamole/adenosine	$^{13}NH_3$	QCA >50%*	14	16	88%	15	18	83%
Bateman TM†	2006	112	dipyridamole	^{82}Rb	>50%*	64	74	86%	38	38	100%
Williams BR**	1994	287	dipyridamole	^{82}Rb	>67%	88	101	87%	99	112	88%
Simone GL**	1992	225	dipyridamole	^{82}Rb	>67%	**	**	83%	**	**	91%
Totals + Weighted Mean		**1460**				**696**	**778**	**89%**	**297**	**333**	**89%**
Weighted Mean excluding R/S						**544**	**603**	**90%**	**160**	**183**	**87%**
Non-weighted Mean								**91%**			**91%**

@ - Study reported that 50 pts in Gould et al 1986 were included. Thus Gould et al not included in mean calculations.
** - Retrospective study; MPI influenced CAG decision; mixed patient and region method for sensitivity / specificity; patients with disease could not be easily determined in one study.
* - Other cut-offs reported; >50% noted here
† - Electronic database, matched cohort design; values derived from reported population, sensitivity and specificity.

N/R = Not reported
R/S = Retrospective
CAG = Coronary Angiogram
QCA = Quantitative Coronary Angiography
SFR = Stenosis Flow Reserve Based on QCA Data

Table 2: PET CAD PROGNOSIS

Author	Year	Patient Number	Stress	Tracer	Outcomes	Follow-up Time (years)	Normal Scan- Annual Event Rate (%/yr)		Abnormal Scan- Annual Event Rate (%/yr)	
							Hard Events	Total Events	Hard Events	Total Events
Yoshinaga	2004	367	dipyridamole	^{82}Rb	death,MI,Rev,Hosp	3.1	0.4	1.7	mild: 2.3 mod/sev: 7.0	mild: 12.9 mod/sev: 13.2
Chow	2005	629	dipyridamole	^{82}Rb	death,MI,Rev,CAG	2.3	0.09	0.98		ECG +ve Normal MP: 1.9
Marwick T	1997	581	dipyridamole	^{82}Rb	death,MI,Rev,UAP	3.4	0.9	4	4	7
Marwick T	1995	Prediction of peri-operative and late cardiac events before vascular surgery*								
MacIntrye	1993	Outcomes in patients with False Negative Thallium-201 SPECT*								

MI = Myocardial Infarction
Rev = Revascularization
CAG = Coronary Angiogram
UAP = Unstable Angina

* See text for details

TABLE 3: PET VIABILITY DIAGNOSIS (EF < 40%)

Author	Year	Number	EF(%)	Tracer	Reference Method	Sensitivity +ve test	Sensitivity Patient/segments with recovery	Sensitivity %	Specificity -ve test	Specificity Patient/segments. without recovery	Specificity %
Bax (meta-analysis) 20 studies	2001	598	36±8	^{18}FDG	WM/EF F/U 4.1m	751	807	93%	417	725	58%
Barrington†	2004	25	36	$^{13}NH_3/^{18}$FDG uptake+MM	WM 8m F/U	6	6	100%	23	25	92%
Bax, Visser*	2001	47	30	^{201}Tl/^{18}FDG SPT MM	WM + EF 3-6m F/U	18	21	86%	24	26	92%
Bax, Fath-Ordoubadi*	2002	34	32	$^{13}NH_3/^{18}$FDG MRGR>60%	WM + EF 4-6m F/U	10	10	100%	17	24	71%
Bax, Maddahi*	2003	47	30	^{18}FDG SPT uptake	EF 6m F/U	17	19	89%	24	28	86%
Gerber*†	2001	178	38	^{18}FDG-MGU %uptake	EF 4-6m F/U	65	82	79%	49	89	55%
Kosoroglou	2004	41	31	MIBI/FDG uptake	WM 3-6m F/U	**	**	90%	**	**	44%
Nowak	2003	42	38	TF/FDG MM ^{15}O-H_2O	WM F/U 6-17m	32	40	80%	23	32	72%
Wiggers*	2001	35	35	$^{13}NH_3/^{18}$FDG uptake+MM	Pt WM F/U 6.1m	14	14	100%	14	21	67%
Totals + Wt'd Mean		**1047**	**33.8**			**913**	**999**	**91%**	**591**	**970**	**61%**
Mean weighted by number of patients								**90%**			**61%**

* = EF recovery used or patient based recovery
† = Values derived from sensitivity, specificity and other values provided.
** = Not reported and cannot be easily determined from data presented
WM = Wall Motion
SPT = SPECT
MM = Mismatch
MRGR = Metabolic Rate of Glucose (Relative)
TF = Tetrafosmin

Table 4: PET VIABILITY PROGNOSIS (EF < 40%)

Citation		Patient Population			Test Method	Mortality Rates			
Author	Year	N	EF	mean FU (months)	Tracer	Viab +ve Rev +ve	Viab +ve Rev -ve	Viab -ve Rev +ve	Viab -ve Rev -ve
Allman (meta-anal)†	2002	3088	32	25	Tl/DE/FDG	3.2%	16.0%	7.7%	6.2%
Allman(PET)†		1029	35	24	perfusion/FDG	6.0%	21.0%	7.0%	8.0%
Eitzman	1993	82	33	12	Rb-NH3/FDG	3.8%	33.3%*	0.0%	8.3%
Di Carli	1994	93	25	14	NH3/FDG	11.5%	23.5%*	5.9%	18.2%
Lee	1994	129	37	17	Rb /FDG	8.2%	14.3%*	5.3%	12.5%
Beanlands	1998	85	26	17	MIBI/FDG	3.2%	28.6%††	-	18.8%
Zhang	2001	123	35	37	MIBI/FDG	0.0%	26.7%**	8.0%	3.8%
Rohatgi	2001	99	22	25	NH3/FDG	0.0%	34.5%**	0.0%	15.2%
Santana	2004	90	26	22	G-Rb/FDG	NR	NR€	NR	NR
Dessideri€€	2005	261	29	34	NH3/FDG	14.5%	28.3%**	10.3%	21.5%
Sawada†††	2005	61	29	48	NH3/FDG	47.4%	83.3%**	57.1%	43.8%
TOTALS/mean €€€		**933**	**30**	**26**		**9.4%**	**30.9%¶**	**11.8%**	**17.7%**

† Meta-analysis of 24 viability studies; rates reported are for all studies in line 1; line 2 is data for 11 FDG PET studies: 7 of which reported outcomes; 4 of which compared event rates in subgroups and had EF<40%; table data derived from reported values and estimated for 1 year follow-up based on rates and mean follow-up reported.

* p <0.05 Viab +ve, rev -ve vs rev +ve for total cardiac event rates.

** p <0.05 Viab +ve, rev -ve vs rev +ve (also vs other groups (Allman, 2002; Zhang 2002)).

†† p<0.05 delayed vs early revasculuarization

€ Values not reported: 11% survival benefit with revascularization in patients with viability and LV remodeling (EDV>260).

€€ Values determined from reported percentages.

††† Pts with Diabetes; LV dysfunction and CAD

€€€ Totals/mean include 8 studies with reported values. Does not include meta-analysis

¶ p <0.05 vs other groups using a Fisher's exact test.

Tl = Thallium-201
DE = Dobutamine Echo
FDG = F-18 Fluorodeoxyglucose
Viab = Viability
Rev = Revascularization

Table 5: 16-SLICE MDCT

	Yr	N Seg	Segment Analysis	Sen	Sp	Patient Analysis	Sen	Sp	Accuracy
Nieman	2002	58	≥ 2 mm	95(82/86)	86(125/145)		100(50/50)	88(7/8)	98% (57/58)
Mollet	2004	128	≥ 2 mm	92(216/234)	95(1092/1150)		100(106/106)	86(18/21)	98% (124/127)
Kuettner	2004	58	ALL	72(54/75)	97(679/700)				97% (58/60)
Martuscelli	2004	61	>1.5 mm	89(83/93)	98(511/520)				
Hoffmann U	2004	33	ALL	70(30/43)	94(371/393)		86 (19/22)	82(9/11)	85% (28/33)
Cademartiniri	2005	40	≥ 2mm	96(88/92)	96(322/336)				
Cademartiniri	2005	60	≥ 2mm	93(93/100)	97(557/572)				
Doregelo	2005	22	≥ 2mm	94(30/32)	96 (216/225)				
Morgan-Hughes	2005	57	ALL	83(75/90)	97(566/585)		100(32/32)	96(24/25)	98% (56/57)
Heuschmid	2005	37	ALL	59(22/37)	96(329/343)				97% (36/37)
Hoffman M	2005	103	≥ 1.5 mm	95(149/157)	98(1117/1139)		96(55/58)	84(38/45)	90% (93/103)
Kefer	2005	52	≥ 1.5 mm	82(64/78)	79(293/369)		92	67	
Schuijf	2005	31	≥ 2mm	93(53/57)	96(179/186)		95(20/21)	80(8/10)	90% (28/31)
Mollet	2005	51	≥ 2mm	95(61/64)	98(537/546)		100(31/31)	85(17/20)	94% (48/51)
Kuettner	2005	72	ALL	82(96/117)	98(804/819)				90% (65/72)
Achenbach	2005	50	≥ 1.5 mm	94(50/53)	96(559/582)		100(25/25)	83(19/23)	92% (44/48)
Aviram	2005	22	> 1.5 mm	86(24/28)	98(255/260)				
Burgstahler	2005	117	ALL	84(294/348)	97(1105/1134)				
Kuettner	2005	124	ALL	85(304/359)	98(1172/1201)		85	98	92% (110/120)
Weight Mean				87(1868/2143)	96(10789/11205)		98(352/359)	86%(140/163)	

Table 6: 64-SLICE MDCT

Author	Yr	N	Segment Analysis	Sen	Sp	Patient Analysis	Sen	Sp	Accuracy
Raff	2005	70	ALL	86(79/92)	95(802/843)		95(38/40)	90(27/30)	93%(65/70)
Leber	2005	55	ALL	79(52/66)	73(29/40)		88(22/25)		
Leshcka	2005	67	≥ 1.5 mm	94(165/176)	97(805/829)		100(47/47)	100(20/20)	100%(67/67)
Mollet	2005	52	ALL	99 (93/94)	95(601/631)		100 (38/38)	92 (12/13)	98%(51/52)
Weighted Mean				91 (389/428)	95(2237/2343)		97(145/150)	94(59/63)	

Table 7: MR ANGIOGRAPHY

Year / Author	Patients (n)	Assessable % (Number of Segments)	Sensitivity % (Number of Segments)	Specificity % (Number of Segments)	PPV % (95% CI)	NPV % (95% CI)
2D breath hold						
1993 Manning	39	98 (147/150)	90 (47/52)	92 (87/95)		
1993 Pennell	7	NA	83 (5/6)	NA		
1996 Mohiaddin	16	90 (43/48)	56 (5/9)	82 (28/34)		
1996 Pennell	39	NA	85 (47/55)	NA		
1997 Post	35	89 (125/140)	63 (22/35)	89 (80/90)		
Total	136				84 (78-90)	86 (82-91)
Weighted mean		93 (315/338)	80 (126/157)	**89 (195/219)**		
3D breath hold						
1999 Kessler	6	NA	60 (3/5)	NA		
2000 van Geuns	38	69 (187/272)	68 (21/31)	97 (151/156)		
2000 Regenfus	50	77 (268/350)	86 (48/56)	91 (193/212)		
2002 Regenfus	32	76 (171/224)	87 (26/30)	91 (129/141)		
2004 Jahnke	40	45 (143/320)	63 (12/19)	82 (102/124)		
Total	166				65 (58-72)	95 (93-97)
Weighted mean		66 (769/1166)	78 (110/141)	**91 (575/633)**		
3D navigator						
1996 Post	20	96 (77/80)	38 (8/21)	95 (53/56)		
1997 Muller	35	NA	83 (45/54)	94 (115/122)		
1997 Kessler	73	52 (236/455)	65 (28/43)	88 (169/193)		
1998 Woodard	10	NA	70 (7/10)	NA		
1999 Sandstede	30	77 (92/120)	81 (30/37)	89 (49/55)		
1999 van Geuns	32	74 (151/203)	50 (13/26)	91 (114/125)		
1999 Kessler	6	NA	60 (3/5)	NA		
2000 Sardanelli	42	86 (234/273)	82 (55/67)	89 (149/167)		
2001 Kim	109	86 (374/434)	83 (78/94)	73 (204/280)		
2002 Plein	10	93 (37/40)	88 (15/17)	85 (17/20)		
2002 Weber	11	70 (62/88)	88 (14/16)	93 (43/46)		
2002 Wittlinger	25	85 (102/120)	75 (18/24)	100 (78/78)		
2002 Regenfus	32	69 (155/224)	60 (15/25)	88 (115/130)		
2002 Watanabe	12	70 (49/70)	80 (12/15)	85 (29/34)		
2002 van Geuns	27	69 (139/201)	46 (12/26)	90 (102/113)		
2003 Bogaert	21	72 (134/186)	56 (15/27)	83 (89/107)		
2003 Ikonen	69	84 (233/276)	75 (64/85)	62 (92/148)		
2004 Jahnke	40	79 (254/320)	72 (26/36)	92 (200/218)		
2005 Gerber	27	100 (294/294)	62 (36/58)	84 (198/236)		
2004 Muller	30	100 (221/221)	85 (35/41)	84 (151/180)		
2005 Sommer	18	87 (109/126)	82 (14/17)	88 (80/91)		
Total	679				61 (58-64)	91 (90-92)
Weighted mean		82 (2953/3731)	73 (543/744)	85 (2047/2399)		
					65 (62-68)	90 (89-91)
TOTAL for 1.5 T	981			87(2600/2997)		
Weighted mean		83 (3441/4147)	72 (749/1043)			
3T						
2005 Sommer	18	86 (108/126)	82 (14/17)	**89 (80/90)**		

Adapted from Schuijf J et al. Meta-analysis of comparative diagnostic performance of magnetic resonane imaging and multislice computed tomography for noninvasive coronary angiography. *Am Heart J*. 2006;151:404-11.

Table 8: DOBUTAMINE STRESS MR CAD DIAGNOSIS - RESULTS TABLE

					Sensitivity			Specificity		
Author	**Year**	**Number**	**Max Dose (µg/kg/min)**	**Reference**	**+ve test**	**Pt. w. CAD**	**% (DSE)**	**-ve test**	**Pt. w.o. CAD**	**%**
van Rugge	1994	39	20	CAG ≥50%	30	33	91	5	6	83
Nagel	1999	172	40+1mg Atropine	CAG ≥50%	94	109	86 (74*)	60	70	86(70*)
Hundley	1999	41**	40+1mg Atropine	CAG ≥50%	37	41	90	5	6	83
Schalla	2002	22	40+1mg Atropine	QCA ≥75%	14	16	88	5	6	83
van Dijkaman†	2002	95	40	CAG ≥50%	41	42	98	NA	NA	NA
Kuijpers†	2003	194	40	CAG ≥50%	65	68	96	NA	NA	NA
Wahl	2004	151	40+2mg Atropine	QCA ≥50%	101	113	89	32	38	84
Paetsch	2004	79	40+2mg Atropine	QCA ≥50%	47	53	89	21	26	80
Totals + Weighted Mean		**893**			**429**	**475**	**90**	**128**	**152**	**84**

* - Values for dobutamine stress echo
** - Total patients in study 153, only 41 patients underwent coronary angiogram which are shown in this analysis
† - Only patients with positive dobutamine stress MR underwent coronary angiogram
CAG = Coronary angiogram
QCA = Quantitative coronary angiography
DSE = Dobutamine stress echo

Table 9: MRI FIRST PASS PERFUSION CAD DIAGNOSIS - RESULTS TABLE

Author	Year	Number	Stress Agent	Reference	Sensitivity			Specificity		
					+ve test	Pt. w. CAD	%	-ve test	Pt. w.o. CAD	%
Al-Saadi	2000	34	Dipyridamole	CAG ≥75%	26	29	90	4	5	83
Schwitter	2001	48	Dipyridamole	CAG ≥75%, PET*	32	37	87(91**)	9	11	85(94**)
Al-Saadi	2002	27	Dobutamine	QCA ≥75%	19	23	81%	3	4	73%
Ibrahim†	2002	39	Adenosine	QCA ≥75%, PET*	17	25	69(86**)	12	14	89(86**)
Nagel	2003	84	Adenosine	CAG ≥75%	38	43	88	37	41	90
Paetsch	2004	79	Adenosine	QCA ≥50%	48	53	91	16	26	62
Plein	2004	68	Adenosine	CAG ≥70%	54	56	96	10	12	83
Kawase	2004	50	Nicorandil	CAG ≥75%	31	33	94	16	17	94
Wolff°	2004	75	Adenosine	QCA ≥70%	11	37	93	29	38	75
Plein	2005	92	Adenosine	CAG ≥70%	52	59	88	27	33	82
Giang#°	2004	51	Adensosine	QCA ≥50%	31	33	93	14	18	75
Totals + Weighted Mean		**647**			**359**	**428**	**84**	**177**	**219**	**81**

* - ^{13}N-ammonia
** - Comparison to second reference
† - Comparison to normal controls
# - Gadolinum dose finding study; results reported for two highest doses (0.10 and 0.15 mmol/kg)
° - Multi-centre trial
CAG = Coronary angiogram
QCA = Quantitative coronary angiography

Table 10: DOBUTAMINE STRESS MR VIABILITY DIAGNOSIS – RESULTS TABLE

Author	Year	Number	EF(%)	Other Reference	Reference Method	Sensitivity			Specificity		
						+ve test	Pt. w. recovery	%	-ve test	Pt. w.o. recovery	%
Dendale	1998	28	45±12		WM/EF 3-4m F/U	9	10	90	11	14	79
Sandstede	1999	25			WM/EF 6m F/U	13	17	77	12	12	100
Baer	2000	103	39±13	TEE	WM/EF 4.9m F/U	24	28	86	22	24	92
Trent	2000	25	54±15		WM/EF 4m F/U	6	6	100	23	25	92%
van Dijkman	2002	95	30		WM + EF 17m F/U	38	39	97	NA*	NA*	NA*
Kramer	2002	22	46±10	DSE	WM + EF 2m F/U	CT	CT	86**	CT	CT	69**
Motoyasu	2003	23	51	LGE	WM 3-11m F/U	CT	CT	89**	CT	CT	80**
Schmidt	2004	40	42±10	FDG PET (F-18)	WM 4-6m F/U	24	25	96	15	13	87
Uemura	2004	20	50	SPECT (Tl^{201})	WM 4m F/U	CT	CT	89**	CT	CT	89**
Gutberlet	2005	20	27±9	SPECT (Tl^{201}), LGE	WM + EF 6m F/U	CT	CT	88**	CT	CT	90**
Totals + Wt'd Mean		**401**				**114**	**125**	**91**	**83**	**88**	**94**
Mean weighted by number of patients											

* Patients without evidence of viability by DSMR were not revascularized
** Reported by segment
CT = Cannot tell from data presented
TEE = Transoesophageal echocardiolgraphy
DSE = Dobutamine stress echocardiography
LGE = Late gadolinium enhancement

TABLE 11: LATE GADOLINIUM ENHANCEMENT MR VIABILITY DIAGNOSIS – RESULTS TABLE

Author	Year	Number	EF(%)	Other Reference	Reference Method	Sensitivity			Specificity		
						+ve test*	Segment w. recovery	%	-ve test**	Segment w.o. recovery	%
Kim	2000	50	43±13		WM/EF 3m F/U	329	256	78	124†	110†	98†
Sandstede	2000	12	CT		WM 3m F/U	47	39	83	26	25	96
Choi	2001	24	CT		WM 2-3m F/U	275	213	77	64	61	95
Gerber	2002	20	CT		WM 7m F/U	170	109	64	219	179	82
Klein	2002	31	28±9	^{18}FDG PET	PET	NA	NA	83	NA	NA	88
Beek	2003	30	51		WM/EF 2-4m F/U	151	119	79	35º	31º	89
Kitagawa	2003	22		SPECT (^{201}TI)	WM 2-4m F/U	196	192	98	68	51	75
Kuhl	2003	26	31±11	^{18}FDG PET, SPECT	PET	NA	NA	96	NA	NA	84
Motoyasu	2003	23	51	DSMR	WM 3-11m F/U	175	146	83	103	74	72
Schvartzman	2003	29	28±10		WM/EF 3-8m F/U	44	36	82	33	27	82
Selvanayagam	2004	52	62±11		WM/EF 5m F/U	190	156	82	88	71	81
Van Hoe	2004	18		DSMR	WM 7-11m F/U	61	56	92	24º	22º	92º
Gutberlet	2005	20	27±9	SPECT (TI^{201}), DSMR	WM + EF 6m F/U	CT	CT	99	CT	CT	94
Totals + Wt'd Mean Mean weighted by number of segments		**357**				**1638**	**1322**	**81**	**784**	**651**	**83**

Table 12: RADIATION

Modality	Radiation Source	Total Dose (mCi)	Radiation Dose (mSv)
SPECT MPI (1 day protocol)	Tc-99m	32-40	9.2-11.4
SPECT MPI (2 day protocol)	Tc-99m	50	14.8
SPECT MPI	Tl-201	2.5-3.0	15.7-18.9
PET MPI	Rb-82		
Camera (3D BGO)		20-40	3.6-7.1
Camera (2D BGO/LSO/GSO and 3D LSO/GSO)		60-120	10.6-21.2
PET MPI	N-13 ammonia	20-40	2.0-4.0
PET FDG		5-15	5.0-15.0 mSv
PET Viability			
Camera (3D BGO)	Rb-82/FDG	10-20/10	6.8-18.6
Camera (2D BGO/LSO/GSO and 3D LSO/GSO)	Rb-82/FDG	30-60/10	10.3-25.6
	N-13/FDG	10-20/10	6.0-17.0
CT (16-slice MDCT)	x-ray		7-15
CT (64-slice MDCT)	x-ray		5-15
Invasive Coronary Angiography	x-ray		2.1-2.5
MRI	N/A		N/A

CT - Computed tomography
SPECT - Single photon emission tomography
MPI - Myocardial perfusion imaging
PET - Positron emission tomography
RB-82 - Rubidium -82
FDG - Fluorodeoxyglucose
MRI - Magnetic resonance imaging

Appendix 1:

NAME	EXPERTISE	INSTITUTION	MEMBERSHIP AFFILIATIONS
Primary Panel Members (Writing Team)			
BEANLANDS, Dr. Rob S.B.	Cardiology, PET, Nuclear Cardiology	University of Ottawa Heart Institute	CCS, CNCS, CANM
CHOW, Dr. Benjamin J.W.	Cardiology, CT Angiography, PET, Nuclear Cardiology	University of Ottawa Heart Institute	CCS, CNCS
DICK, Dr. Alexander	Cardiology, Cardiac MRI	Sunnybrook & Women's College HSC University of Toronto	CCS, CanSCMR
FRIEDRICH, Dr. Matthias G.	Cardiology, Cardiac MRI	Foothills Medical Centre, University of Calgary	CCS, CanSCMR*
GULENCHYN, Dr. Karen	Nuclear Medicine, PET	Hamilton HSC, McMaster University	Chair-Standards of Practice (2005-06) CANM*, CNCS*
KIESS, Dr. Marla	Cardiology, Nuclear Cardiology	St.Paul's Hospital , University of British Columbia	CCS, CNCS*
LEONG-POI, Dr. Howard	Cardiology, Echocardiography	St. Michael's Hospital, University of Toronto	CCS
MILLER, Dr. Robert M.	Radiology, CT, MRI	Halifax Infirmary, Dalhousie University	CAR*
NICHOL, Dr. Graham	Clinical Epidemiology, Cost Analysis	Harborview Prehospital & Clinical Trial Center University of Washington	CCS
Secondary Panel Members:			
FREEMAN, Dr. Michael	Cardiology, Nuclear Cardiology	St. Michael's Hospital, University of Toronto	CCS, CNCS
BOGATY, Dr. Peter	Cardiology	Quebec Heart Institute, Universite Laval	CCS
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HUDON, Dr. Gilles	Radiology	Montreal Heart Institute, Universite de Montreal	CAR
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GRAHAM, Dr. John	MRI Fellow	Sunnybrook & Women's College HSC, University of Toronto	

**Current Executive*

Appendix 2:

The ACC/AHA Classifications I, II, and III are used to summarize indications as follows:

Class I: Conditions for which there is evidence and/or general agreement that a given procedure or treatment is useful and effective.

Class II: Conditions for which there is conflicting evidence and /or a divergence of opinion about the usefulness/efficacy of a procedure or treatment.

Class IIa: Weight of evidence/opinion is in favor of usefulness/efficacy.

Class IIb: Usefulness/ efficacy is less well established by evidence/ opinion.

Class III: Conditions for which there is evidence and/or general agreement that the procedure/treatment is not useful/ effective and in some cases may be harmful.

Levels of evidence for individual class assignments are designated as:

A = Data derived from randomized clinical trials

B = Data derived from a single randomized trial, or from nonrandomized studies

C = Consensus opinion of experts

Techniques considered investigational are not further classified.

In considering the use of a specific technique in individual patients, the following factors are important:

1) The quality of the available laboratory and equipment used for performing the study and the quality, expertise, and experience of the professional and technical staff performing and interpreting the study.

2) The sensitivity, specificity, and predictive accuracy of the technique.

3) The cost and accuracy of the technique compared with that of other diagnostic procedures.

4) The effect of positive or negative results on subsequent clinical decision making.

(*Klocke FJ et al. ACC/AHA/ASNC Guidelines for the Clinical Use of Cardiac Radionuclide Imaging. JACC 2003;42(7):1-69*)