Is cardiac magnetic resonance imaging assessment of myocardial viability useful for predicting which patients with impaired ventricles might benefit from revascularization?

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Summary
A best evidence topic in cardiac magnetic resonance imaging (MRI) was written according to a structured protocol. The question addressed was: what is the role of cardiac magnetic resonance (CMR) imaging in viability assessment of ischaemic cardiomyopathy? Altogether more than 164 papers were found using the reported search; of which, 6 represented the best available evidence to answer the clinical question and an additional 4 were found by crosschecking the reference lists for further ‘best available evidence’ papers. The authors, journal, date and country of publication, patient group studied, study type, relevant outcomes and results of these papers are tabulated. Using late-gadolinium enhancement-cardiac magnetic resonance (LGE-CMR) imaging, infarcted myocardium can be identified by the presence of hyperenhanced signal. The extent of myocardial hyperenhancement correlates inversely with improved myocardial contractility following surgical or per-cutaneous revascularization. Furthermore, CMR is able to assess not only viability, but also make gold-standard assessment of ventricular function and volume as well as identify stress perfusion defects, each of which is relevant to estimating patient prognosis. National bodies have also begun to formally recommend CMR imaging for cardiac viability assessment. For example, the Canadian Cardiovascular Society (CCS) has stated that ‘assessment of myocardial viability in patients with left ventricle dysfunction or akinetic segments for predicting recovery of ventricular function following revascularization is a class I indication for the use of LGE-CMR’. We conclude that cardiac MRI is an excellent tool for predicting myocardial viability, in the context of acute and chronic ischaemic heart disease whether subsequent revascularization is achieved by surgical or percutaneous means. In addition, the versatility of CMR imaging makes it an increasingly attractive tool for the complete assessment of the patient with ischaemic cardiomyopathy.

Keywords: Ischaemic cardiomyopathy • Cardiac MRI • Myocardial viability

INTRODUCTION
A best evidence topic was constructed according to a structured protocol. This is fully described in ICVTS [1].

THREE-PART QUESTION
In patients being considered for surgical revascularization is Cardiac MRI scanning effective in predicting ischaemic reversibility.

CLINICAL SCENARIO
You are at an multi-disciplinary team meeting to discuss the case of a patient with worsening angina on maximal anti-anginal therapy. He has left ventricular systolic dysfunction, an ejection fraction of 30% and NYHA class II heart failure. Coronary angiography showed an occluded left anterior descending artery and flow-limiting coronary artery stenoses in his left circumflex artery and right coronary artery. You are asked to take him on for coronary artery bypass graft (CABG), but are concerned that there may not be sufficient viable myocardium. The cardiologist suggests a cardiac MRI scan to assess viability. You are not sure of the additional benefit of this new test so resolve to look this up.

SEARCH STRATEGY
MedLine 1948 to July 2011 using OVIDSP interface. (exp Myocardial Revascularization/ or revascularization.mp.) AND viability.mp AND (exp magnetic resonance imaging/ OR MRI.mp OR CMR.mp)

SEARCH OUTCOME
A total of 164 papers were found using the reported search. Six papers were identified, relevant to the best evidence topics subject, providing best available evidence to answer the question. An additional four relevant papers were found by cross-checking the references of the extracted papers. These are presented in Table 1.
<table>
<thead>
<tr>
<th>Author, date and country</th>
<th>Study type</th>
<th>Patient group</th>
<th>Outcomes</th>
<th>Key results</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kim et al., 1999, Circulation, USA</td>
<td>Basic science report</td>
<td>18 dogs sustained a myocardial infarction through coronary artery occlusion. 8 dogs sustained reversible ischaemic injury with the use of a reversible hydraulic occluder</td>
<td>LGE histo-pathology</td>
<td>Level of LGE was raised in acute infarct hearts (29±5% of normal) but not in reversible ischaemic injury hearts (98±6% of normal). LGE was also seen in chronically infarcted myocardium (253±54% of normal). MRI hyperenhancement correlated virtually identically with histopathology at 8 weeks (R = 0.97)</td>
<td>Study confirming the utility of LGE in identifying infarcted myocardium</td>
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<tr>
<td>Kim et al., 2000, N Engl J Med, USA</td>
<td>Prospective validating diagnostic cohort study (level 1)</td>
<td>50 patients undergoing elective revascularization with regional wall motion abnormality without unstable angina or NYHA IV heart failure</td>
<td>Myocardial contractility</td>
<td>Contractility post-revascularization increased in 78% of myocardial wall sections with no hyperenhancement and increased in 2% of sections with hyperenhancement &gt;75% of tissue. Mean hyperenhancement in dysfunctional myocardium with improved contractility = 10±7% and in dysfunctional myocardium without improved contractility = 41±14% (P &lt; 0.001)</td>
<td>Landmark study showing a relationship between the trans-mural extent of viability and the likelihood of functional improvement following revascularization</td>
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<tr>
<td>Choi et al., 2001, Circulation, USA</td>
<td>Prospective validating diagnostic cohort study (level 1)</td>
<td>24 patients with MI acutely revascularized (PCI or lysis) underwent MRI if no previous MI</td>
<td>Myocardial contractility</td>
<td>LGE &lt;25% of wall thickness was found to be the best predictor of contractile improvement as measured by ejection fraction (P &lt; 0.005), in comparison to creatine kinase-MB and total infarct size</td>
<td>In the setting of acute MI, trans-mural extent of LGE correlates with improved function and therefore viability</td>
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<td>Selvanayagam et al., 2004, Circulation, UK</td>
<td>Prospective validating diagnostic cohort study (level 1)</td>
<td>56 patients undergoing elective CABG for CAD. Excluded if &gt;75 years, renal failure or severe heart failure</td>
<td>Myocardial contractility</td>
<td>Following CABG, improvement in contractility was inversely related to extent of trans-mural HE. Regional function improved in 86% of myocardial segments with no hyperenhancement and 4% of myocardial segments with &gt;76% trans-mural hyperenhancement</td>
<td>Post-CABG, extent of LGE predicts viable myocardium</td>
</tr>
<tr>
<td>Ichikawa et al., 2005, J Am Coll Cardiol, Japan</td>
<td>Prospective validating diagnostic cohort study (level 1)</td>
<td>18 patients. First MI. Single vessel PCI. Stable</td>
<td>Myocardial contractility</td>
<td>Following acute MI, thickness of non-enhanced myocardial wall was a better predictor of viability than the percentage of trans-mural hyperenhancement (ROC area = 0.650 vs. 0.594, P &lt; 0.05)</td>
<td>Similar study to Choi et al., but suggested that non-enhanced wall thickness is more importantly an assessment of viability than the extent of LGE</td>
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<tr>
<td>Welthofer et al., 2004, Circulation, Germany</td>
<td>Prospective, blinded within-patient comparison of dobutamine stress MR and LGE (level 1)</td>
<td>29 patients. CAD and angina. LV &lt;45%. Wall motion abnormalities. No infarction in last 2 months. Elective revascularization</td>
<td>Myocardial contractility</td>
<td>3 months following revascularization, dobutamine stress MRI was more powerful in predicting improvement in myocardial contractility than LGE. (ROC area = 0.838 vs. 0.728, P &lt; 0.05)</td>
<td>In patients with stable CAD revascularized with PCI or surgery, it was shown that dobutamine stress MRI was better than LGE-MRI</td>
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<td>Pegg et al., 2010, J Cardiovasc Magn Reson, USA</td>
<td>Prospective validating diagnostic cohort study (level 1)</td>
<td>33 patients. CAD (3 VD/LMS). Reduced LV systolic function. Elective CABG</td>
<td>Myocardial contractility</td>
<td>6 months post-revascularization, improvement in ejection fraction was best predicted by patients with ≥10 viable + normal myocardial segments (i.e., trans-mural LGE &lt;50%) with a sensitivity of 95% and specificity of 75%. Patients with &lt;10 viable + normal segments showed no improvement in global LV function</td>
<td>This paper extended the work of Selvanayagam et al. The high spatial and temporal resolution of CMR showed that patients with ≥10 or more viable + normal segments are likely to have improved LV function following CABG</td>
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<tr>
<td>Wu et al., 2007, J Nucl Med, Japan</td>
<td>Prospective validating diagnostic cohort study (level 1)</td>
<td>29 patients. Stable CAD and LV dysfunction. Elective CABG</td>
<td>Myocardial contractility</td>
<td>Comparison of contrast-enhanced MRI with 18F-FDG PET/201Tl SPECT. Extent of LGE on MRI correlated negatively with myocardial viability detected with PET/SPECT</td>
<td>This paper demonstrated that contrast-enhanced MRI and PET/SPECT were equally effective at demonstrating viability</td>
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<tr>
<td>West et al. 2010, Curr Probl Cardiol, USA</td>
<td>Review article</td>
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<td>A review of the role of CMR in myocardial infarction, viability and cardiomyopathy</td>
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**Table 1: Best evidence papers**
RESULTS

Three imaging modalities are routinely used for assessment of myocardial viability; 18F-fluorodeoxyglucose (18F-FDG) combined with positron emission tomography (PET), dobutamine stress echocardiography (DSE) and late-gadolinium enhancement cardiac magnetic resonance (LGE-CMR). Traditionally, PET scanning has been viewed as the gold-standard for viability assessment [2]. However, Wu et al. [3] demonstrated that 18F-FDG-PET and LGE-CMR were comparable in their ability to identify viable myocardium in patients undergoing CABG for chronic coronary artery disease. Also, Pegg et al. [4] demonstrated that LGE-CMR prediction of viable myocardium and improvement in left ventricle (LV) ejection fraction post-revascularization compares very favourably with both PET and DSE. The following section outlines the evidence for the use of CMR in viability assessment.

Using the canine animal model, Kim et al. [5] demonstrated the value of LGE-CMR in identifying infarcted and viable myocardium in ischaemic hearts. Infarcted myocardium showed clear hyperenhancement at 3-day and 8-week post-insult, which matched accurately with histological findings. Ischaemic but not infarcted myocardium showed no hyperenhancement regardless of whether there was a regional wall motion abnormality or not.

Kim et al. [6] then published the landmark study in this field. A total of 50 patients with flow-limiting coronary artery disease and left ventricular dysfunction were imaged before and after elective revascularization. As the extent of myocardial trans-mural hyper-enhancement increased, the percentage improvement in myocardial contractility decreased. If >50% of myocardial wall thickness showed hyperenhancement, <15% of myocardium showed any improvement in contractility. Reversible and irreversible myocardial injury was delineated in humans. Furthermore, the extent of irreversible myocardial damage was quantified and correlated with the likelihood of improvement in the regional wall motion. Myocardium with <50% hyperenhancement is consequently regarded as potentially viable in routine practice.

A similar study was performed by Choi et al. [7] which showed that LGE-CMR imaging could predict improvement in myocardial contractility in patients with an acute myocardial infarction (MI). A total of 24 patients were scanned 7 days and then 2-4 months following an acute MI. Choi et al. also found that areas of dysfunctional myocardium 7 days post-MI were more likely to show improved contractility at 2-4 months the lesser the extent of trans-mural late-gadolinium hyperenhancement.

Selvanayagam et al. [8] acknowledged the above findings and utilized LGE-CMR to predict myocardial viability in patients undergoing CABG. A total of 52 patients underwent LGE-CMR imaging pre-operatively, 6 days and 6 months post-operatively. Post-operatively, myocardial contractility improved by at least one grade in 57% of myocardial segments analysed. Furthermore, there was a strong correlation between the extent of trans-mural hyperenhancement and improved contractile function, confirming the value of contrast-enhanced MRI in assessment of viability pre-CABG.

Pegg et al. [4] extended this work performing LGE-CMR imaging pre-operatively, 6 days and 6 months following CABG in 33 patients with LV systolic dysfunction and stable coronary artery disease. They analysed myocardial contractility and demonstrated a consistent improvement in global systolic function if patients had ≥10 viable + normal segments (based on the American Heart Association 17-segment model). This was 95% sensitive, which compared favourably with the ability of PET and DSE to predict functional recovery.

Ichikawa et al. [9] used a slightly different approach to viability assessment using LGE-CMR. They demonstrated in 18 MI patients who were acutely revascularized, that in damaged territories, the thickness of non-enhanced myocardium was a better predictor of viable myocardium than the percentage of trans-mural late-gadolinium hyperenhancement.

Myocardial viability can also be predicted by assessment of contractile activity in response to a pharmacological stress, such as dobutamine. Wellhöfer et al. [10] compared the efficacy of LGE-CMR and dobutamine stress MRI in predicting myocardial viability in patients undergoing revascularization (CABG or PCI). Both modalities were effective in predicting myocardial viability; however, dobutamine stress MRI was superior to contrast-enhanced MRI, particularly in myocardium with non-trans-mural hyperenhancement. Whether this superiority would make a significant difference to clinical decision-making is uncertain.

In a review article by West et al. [11], the authors highlighted the importance of the studies by Kim et al. [6] and Wellhöfer et al. [10] showing the value of LGE-CMR for predicting functional recovery of myocardium following revascularization and the merits of dobutamine stress MRI in predicting contractile reserve of myocardium with non-trans-mural infarction.

Finally, CMR is able to assess not only viability, but also make gold-standard assessment of ventricular function and volume and identify stress perfusion deficits, each of which is relevant to
estimating patient prognosis [12]. Additionally, national bodies such as the Canadian Cardiovascular Society are formally recommending LGE-CMR for assessment of viability and recovery following revascularization [13].

**CLINICAL BOTTOM LINE**

Cardiac MRI is a useful tool for predicting myocardial viability in acute and chronic ischaemic heart disease whether subsequent revascularization is achieved by percutaneous or surgical means. Although patient numbers are relatively small, the current data show the efficacy and safety of LGE-CMR imaging in assessment of viability, whilst there is also evidence to recommend the use of dobutamine stress MRI in the assessment of viability.

**Conflict of interest:** none declared.

**REFERENCES**