Cardiac MRI Guidance For Coronary Artery Revascularisation

Stigi Joseph MD, DM, Fellow in Interventional Cardiology & Cardiac MRI (ICPS Paris)*

Cardiac MRI is recognized as a reliable diagnostic tool for evaluation of cardiac anatomy and function. Coronary artery revascularization based on pure anatomy alone is an imperfect technique and there are many diagnostic methods for anatomy - physiology correlation. Cardiac MRI has immense potential in such correlation and thus serves as a guidance tool for coronary artery revascularization, but it is underutilized. Two important aspects of Cardiac MRI evaluation are Myocardial Stress Perfusion imaging to detect ischemia and delayed enhancement to assess cardiac viability. Cardiac MR is also used for assessing cardiac function as well as anatomic details. The usefulness of Cardiac MRI in coronary artery anatomy and plaque structure delineation are evolving. This article discusses how cardiac MRI helps in anatomy – physiology correlation of coronary artery disease.

**MYOCARDIAL STRESS PERFUSION MR IMAGING**

Non invasive stress test prior to invasive coronary angiogram is a usual practice in assessment of chronic stable angina. There are many reasons for non invasive stress testing prior to coronary angiogram.

(A) The diagnostic yield of coronary angiogram is low\(^1\). In an analysis of US National Cardiovascular Data Registry, Patel et al states that the prevalence of obstructive CAD patients referred for coronary angiogram was only 37.6%. This analysis included 1,49,739 patients who underwent Coronary angiogram from January 2004 through April 2008. Of the 3,98,978 patients who underwent CAG during this period, only 149,739 patients had obstructive CAD defined as stenosis of 50% or more of the diameter of the left main coronary artery or stenosis of 70% or more of the diameter of a major epicardial coronary artery. 39.2% of the patients had no coronary artery disease (defined as <20% stenosis in all vessels). The remaining had intermediary lesions.

(B) The event free survival with coronary artery revascularization is better than optimal medical therapy if the ischemic myocardium is > 10% and if the intervention reduces the burden by 50% (analysis of COURAGE\(^2\) and COURAGE trial nuclear sub study\(^3\)).

(C) In anatomic assessment of coronary artery disease, many stenosis are intermediary lesions. Inter individual variations in assessing the lesion significance is well known. The functional significance of these intermediary lesions are not clear and need further assessment to decide on revascularization. In the De FACTO study\(^4\) (CT Angiogram analysis of coronary arteries) 33% of the vessels studied were having intermediary lesions (30-69% as defined in the study). Of these 71% were lesions between 30-49% and 29% with lesions 50-69% stenosis. 22% of lesions in the group 30-49% stenosis and 27% in the group with 50-69% stenosis were functionally significant.

\* Senior Consultant Interventional Cardiologist, Little Flower Hospital & Research Centre, Angamaly, Kerala, India. drstigi@yahoo.com

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An ideal non invasive stress test should be able to diagnose ischemia and predict ischemic burden accurately.

A reversible perfusion defect with stress is the primary diagnostic criteria for ischemia in Stress Myocardial Perfusion MR imaging. Reversible perfusion defect is defined as persistent delay of enhancement in at least one myocardial segment during first pass of contrast agent for >3 heart beats after maximum signal intensity in the cavity of the LV that does not correspond to perfusion defect at rest. Apart from the reversible perfusion defect, myocardial segments also show wall motion abnormalities with stress. These are classified as normal, hypokinetic, akinetic and dyskinetic. This wall motion details also help in ischemia detection. Thus in stress CMR, myocardial segments can be classified as:

a) Normal (non ischemic) - no perfusion defect, no wall motion abnormality.

b) Ischemic - Stress perfusion defect with or without wall motion abnormality.

c) Scar tissue - Akinetic or dyskinetic segments with delayed hyper enhancement.

(Delayed Hyper Enhancement will be discussed in detail in the next section).

For the ease of description and identifying the vascular territory, Left Ventricular myocardium is divided into 17 or 21 segments. This help in quantification of the myocardial ischemic burden.

**Evidences for Stress Perfusion CMR imaging.**

1. In a metaanalysis by Kiran R Nandallur et al, of patients from 37 studies showed a sensitivity of 91% and specificity of 81% with stress perfusion CMR (analysis of 1183 patients) and sensitivity of 83% and specificity of 86% with stress induced Wall Motion Abnormality (analysis of 735 patients) in diagnosing CAD. In the same metaanalysis Perfusion imaging showed a sensitivity of 84% and specificity of 85% in detecting the coronary artery territory and the stress induced Wall Motion Abnormality showed sensitivity of 79% and specificity of 93% for coronary artery territory involvement.

2. Comparison with other Non invasive modalities. SPECT has an overall sensitivity and specificity of is 86% and 74% and Dobutamine stress Echocardiography has an overall sensitivity and specificity of 80% and 84%. Many studies have compared stress CMR and SPECT. In the multi centre CE-MARC Trial both had equal specificity and positive predictive value while CMR had better sensitivity and negative predictive value. Unlike SPECT there were no significant gender differences in the diagnostic performance of stress CMR.

**Table 1. Stress CMR – SPECT comparison.**

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive Predictive Value</th>
<th>Negative Predictive Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stress CMR</td>
<td>86%</td>
<td>83%</td>
<td>77%</td>
<td>90%</td>
</tr>
<tr>
<td>SPECT</td>
<td>66%</td>
<td>82%</td>
<td>71%</td>
<td>79%</td>
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</table>

**Advantages of CMR.**

I. Overall performance of stress perfusion cardiac MRI is comparable to both SPECT and Dobutamine Stress Echo with higher sensitivity.

II. It has no attenuation artifacts, so it has equal sensitivity in both males and females.

III. Stress MRI has superior spatial resolution compared with SPECT. The distinction between sub endocardial and transmural defect is better with CMR.

IV. It has no radiation exposure.

**Stress MRI artifacts**

1. Movement artifacts.

2. Sub endocardial rim artifacts. This may be confused with myocardial perfusion defects. Rim artifacts appear as dark lines at the border of myocardium and blood flow. Under sampling from low spatial resolution is the major reason for endocardial rim artifacts.

**CARDIAC MRI FOR ASSESSMENT OF VIABILITY.**

Viability assessment before revascularization is important in ischemic cardiomyopathy. Not all patients with ischemic cardiomyopathy show improvement in LV function after revascularization. Nearly 1/3rd of dysfunctional LV segments improve with revascularization and 40% show overall improvement in LV function. The expected benefits with revascularization are improvement in symptom status and exercise capacity, improvement in survival and prevention of sudden cardiac death.

Improvement in regional and globular LV function are of paramount importance in achieving these goals. In an analysis of 3,003 patients from 105 studies having 15,045 dysfunctional segments by non invasive testing 53% (7,941) showed segmental improvement after revascularization. Of these, 749 segments (84%) were viable according to the imaging modalities.

Improvement in overall LV function is more important than segmental improvement. The amount of viable tissue needed for improvement in
LV function differed in different studies, but available evidence suggests that >20% of the viable myocardium is needed for overall improvement in LV function. It is also known that those patients with >20% of viable myocardium shows improvement in LV dimensions after revascularization. Patients with predominantly scar tissue shows ongoing adverse LV remodeling with increase in both LV diastolic and systolic volumes.

In a metaanalysis by Allman et al, the importance of viability prior to revascularization was underscored. In his analysis involving 3,088 patients from 24 studies the annual death rate was 3.32% in patients with viable myocardium who underwent revascularization, while it was 16% in those who had viable myocardium who were treated medically. In those with non viable myocardium the annual death rate was 7.7% after revascularization and 6.2% with medical therapy. This shows that those with viable myocardium should undergo revascularization, while medical therapy is better for patients with non viable myocardium.

How to assess Myocardial viability by CMR?

1) Rest cine MRI with SSFP can provide accurate assessment of LV wall thickness at rest, resting wall motion abnormality as well as systolic wall thickening. However this is not accurate as both viable and necrotic myocardium may show these features.

2) Inotropic stimulation with low dose Dobutamine is reliable means for predicting functional recovery. Compared with Echocardiography MRI has the advantage of relatively low inter individual variability.

3) Late Gadolinium enhanced MRI: This is the hallmark of viability assessment.

Criteria for viability

1. LV end diastolic wall thickness >5.5mm. Studies with F18-FDG PET and CMR has shown that regions with LV end diastolic wall thickness <5.5mm has reduced glucose uptake while areas with LV end diastolic wall thickness >5.5 mm has preserved glucose intake.

2. Low dose Dobutamine induced systolic wall thickening >2.0mm. This has a sensitivity of 89% and specificity of 94%.

3. Late Gadolinium enhancement (Delayed Hyper Enhancement) >50% of the myocardial thickness. Even very thin myocardium without late Gadolinium enhancement have the potential for increase in thickness and recovery of function after revascularization.

LGE (Delayed Hyper Enhancement) is useful in detecting acute Myocardial Infarction with a sensitivity of 99% and chronic Myocardial Infarction with sensitivity of 94%. T2 weighted imaging in acute MI will identify the salvageable myocardium. LGE performed 5 minutes after contrast injection identifies micro vascular obstructions (no reflow). This is seen as dense hypo enhanced area surrounded by bright region of infarct.

Basics for Late Gadolinium enhanced MRI

Gadolinium does not cross the cellular membrane and is distributed in the extra cellular space only. In normal myocardium myocytes are densely packed and 80% of water space is intra cellular. So the volume of distribution in normal myocardium is quite small (20%). In acute infarctions the myocytes cell membranes are ruptured so the Gadolinium enters into the intra cellular space. This increases the concentration of Gadolinium at the tissue level resulting in hyper enhancement. Myocardial scar is characterized by dense collagenous matrix. Here the interstitial space between collagen fibers are significantly greater than the interstitial space between myocytes in normal myocardium. So the contrast distribution in scar is also higher resulting in hyper enhancement.

Protocol

CMR can be performed with 1.5T or 3T systems. Stress MR images are better with 3T systems while Delayed hyper enhancement is better with 1.5T systems.

Stress agents

Coronary vasodilator agents

<table>
<thead>
<tr>
<th>Agent</th>
<th>Dose</th>
<th>Half Life</th>
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<tbody>
<tr>
<td>Adenosine</td>
<td>140 mcg / Kg / min. May increase to 210 mcg / kg/min.</td>
<td>10 seconds</td>
</tr>
<tr>
<td>Regadenoson</td>
<td>0.4mg single injection.</td>
<td>2-3 minutes</td>
</tr>
<tr>
<td>Dipyridamole</td>
<td>0.56mg / kg IV over 4 min.</td>
<td>23 minutes</td>
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Dobutamine - Upto 40mcg / kg / min. with or without iv Atropine upto 2 mg is also used as stress agent. This has the advantage for better assessment of associated Wall Motion Abnormalities.

Gadolinium – The perfusion agent

The dose of the Gadolinium contrast should be as low as possible. For perfusion imaging 0.05 - 0.1 mmol/kg wt and for delayed hyper enhancement 0.1 - 0.2mmol/kg wt is recommended.

Gadolinium should be avoided in patients with stage IV or V chronic kidney disease (estimated GFR <30 ml / min / 1.73 meter<sup>3</sup>), patients with acute renal failure, those on dialysis and those with chronic liver disease, due to concerns regarding nephrogenic systemic fibrosis.

LV structure and function analysis are done with Steady State Free Precession (SSFP) cine
acquisitions in held expiration, with a slice thickness of 6-8 mm and 2-4 mm inter slice interval. This is followed by administration of stress agent and then the contrast agent (at an infusion rate of 3-7 ml/sec followed by saline flush). Breath hold starts with the administration of contrast agent and images are taken for 40 - 50 heart beats. First – pass perfusion images are taken with T1 – weighted inversion - recovery gradient - echo sequence. After a washout period of 10 minutes rest images are taken. If stress images are normal and free of artifacts, rest perfusion imaging may be avoided. If rest imaging are taken, same dose of Gadolinium is repeated.

After 10-15 minutes of delay the contrast enhanced images are taken with T1-weighted inversion - recovery gradient - echo sequences.

**Segmental Analysis**

After the acquisition of images segmental analysis is done as shown below.

**Diagram A**

**Diagram B**

**Coronary Artery Territories**

**Case 1**

Middle aged male presented with LVF. ECG evidence of evolved AWMI. Echo showed severe LV dysfunction and akinetic thinned mid - distal LAD territory. After the CMR evidence of viable myocardium he underwent revascularization.

**CMR Delayed Hyper Enhancement**

DHE in the four chamber view shows uptake of the mid apical septum and Lateral wall and Apex. There is no residual myocardium in the Apex suggesting non viable area, while normal myocardial thickness in the septum and Lateral Wall is > 5mm suggesting these areas are viable.

DHE:Infarct myocardium

No DHE:The normal myocardial thickness is >50% of the total myocardial thickness suggesting viable segments.

1. basal anterior
2. basal anteroseptal
3. basal inferoseptal
4. basal inferior
5. basal inferolateral
6. basal anterolateral
7. mid anterior
8. mid anteroseptal
9. mid inferior
10. mid inferior
11. mid inferolateral
12. mid anterolateral
13. apical anterior
14. apical septal
15. apical inferior
16. apical lateral
17. apex
Case 2
63 year old male presented with class III dyspnoea of 3 weeks duration. ECG evidence of evolved AWMI. Echo showed severe LV dysfunction and akinetic and thinned LAD territory. CMR showed non viable mid-distal LAD territory and was kept on medical follow up. CMR also showed LV apical clot and was started on oral anticoagulants.

MRI for assessing prognosis in CAD
In a meta analysis of 19 studies involving 11,636 patients, the combined outcome annualized events rates were 4.9% for a positive versus 0.8% for a negative stress CMR (p < 0.0001), 2.8% versus 0.3% for cardiovascular death (p < 0.0001), and 2.6% versus 0.4% for MI (p < 0.0005) The presence of late gadolinium enhancement was also significantly associated with a worse prognosis. The annual event rates for LGE was also analyzed. Macwar et al, found that the MACE end points defined as death, non fetal MI or revascularization was 0.5% in those with normal MRI, 2.4% in the scar group, and 2.6% in the ischemia group.

Similarly in an analysis of 1,369 patients with Dobutamine stress CMR, Kelle et al found that those patients with stress-inducible WMA, who underwent medical therapy demonstrated a trend to a higher cardiac event rate (8.0%) than those with early revascularization (5.4%). Patients with normal DCMR and medical therapy or early revascularization demonstrated similar cumulative cardiac event rates (3.1% vs. 3.2%)15.

These evidences shows that CMR has excellent prognostic value in CAD.

Conclusion
We have discussed the importance of non invasive testing prior to invasive angiogram and how the quantification of ischemic burden helps in the coronary interventions. The importance of viability testing in patients with LV dysfunction prior to revascularization has also been discussed. We have also seen how CMR help in analyzing these factors. CMR is an evolving technique and newer modalities like contrast enhancement MR angiogram (CEMRA) are coming up which are helpful in non invasively visualizing the coronary artery stenosis.

Acknowledgments
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Case 3
Middle aged male presented with atypical chest pain. He underwent stress CMR, which shows stress perfusion defect involving the septum (dark area).

63 years old gentleman had Acute Anterior Wall Myocardial Infarction (delayed presentation). CMR for Cardiac viability shows non viable mid-distal LAD territory. The picture shows uptake of the contrast in the septum, Anteroapex, Anterior Wall and Anterolateral segments (White area). There is no normal myocardium in these segments suggesting non viable myocardium. There is a crescent shaped dark area adjacent to the infract segment in the LV cavity which is LV clot. The normal LV cavity is grey as seen in the picture. Normal myocardium shows no hyper enhancement (Infersespetum, Inferior Wall & Laberal Wall).


