THE ROLE OF CARDIAC MAGNETIC RESONANCE IMAGING IN PATIENTS WITH ISCHEMIC HEART DISEASE

ABSTRACT: Over the last decade, cardiovascular magnetic resonance (CMR) imaging has emerged as a powerful non-invasive imaging modality with pivotal role in the evaluation and management of patients with coronary artery disease. In particular, it quantifies ventricular function, detects myocardial ischemia and scar, visualizes myocardial edema and hemorrhage. CMR provides high resolution images that are not limited by acoustic window, and without the use of radiation or iodine contrast, hence being an attractive alternative to other non-invasive modalities.

In this paper we present four different cases illustrating the role of CMR in the diagnosis of patients with known or suspected coronary artery disease, how it provides prognostic information and may guide or alter the management.

Keywords: Cardiovascular magnetic resonance, coronary artery disease, viability

INTRODUCTION

When evaluating patients with known or suspected ischemic heart disease, cardiovascular magnetic resonance (CMR) imaging has emerged over the last decade as a powerful and "one stop shop" non-invasive imaging modality. CMR has demonstrated usefulness in several manners: 1) Evaluation and quantification of ventricular function and wall motion abnormality [1]; 2) detection of myocardial ischemia using pharmacological stress with either adenosine perfusion [2] or dobutamine [3]; 3) evaluation of myocardial scar [4], edema [5], no-reflow [6], tissue hemorrhage [7]; and 4) visualization of anomalous coronary arteries [8] and to a lesser extent proximal coronary artery disease (CAD) [9].

The roles of echocardiography, nuclear imaging, and cardiac computed tomography (CCT) have been well established in the assessment of CAD [10]. CMR, however, has several advantages and has proven to be a strong competitor (Table I). When compared to dobutamine echocardiography for instance, CMR provides images with higher contrast to noise ratio, better delineation of endocardial border, and is not compromised by poor acoustic window. While the use of contrast with echocardiography improves accuracy of testing [11], the availability and cost of contrast agents maybe be a limitation in certain countries such as Lebanon. While radiouclide imaging is widely used for the detection of coronary artery disease (CAD), perfusion CMR has many potential advantages: 1) It has more than an order of magnitude improvement in spatial resolution (typical voxel dimensions, CMR 3.0 x 1.8 x 8 mm = 43 mm³ versus SPECT 10 x 10 x 10 mm = 1000 mm³); 2) the ability to identify regional differences in flow over the full range of coronary vasodilation (i.e. no plateau in signal at high flow rates, as seen with radionuclide tracers) and differences in endocardial and epicardial flow [12]; 3) it lacks ionizing radiation; and 4) has a shorter examination time (≈ 30-45 minutes for a full CMR study ver-
sus 2-3 hours and sometimes 2 days for nuclear studies). Finally, while CCT provides high quality anatomical assessment of the coronary arteries, it still lacks physiologic assessment of ischemia, although work is in progress but hindered by the high iodine-contrast volume and radiation burden required for such an evaluation.

CMR, however, has limitations; it is more prone to artifacts, particularly arrhythmia; cannot be performed in patients with claustrophobia, or those with intracardiac devices such as pacemakers or defibrillators; and Gadolinium (Gd) contrast cannot be administered to patients with significantly impaired renal function because of potential risk of nephrogenic systemic fibrosis [13].

When CMR is appropriately ordered, it contributes to patient management and affects future therapeutic decisions, and may do so in a cost effective manner. As an autonomous diagnostic modality, CMR prevents layered testing and may serve as a gate keeping function, highlighting the prudent use of cost effective technology. In the current paper, we opted to illustrate the potential use of this technology through several cases.

CASE 1

This is a 57-year-old male with history of diabetes mellitus, hypertension, and a former smoker, who presented to the emergency complaining of chest pain for the last three days. He describes the pain as dull, on and off, non-radiating, but also experienced shortness of breath. He took antacid and had minimal relief. Shortly after arrival to the emergency room, he was chest pain free. His physical exam was unremarkable except for mild bilateral rales. His electrocardiogram showed Q waves in leads V1-V4 but no ST elevation. The first set cardiac enzymes were positive with troponin-T 10 ng/ml.

Because the pain had started over 48 hours before presentation and as he was chest pain free, a viability study was ordered. CMR was performed (Figure 1) and showed significant wall motion abnormality in the left anterior descending (LAD) distribution on the cine images with severe hypokinesis to akinesis of the antero-septal and anterior wall (base to apical) (first and second rows). T2 imaging demonstrated increased signal intensity in the LAD distribution consistent with tissue edema (third row). On late gadolinium enhancement (LGE) imaging, there was a transmural scar (arrow) involving the LAD distribution with > 75% transmurality suggesting no residual viability in that territory. Furthermore, there were scattered “dark” areas in the mid-myocardium consistent with no reflow phenomenon (arrow head).

**TABLE 1**

| COMPARISON OF MULTI-IMAGING MODALITIES IN THE ASSESSMENT OF CHEST PAIN |
|---------------------|---------------------|---------------------|
| **Echo** | **Nuclear** | **CT** | **CMR** |
| **CORONARY ANATOMY** | – | – | +++ | ++ |
| **ISCHEMIA** | ++ | ++ | + | ++ |
| **VIABILITY/SCAR** | ++ | ++ | + | +++ |
| **Tissue Characteristics** | edema/hemorrhage/ | no reflow | – | – | + | +++ |
| **LEFT VENTRICULAR FUNCTION** | ++ | ++ | ++ | +++ |
| **RIGHT VENTRICULAR FUNCTION** | ++ | – | ++ | +++ |
| **AORTIC PATHOLOGY** | + | – | +++ | +++ |
| **PULMONARY ARTERIES** | – | – | +++ | ++ |
| **PERICARDIUM** | + | – | ++ | +++ |

Echo: echocardiography CT: CAT scan CMR: cardiovascular magnetic resonance

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**Figure 1**

1st & 2nd rows
Cine images revealing wall motion abnormality in the left anterior descending (LAD) artery distribution.

3rd row
On T2 imaging, there is increase signal intensity in the myocardium in the LAD distribution consistent with tissue edema.

4th row
On late gadolinium enhancement (LGE) imaging, there is a transmural scar in the corresponding LAD distribution with evidence of “dark area” in the mid-myocardium which is consistent with microvascular obstruction (arrow head).
Discussion
The "wavefront phenomenon" of myocardial cell death was first described by Reimer and Jennings in the 1970s, and refers to the fact that as the severity and/or duration of ischemia increases, myocardial necrosis progresses from the endocardium towards the epicardium [14-15]. Work by Kloner et al. revealed that behind this "wavefront" of necrosis subregions of severe microvascular injury may also exist which impede microvascular perfusion, particularly at the infarct core [16-17]. Until recently, determining the transmural extent of necrosis and the extent of microvascular injury has largely been limited to histopathologic analysis. Advances in non-invasive imaging, however, have allowed elucidation of these different infarct patterns and revealed that myocardial tissue characterization can be useful in predicting recovery of function, guiding therapy, and predicting prognosis [18-20].

Contrast-enhanced MRI has emerged as a useful tool to examine infarct characteristics. Four different zones of myocardium can readily be defined by MRI after an ischemic event: (1) non-necrotic, stunned tissue; (2) necrotic tissue without microvascular damage; (3) necrotic tissue with microvascular damage; (4) remote, normal tissue. These zones are defined by examining contractility using cine MRI, tissue characteristics, and late Gd enhancement as illustrated. In the case of myocardial necrosis hyperenhanced (‘bright’) areas reflect necrotic tissue with intact microvasculature, while hypo-enhanced (‘dark’) areas within areas of hyperenhancement reflect necrotic tissue with damaged microvasculature (‘no-reflow’ zones) and are associated with worse prognosis.

Kim et al. [21] first reported that delayed enhancement DE-CMR could be used to predict functional improvement after revascularization. The likelihood of functional improvement for a given region was inversely related in a progressive stepwise fashion to the transmural extent of scar by DE-CMR. For example, 78% of segments without scar improved contractility after revascularization, while less than 2% of segments with ≥ 75% scar transmurality recovered, and with a negative predictive value of 92% for a cutoff of 50% scar. In other words, scar with > 50% transmurality have less than 10% chance of recovering function after revascularization.

In addition, CMR studies have shown microvascular obstruction to be a highly dynamic process [22-26], and an independent predictor of postinfarct complications, including cardiovascular death, congestive heart failure, reinfarction, or stroke, and a predictor of left ventricular remodeling [27].

Since many imaging modalities that assess no reflow were not well suited for assessing infarct size and extent of transmurality, it has not always been clear whether the link between no reflow and adverse outcomes is causal or merely associative. CMR, being well suited for simultaneously assessing multiple infarct characteristics, has helped to shed light on this issue.

In the current case, left heart catheterization was performed and showed an occluded LAD. Given the absence of viability seen on CMR, revascularization was not performed.

CASE 2
This is a 45-year-old male with hypertension, dyslipidemia, active smoker, who was referred because of abnormal echocardiogram done on routine screening and which showed hypokinetic inferior wall.

The patient reports occasional dyspnea on exertion and sharp chest pain upon climbing a flight of stairs. He underwent adenosine stress CMR to assess the amount of myocardium at risk and scar tissue.

In cine imaging, the inferior wall was hypokinetic, while the other walls had normal thickening (Figure 2, top row). Stress perfusion was performed with adenosine

Figure 2
1st & 2nd rows
Cine images of the left ventricle (short axis base to apex) revealing hypokinesis of the inferior wall.
3rd row
On adenosine perfusion, there are two areas of hypoperfusion; one in the LAD territory and another one in the right coronary artery (RCA) distribution (arrow head).
4th row
On LGE, there is a transmural scar in the RCA distribution (arrow head) but full viability in the LAD territory. This represents LAD inducible ischemia and old RCA infarct.
and showed two areas of hypoperfusions: the LAD territory (anterior walls) and right coronary artery (RCA) distribution (inferior walls) from base to apical areas. Delayed enhancement showed normal viability and no scar in the LAD distribution; however, there was a transmural scar in the inferior wall (75% of the segment). The interpretation of the study was ischemia in the LAD territory and an old infarct in the RCA distribution.

**Discussion**

The diagnostic accuracy of CMR in the assessment of CAD is well established. Stress CMR can be performed using adenosine stress perfusion similar to nuclear imaging, or dobutamine CMR similar to dobutamine echocardiography [28]. Lee et al. [29] compared perfusion CMR to technetium-99m (99mTc) sestamibi and 201-Thallium (201Tl) SPECT imaging in the quantification of regional differences in vasodilated blood flow in viable myocardium. When circumflex microsphere flow was reduced by ≥50%, perfusion defects were apparent on the MR images both by visual inspection and by analysis of the signal intensity curves. In contrast, with SPECT imaging, perfusion defects were not evident until flow was reduced by at least 85%. In a meta-analysis of 21 studies comparing stress CMR with coronary angiography, and consisting of 1233 patients with known or suspected CAD, the sensitivity and specificity of perfusion CMR for detecting obstructive CAD were 84% and 80%, respectively. When cine-imaging and delayed enhancement were incorporated during the interpretation algorithm, the diagnostic performance [30] improved significantly and yielded a sensitivity of 89%, specificity of 87%, and diagnostic accuracy of 88% for the detection of CAD (major coronary artery with stenosis ≥70% or left main stenosis ≥50%). Detection of CAD can also be assessed using dobutamine CMR with similar sensitivity and specificity to adenosine CMR [31-33]. Also, perfusion CMR has been evaluated in patients with prior coronary artery bypass graft (CABG) and had 85% and 90% accuracy in detecting native vessel territory and bypass graft ischemia, respectively [34]. Furthermore, the presence of perfusion abnormality has been shown to be predictive of adverse outcomes [35-37].

**CASE 3**

This is a 38-year-old male with family history of CAD, former smoker, and no prior medical history, who has been doing well until three months ago when he started having dyspnea on exertion. He denied chest pressure. Recently, he started having orthopnea, and paroxysmal nocturnal dyspnea, but no palpitations or syncope. He was a social drinker, and denied travel history, or prior transfusions. An echocardiogram showed depressed ejection fraction (EF 30-35% visual assessment) with regional wall motion abnormalities in the LAD territory.

Stress CMR was performed to assess for scar in the LAD distribution, the presence of ischemia and myocardial jeopardy. Cine CMR showed depressed left ventricular EF (35%) with akinesis of the anterior wall (Figure 3). Stress perfusion showed significant perfusion abnormality in the LAD distribution. However, delayed enhancement imaging showed normal viability and no evidence of scar. The study was interpreted as significant LAD ischemia and secondary myocardial hibernation with regional wall motion abnormality. The patient underwent...
left heart catheterization that showed 99% proximal LAD stenosis, which was subsequently stented. Two months later, patient presented for follow-up. He was asymptomatic, and his LV systolic function returned to normal.

**Discussion**

The insult to myocardial cells subjected to chronic ischemia promotes an initially "adaptive" response from the cell, aimed at protecting cellular integrity. During this process, the cell initially stops contracting, and later looses its contractile elements. Failure of cellular integrity results in the formation of scar tissue. The term hibernation is used to describe a dysfunctional myocardium that retains viability and has potential for improvement with revascularization. [38-40].

The process of hibernation in chronically underperfused myocardium involves a continuum of downregulation of myocyte metabolism that eventually leads to reductions in mitochondrial numbers, reduction in functional myofibrillar elements, and differentiation of cells. At some point on this continuum, the ability of the cell to recover contractile function becomes compromised. Hence the observation that hibernating myocardium revascularized "too late" does not recover contractile function promptly, if at all [41].

CMR imaging has a unique role for non-invasive assessment of myocardial viability. The combination of cine imaging, stress testing, and delayed hyper enhancement provides the most complete assessment of myocardial viability. In fact, CMR is the only non-invasive modality to visually detect scar (using delayed enhancement), and assess contractility reserve (using dobutamine stress protocol); it therefore combines information delivered from both FDG-PET and dobutamine echocardiography in one study, and therefore has one of the highest sensitivities and specificities for assessing viability and hibernation [42].

**CASE 4**

This is a 42-year-old female who presented to the ER with sharp chest pain for five days, nausea and shortness of breath. She had no cardiovascular risk factors. Her physical exam was unremarkable.

Echocardiogram showed normal left ventricular ejection fraction (LVEF). Her electrocardiogram was normal. Cardiac enzymes showed troponin 1.5 ng/mL, CK-MB 15 μg/L.

CMR was performed (Figure 4) and showed increased signal intensity on T2 and T2 STIR signifying tissue edema. Late Gd enhancement was performed and showed delayed enhancement in a non-CAD distribution, involving the epicardial and mid-myocardium of the anterior, septal and inferior walls, consistent with myocarditis. Retrospectively, patient did recall having an upper-respiratory infection one week prior.

**Discussion**

In the current case, CMR made the diagnosis of myocarditis as the cause of chest pain and myocardial injury with troponin leak. While clinical history often provides clues to the diagnosis of myocarditis, sometimes the history or symptoms could be vague and a diagnostic test is required. In the current case, a left heart catheterization was not performed since CMR non-invasively made the diagnosis, and the patient was treated conservatively and recovered. CMR can also provide insights into other causes of chest pain such as aortic pathology (dissection, intramura- ral hematoma), pericarditis (by assessing for pericardial inflammation), and can sometimes detect large pulmonary embolus at no additional cost to the patient or significantly prolonging scan time.

**CONCLUSION**

CMR plays an important role in the evaluation of ischemic heart disease. When combined with delayed enhancement and cine-CMR, the sensitivity, specificity, and diagnostic accuracy of the multi-component stress perfusion CMR exam rival other currently available modalities for the evaluation of myocardial ischemia [43]. Importantly, CMR perfusion stress testing has been

**FIGURE 4**

1st row
T2 images of left ventricular myocardium (short axis view) showing increased signal intensity which is consistent with tissue edema (asterix).

2nd row
LGE in the in septal, inferior and inferolateral wall in the mid-myocardium and epicardial distribution (arrow heads), sparing the endocardium (non-coronary artery distribution). This pattern is commonly seen in myocarditis.
deemed appropriate for the evaluation of chest pain syndromes in patients with intermediate probability of coronary artery disease (CAD) and for ascertaining the physiologic significance of indeterminate coronary artery lesions [44]. Similarly, dobutamine stress CMR is an alternative modality, particularly for patients with contra-indications for adenosine, or in whom contractility reserve needs to be assessed. Furthermore, CMR elegantly defines myocardial viability, transmurality of scar, and predicts tissue contractile recovery post revascularization [45]. CMR also provides important prognostic information [45]. Not only can it evaluate ischemic chest pain, but may also prove useful in less likely though still common scenarios such as anomalous coronary arteries, myocarditis, aortic pathology, pericardial disease and others. There is an increasing role for metabolic imaging, strain associated with dobutamine CMR [46] and better assessment of the coronary arteries using stronger magnetic fields. While CMR availability and cost remain some of its main challenges, there is growing interest and need for such non-invasive modality which may become truly a “one-stop shop”.

REFERENCES

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