MRI assessment of left ventricle myocardial viability in patients with chronic coronary artery disease in comparison with single photon emission computed tomography

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Abstract

Background: Coronary artery disease (CAD) is highly prevalent in developed countries and is a leading cause of death. Diagnostic imaging plays an important role in the proper assessment and management of CAD. Myocardial perfusion is evaluated by SPECT in most patients today; however, this technique exposes patients to radiation and its diagnostic accuracy is sometimes limited by relatively low spatial resolution and artifacts from photon scatter and tissue attenuation. Scintigraphy defects may not be apparent until 10 g of tissue is infarcted. Thus, because a sizable threshold of damage is required, SPECT may miss small or subendocardial MI. Advances in rapid magnetic resonance imaging technology and its application to cardiac imaging have shown that MR imaging has tremendous potential for evaluation, a shortened examination time (25 to 40 min), good safety and tolerability profile, and detection of small subendocardial infarcts.

Aim: assessment of myocardial viability in patients with chronic coronary artery disease by magnetic resonance imaging in comparison with single photon emission computed tomography (SPECT).

Patients and Methods: This prospective study include examination of 10 adult patients (each patient has 3 coronary arteries, so we examined 30 coronary arteries and their myocardial territories) known to have chronic ischemic heart disease in Cairo university by MRI and SPECT with conventional angiography as a standard reference. MRI done by using 1.5T machine, using SENSE (sensitivity encoding) cardiac coil (6 element phased-array coil, receive only), functional cine images, first pass perfusion images and delayed enhancement images were acquired. SPECT study was done by 2-day exercise/rest gated SPECT imaging with Tc-99m sestamibi. Conventional coronary angiography was done using a trans-femoral approach to selectively inject the left and right coronary systems sequentially. The results of cardiac MRI subdivided into three groups: (a) Myocardial ischemia was defined as: either 1- Cardiac segment with motion abnormality or perfusion deficit at first-pass perfusion MR imaging consistent with no hyperenhancement at delayed-enhancement MR imaging. Or 2- Cardiac segment of subendocardial enhancement (25 % thickness scar) with motion abnormality. (b) Myocardial scarring is defined as: either 1- Cardiac segment with myocardial delayed enhancement having $\geq 75\%$ thickness scar. Or 2- Myocardial thickness less than 6 mm in diastole. (c) Mixed myocardial ischemia and scarring is defined as: Cardiac segment with myocardial delayed enhancement of near 50 % (>25% and <75%) thickness scarring. The results of SPECT were obtained by comparison between resting and exercise images to detect areas with fixed defects (scar) and those with reversible defects (ischemia). A defect was considered to be *fixed (scarred)* when there was no change between the stress and rest images, partially reversible (mixed ischemia and scar) when there was an improvement in tracer uptake of at least 1 grade between stress and rest images, totally reversible (ischemic) when there was normalization of uptake at rest images. In coronary angiography a reduction of the luminal diameter 70% or more in a major epicardial coronary artery or the major branches was considered to be a relevant stenosis. The angiographic results were classified as one-, two-, or three-vessel disease.

Results: Both CMR and SPECT are accurate in detection of diseased coronary arteries with statistically significant P values. The overall patient based sensitivity, specificity, PPV, NPV and accuracy of cardiac MRI for the detection of diseased coronary artery were 94% (15 of 16 territories), 100% (14 of 14), 100% (15 of 15), 93% (14 of 15) and 97% (29 out of 30) respectively while the overall sensitivity, specificity, PPV, NPV and accuracy of SPECT for the detection of coronary artery stenosis were 88% (14 of 16), 93% (13 of 14), 93% (14 of 15), 87% (13 of 15) and 90% (27 out of 30) respectively. Both modalities CMR and SPECT show no statistically significant difference in detection of ischemic and scarred left ventricle myocardial segments although the sensitivity of MRI was higher than SPECT in detection of transmural scarring. As regard detection of complications CMR detected 1 intraventricular thrombus that was missed by SPECT.

Conclusion: CMR is an accurate tool for assessment of coronary artery disease and myocardial viability as regard ischemia, scarring with great capability for detection of transmural extension of scarring and prediction of recovery. MRI can detect complications like ventricular thrombus that was missed by SPECT. Other advantages of MRI are time saving, lack of ionizing radiation and detection of left ventricular volumetrics and wall motion abnormalities.

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Keywords: myocardial viability, Cardiac magnetic resonance imaging, SPECT, coronary artery disease.

INTRODUCTION

Coronary artery disease (CAD) is highly prevalent in developed countries and is a leading cause of death (1). Diagnostic imaging plays an important role in the proper assessment and management of CAD. Myocardial perfusion is evaluated by single photon emission computed tomography (SPECT) in most patients today; however, this technique exposes patients to radiation and its diagnostic accuracy is sometimes limited by relatively low spatial resolution and artifacts from photon scatter and tissue attenuation. Scintigraphy defects may not be apparent until 10 g of tissue is infarcted. Thus, because a sizable threshold of damage is required, SPECT may miss small or subendocardial MI.

Practical advantages of cardiac magnetic resonance (CMR) include the lack of ionizing radiation, a shortened examination time (25 to 40 min), good safety and tolerability profile, and detection of small subendocardial infarcts.

Advances in rapid magnetic resonance imaging technology and its application

to cardiac imaging have shown that MR imaging has tremendous potential for evaluation of cardiac disease ^{(2-4).}

MR imaging has been hailed as the single modality capable of defining cardiac anatomy and function, myocardial perfusion, myocardial viability, and coronary artery anatomy (5,6).

The hallmark of CAD at cardiac MR imaging (CMR) includes wall-motion abnormalities with or without reduced systolic function, diastolic dysfunction, progressive chamber enlargement, wall thinning, perfusion defects at pharmacologic stress, and myocardial scar contacting the subendocardium within a coronary territory.

PATIENTS AND METHODS

Patients: 10 patients with known chronic coronary artery disease were enrolled in the study between January 2010 and August 2015 (each patient has 3 coronary arteries, so we examined 30 coronary arteries and their myocardial territories).

All patients underwent cardiac MRI,

conventional coronary angiography and stress-rest SPECT study within 3 weeks. All these patients presented with ischemic chest pain or suspected progression of known coronary artery disease. The clinical and laboratory investigations were evaluated.

Inclusion criteria: patients with ischemic heart disease, with sinus heart rhythm, able to hold breath for accepted time (10-20 seconds) and normal serum creatinine.

Exclusion criteria: hemodynamic instability, atrial fibrillation, contraindications for MR imaging; claustrophobia, patients with pacemaker or metal implants, contraindication for contrast material including known allergy and renal insufficiency (serum creatinine more than 1.4 mg\dl).

Methods: include:

1- <u>MRI:</u>

No special instructions are required prior to the examination. Medications are not to be discontinued. First, a short medical history was taken. Patients were then screened for contraindication to MR imaging. All undergarments containing nylon or metal were removed. The former may cause artifacts because of static electricity and the latter can cause image degradation. Before the examination; the heart rate and rhythm were evaluated. To evaluate patients ability of breath-withholding for relatively long time; they were asked to perform a deep inspiration and to hold their breath without pushing (i.e., Valsalva maneuver). The MRI examination was done by A Philips Achiva. Netherland (1.5)Tesla) superconducting magnet in radiology department -Cairo university. SENSE (sensitivity encoding) cardiac coil (6 element phased-array coil, receive only) was used.

Imaging protocol:

All patients received 18-gauge intravenous line to allow administration of the contrast agent. The patients underwent a standard MR examination that included the following steps:

1.Scout images were acquired in orthogonal orientations for planning of the final long-axis and short-axis views.

2.Functional cine images: were using electrocardiographic acquired gated, breath hold balanced turbo field echo (b-TFE) sequence in short axis view. Eight to eleven short-axis views 1 cm apart, were obtained during repeated breath-holds, starting from the mitral valve insertion and covering the entire left ventricle with the following parameters:

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TR/TE: 4.4/2.5	FOV: 300
Phases: 25	NSA: 1
Matrix: 128x128	Bandwidth: 125
kHz	
Flip angle: 15°	Scan Time:
0.07-0.12 sec.	
Slice thickness: 8mm	Slice number:
8-11	

3. First pass rest perfusion imaging

It is performed by intravenous bolus of 0.025 mmol/kg injection of gadopentetate dimeglumine (Magnevist) at an injection rate of 5 mL/sec followed by a flush of 20 mL of saline solution at the same rate. Scanning was started about 10 seconds after the starting of contrast injection and continues for about 1 minute. Breath-hold first-pass perfusion MR imaging was performed by using a hybrid gradient echo-planar imaging pulse sequence. This pulse sequence yields three sections (at basal, mid-cavitary and apical levels) in the short-axis view covering the entire left ventricle every other heart beat with the following parameters:

TR/TE: 2.9/1.46 FOV: 350

Phases: 25	NSA: 1
Matrix: 128 x 128	Bandwidth: 125
kHz	
Flip angle: 20°	Scan Time: 1
sec	

Slice thickness: 8mm Slice number: 3 **4. An additional bolus** of 0.1-0.2 mmol/kg gadopentetate dimeglumine immediately after ending the rest perfusion scan.

5. Additional functional cine images were acquired using similar parameters to the previously described cine sequences. Four to six long-axis views (Two or Four chamber views), 1 cm apart, were obtained during repeated breath-holds.

6. Standard delayed gadolinium enhancement imaging was performed by using Segmental inversion recovery balanced turbo field echo (IR-b-TFE), starting 10–20 min after the last injected intravenous bolus of contrast). Contrastenhanced images were acquired in the same orientation as the cine images (short axis plane) and at least one of the long axis plane with the following parameters:

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TR/TE: 3.8/1.86	FOV: 300
TI: 260-350	NSA: 1
Matrix, 128x128	Bandwidth:
125 kHz	
Flip angle: 15°	Scan Time: 9-
15 sec.	
Slice thickness: 8mm	Slice number:
8-11	

The mean time of the MR imaging examination was 40 minutes. All patients underwent the complete MR imaging examination without severe complications.

MR Image analysis:

Images (DICOM) were transferred to a workstation equipped with a dedicated cardiac software package for further post-processing analysis: tissue characterization and segmental analysis was done. Images of delayed enhancement (DE) on MRI were evaluated using a 17-segment model. The basal, mid-ventricular, and apical segments were evaluated on short-axis images, whereas the apical cap was evaluated on a 2 or four-chamber longaxis planes. In the contrast-enhanced MRI, the average segmental thickness of DE on cardiac MRI was graded visually using the following scale: 0 = noenhancement, 1 = 1% - 25%, 2 = 26% - 25%50%, 3 = 51% - 75%, and 4 = 76% - 100%of enhancement.

The results of cardiac MRI subdivided into three groups: (a) Myocardial ischemia was defined as: either 1-Cardiac motion segment with abnormality or perfusion deficit at firstpass perfusion MR imaging consistent with no hyper-enhancement at delayedenhancement MR imaging. Or 2-Cardiac segment of subendocardial enhancement (25 % thickness scar) with motion abnormality. (b) Myocardial scarring is defined as: either 1- Cardiac segment with myocardial delayed enhancement having \geq 75% thickness scar. Or 2- Myocardial thickness less than 6 mm in diastole. (c) Mixed myocardial ischemia and scarring is defined as: Cardiac segment with myocardial delayed enhancement of near 50 % (>25% and <75%) thickness scarring.

2- <u>SPECT study</u>: was done by 2-day exercise/rest gated SPECT imaging with Tc-99m sestamibi.

The results of SPECT were obtained by comparison between resting and exercise images to detect areas with fixed defects (scar) and those with reversible defects (ischemia). A defect was **fixed** (**scarred**) when there was no change between the stress and rest images, **partially** reversible (mixed ischemia and scar) when there was an improvement in tracer uptake of at least 1 grade between stress and rest images, totally reversible (ischemic) when there was normalization of uptake at rest images.

3- <u>Conventional coronary angiography</u>: was done using a trans-femoral approach to selectively inject the left and right coronary systems sequentially.

A reduction of the luminal diameter 70% or more in a major epicardial coronary artery or the major branches was a relevant stenosis. The angiographic results were classified as one-, two-, or three-vessel disease.

The results were compared, and statistical tables were created according to the number of affected territory (one vessel disease, two vessel disease and three vessel disease) and the specific diseased territory (LAD, LCx, and RCA).

The results of cardiac MRI for ischemia and viability compared to the SPECT findings, guided by the conventional angiographic findings. These comparative results are analyzed, based on findings of many recent studies performed in last five years (as Bondarenko et al 2008), in which they proved that 50% of the segmental extent of hyper enhancement in CE–MRI would be a good discriminator for functional recovery after revascularization.

So, myocardial segments with more than 50% thickness scarring (\geq 75% thickness considered scar) as nonviable myocardial segment. While myocardial segments having less than or near 50% scarring thickness with motion abnormalities, (with or without resting perfusional defect). considered as ischemic or mixed scared and ischemic myocardial tissue respectively, that still have viable myocardial tissue with high probability to recovery.

Myocardial segments were assigned to the three-major coronary arterial territories according to the American Heart Association standardized myocardial segmentation.

RESULTS

Our results show that among 30 territories examined by coronary angiographic study, 16 territories were diseased. We found 9, 4 and 3 affected territories (occluded or with hemodynamically significant stenosis \geq 70% luminal reduction) corresponding to LAD, LCx and RCA territories respectively. The distribution of the affected territories is illustrated in (chart 1).



Chart 1. Ratios according to number of each affected territory.

The overall patient-based sensitivity, specificity, PPV, NPV and accuracy of cardiac MRI for the detection of diseased coronary artery were 94% (15 of 16 territories) (one is false negative), 100% (14 of 14), 100% (15 of 15), 93% (14 of 15) and 97% (29 out of 30) respectively.

The overall sensitivity, specificity, PPV, NPV and accuracy of SPECT for the detection of coronary artery stenosis were 88% (14 of 16) (two are false negative), 93% (13 of 14) (one is false positive), 93% (14 of 15), 87% (13 of 15) and 90% (27 out of 30) respectively.

Regarding the findings of cardiac MRI and SPECT we found the following:

- **For Ischemic territories:** Cardiac MRI detected 3 pure ischemic territories, matching with 2 pure ischemic territories detected by SPECT study. Among these 3 ischemic territories detected by the Cardiac MRI, only one territory is detected by perfusional defect, while the rest 2 ischemic territories are detected with subendocardial scarring and motion abnormality.
- For transmural scarred territories: Cardiac MRI detected myocardial segments corresponding to 9 transmural scarred territories, matching with 5 transmural scarred territories detected by SPECT study.
- For mixed ischemic and scarred territories: MRI detected myocardial segments corresponding to 3 mixed ischemic and scarred territories, matching with 7 mixed ischemic and scarred territories detected by SPECT study.

Among the 16 diseased territories, near total thickness delayed enhancement (indicating non-viable myocardial scarred segments) was detected corresponding to 9 territories. On the other hand, the other diseased myocardial segments correspond to 6 diseased territories which still showed variable thickness of viable ischemic myocardial tissues, distributed as follows:

3 territories of ischemic myocardial segments (showing subendocardial scarring in cardiac MRI studies).

3 territories of mixed scarred and ischemic segments.

- For myocardial scarring (non-viable tissue): Among the diseased 16 territories, cardiac MRI detected 60% (9 out of 15) and SPECT detected 36% (5 out of 14) of non-viable (transmural scarred) diseased territories.

- For detection of complications:

CMRI detected one intraventricular thrombus and 20 mitral insufficiency that were missed by SPECT.

ILLUSTRATED CASE

40 years old man diagnosed as ischemic since 1 year. To whome MRI, SPECT and selective conventional coronary angiography were done.

Coronary angiographic findings (Fig. 1):

- **§** Moderately stenotic lesion at LAD territory, inducing about 40-50% luminal reduction (arrow in fig. 1).
- **§** No obstructive lesions detected.
- **§** LCx and RCA are free of significant disease.

Figure 1. Conventional angiographic findings; case 1. **A-B Left coronary system. C: Right coronary system.** Arrow refers to the stenotic lesion at LAD territory.

Gated SPECT findings:

Large myocardial scar along the apex, septum, anterior and inferoapical segments

(Figure 2).



Figure 2. SPECT findings in case 1. **A-B:** Short axis. **C-D**: Vertical and horizontal long axis., first row is stress images and second row is rest images. Arrows refer to persistent fixed defect (decreased tracer uptake) in stress and rest images denoting large scar along the apex, septum, anterior and infero-apical segments of the left ventricular wall.

Cardiac MRI Findings:

The cardiac MRI confirmed presence of myocardial scarring along LAD territory.

A. <u>Cine Sequences</u> (Figures 3 and 4) :

- § Globally. The left ventricle shows moderate dilatation.
- **§** Thinning (less than 6 mm thickness) and akinesia of the anterior, anteroseptal and septal segments of the left ventricular wall at the mid-cavitary and apical levels.



Figure 3. MR findings in case 1. ECG gated TFE cine sequence in four chamber plane of the heart in diastole (A) and in systole (B). Showing moderate dilatation of the left ventricle. Arrows refer to the thinning of the anteroseptal and septal segments of the left ventricular wall at the mid-cavitary and apical levels.

Left ventricular function is as follows:

- Left ventricular ejection fraction:
- Left ventricular end diastolic volume: 252 mls
- Left ventricular end systolic volume: 138 mls
- Left ventricular stroke volume: 114 mls
- B. <u>Tissue characterization</u>:



Figure 4. MR findings in case 1. A-E: ECG gated TFE cine sequence in short axis plane of the heart in diastole. F-H: ECG gated TFE cine sequence in short axis plane of the heart in systole. Arrows refer to the thinning of the anteroseptal and septal segments of the left ventricular wall at the mid-cavitary and apical levels.

45 %

§ In the dynamic sequence, there is an anterior and anteroseptal perfusion defect at mid-cavitary and apical level (*Figure 5*).



Figure 5. MRI findings in case 1. ECG gated dynamic 2D EPI sequence in short axis plane at the mid-cavitary level. Arrows refer to perfusion defect at the anteroseptal wall at the mid cavitary level.

§ In the 3D IR sequence, there is transmural (75-100%) enhancing scar at the left ventricular wall involving anterior, anteroseptal and septal segments at the mid-cavitary and apical levels and extends to involve the cardiac apex circumferentially (*Figure 6*).

DISCUSSION

Within the past decade, cardiac MR imaging has emerged as the standard of reference for the assessment of functional and structural myocardial abnormalities in different cardiac diseases (7,8). Imaging of IHD is not limited to the mere visualization of coronary arteries for detection of stenotic or occluded coronary arteries. Accurate and early identification of viable myocardium is also important, especially for treatment modalities and prognosis. During the past decade, CMR has evolved from a research tool performed in a few selected centers to a clinical diagnostic tool that is recognized as the standard in the quantitative gold assessment of left ventricular function. It is now established as a comprehensive clinical tool offering cardiologists different information on cardiac function, and tissue characteristics. It accurately assesses ischemia, inflammation and viability ⁽⁹⁾.

In our study, the overall patient-based sensitivity, specificity, PPV, NPV and



Figure 6. MRI findings in case 1: Post Gd DTPA 3D IR sequence in short axis plane (A-E images), in four chamber plane (F image). Arrows refer to the transmural enhancing scar involving the anterior, anteroseptal, septal and apex segments of the left ventricle.

accuracy of cardiac MRI for the detection of coronary artery stenosis were 94% (15 of 16 territories), 100% (14 of 14), 100% (15 of 15), 93% (14 of 15) and 97% (29 out of 30) respectively. While the overall sensitivity, specificity, PPV, NPV and accuracy of SPECT for the detection of coronary artery stenosis were 88% (14 of 16), 93% (13 of 14), 93% (14 of 15), 87% (13 of 15) and 90% (27 out of 30) respectively. In agreement with our results, in 40 patients, Sakuma et al 2005⁽⁷⁾, compared CMRI to SPECT, followed by conventional coronary angiography as a standard. The study showed a comparable sensitivity and specificity for CMRI and SPECT, MRI had a sensitivity of 87-90 % and specificity of 85 %. More precisely, for patients having significant stenosis in at least single CA the sensitivity was 81 % for MRI and 81 % for SPECT. The specificity was 68.4 % for MRI and 63.2 % for SPECT. A study performed by Kitagawa K et al, 2008 ⁽¹⁰⁾, obtaining first-pass contrast-enhanced MR images

followed by LGE MRI with a 1.5-T system in 50 patients with suspected CAD. The sensitivity and specificity of this study by two observers, ranged between 84% and 89% and specificity ranged between 71% and 79% for detection of individual diseased coronary artery. In a study by Ishida N et al 2003 (II), the overall sensitivity and overall specificity of MR imaging for depicting > 70% diameter stenosis in individual coronary arteries were 84% (109 of 130 arteries) and 82% (150 of 182 arteries), respectively. The sensitivity and specificity of SPECT for depicting stenosis in individual coronary arteries in 69 patients were 64% (55 of 86 arteries) and 79% (96 of 121 arteries), respectively.

In our study, the sensitivities of MR imaging for depiction of single-, double-, and triple-vessel stenosis were 100 % (4 of 4 vessels), 83 % (5 of 6 vessels), and 100 % (9 of 9 vessels). In a study by Ishida N et al 2003, they were 85% (33 of 39 patients), 96% (22 of 23 patients), and 100% (15 of 15 patients), respectively. The overall sensitivity of MR imaging for depicting at least one coronary artery with significant stenosis was 90% (69 of 77 patients). In our studv there was no statistically significant difference between CMR and SPECT detection of ischemic in myocardial tissues with P value = 0.199. Recently, Gebker R et al 2008 (12) study performed in 101 patient with suspected and known CAD, using combined stress and rest perfusion MR imaging with delayed enhancement (DE) imaging. Per-patient analysis, the overall patient based sensitivity and specificity for the myocardial detection of ischemic territories secondary to coronary artery stenosis were 90% and 71% respectively. Near similar results was

found early by *Ishida N et al 2003* with sensitivity of 84%. These high sensitivity values is likely contributed for combination of stress first pass perfusional images to MR protocol in other published studies. And so, these results highlight the role of rest-stress myocardial perfusional imaging in detection of ischemic (viable) myocardial territory corresponding to flow limiting coronary artery. In our study CMR has higher sensitivity and values in specificity detection of myocardial scarring than SPECT especially the subendocardial scars, CMR detected 60% and SPECT detected 35%. In a study by Wagner et al, 2003 ⁽¹³⁾. CE-MRI was able to detect 92% of histologically confirmed subendocardial infarcts but a significant proportion was missed by SPECT, which could only detect 28% of these subendocardial infarcts. The high spatial resolution of MRI allows for a more accurate determination of the transmural extent of viability as opposed to a binary classification of a myocardial wall segment as either viable or not, as determined by nuclear medicine techniques and echocardiography. This distinction is critical because it has been repeatedly shown that revascularization of patients with viable myocardium leads to significant improvement in clinical outcome. Thus CE-MRI has become the gold standard for assessment of myocardial viability (Kühl HB et al, 2006)⁽¹⁴⁾. Based on results concluded by many published studies during the last decade for the predictive power of hyper enhancement by CE-MRI for functional recovery after revascularization, it proved that 50% of the segmental extent of hyper enhancement in CE-MRI would be a good discriminator for recoverv functional after

revascularization. So segments with 50% or less thickness scarring, considered as viable ischemic myocardial tissue, having high probability to recovery. As a result, the cardiac MRI shows higher sensitivity than SPECT in detection of mvocardial scarring and thus determination for myocardial viability. Thus, CE-MRI may be especially important in identifying myocardial viability in patients with a thin myocardial wall (Kühl HB et al, 2006). Syed MA et al, 2005 (15) stated that the akinetic left ventricular region with diastolic wall thickness less than 6 mm is considered to represent unviable scar, especially if dobutamine stimulation does not increase wall thickening.

Role of cardiac MRI in diagnosis of complications of myocardial infarction: In our study, CMR detected small LV thrombus in one patient and 20 mitral insuffeciency that were not diagnosed by SPECT. Srichai MB et al, 2006 (16) evaluated a protocol combining cine- and DE-CMR for the diagnosis of LV thrombus in patients with advanced ischemic cardiomyopathy undergoing surgical LV reconstruction. Among 160 patients (in whom there was surgical and/or pathological confirmation of thrombus), CMR showed higher sensitivity and specificity (88% and 99%, respectively) than trans-thoracic (23%, 96%) and trans-esophageal (40%, 96%) echocardiography.

CONCLUSION

CMR is considered the gold standard for global assessment of LV myocardial structure and function, with intraobserver and interobserver agreement superior to other modalities. Cardiac MRI as a noninvasive modality in evaluation of the coronary artery disease is valuable in:

-Detection of diseased coronary territory in patients suspecting or known to have CAD with high sensitivity and specificity.

-Differentiation between ischemic and nonischemic dilated cardiomyopathy. -Assessment of myocardial viability, delineation of myocardial scarring with no need of stress agents, and thus it is necessary to preoperatively predict the functional recovery.

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