

DEBATE ARTICLES: WHICH IMAGING IS THE BEST FOR DETECTING CAD ?— REVIEW ARTICLE

Advanced Noninvasive Cardiac Imaging using Cardiac Magnetic Resonance Imaging in the Diagnosis and Evaluation of Coronary Artery Disease

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Abstract

The purpose of this review article is to describe the essential characteristics of cardiac magnetic resonance imaging (MRI) in the evaluation of coronary artery disease in comparison with other noninvasive imaging modalities. Recently, technical advances and improvements in cardiac MRI have provoked increasing interest regarding its clinical role in the diagnosis and evaluation of coronary artery disease. Major advantages of cardiac MRI in comparison with other noninvasive imaging tests include its excellent spatial resolution and the characterization of myocardial tissue. These features allow the accurate assessment of ventricular volume and function, as well as clear delineation of infarcted tissue from normal myocardium. Further, myocardial ischemia can also be assessed by cardiac MRI upon pharmacological stress testing. In addition, coronary MR angiography has emerged as a possible alternative to X-ray angiography for visualizing the coronary arteries. The capability to perform comprehensive evaluations of ventricular function and myocardial perfusion and viability, as well as to assess the coronary anatomy, is a major strength of cardiac MRI.

Keywords: Coronary artery disease, Diagnosis, Gadolinium, Magnetic Resonance Imaging, Myocardial infarction

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Recently, various noninvasive cardiac imaging modalities have been widely used for the diagnosis and evaluation of coronary artery disease (CAD). Among these, cardiac magnetic resonance imaging (MRI) has several important advantages over other imaging modalities such as coronary computed tomographic angiography (CCTA) and nuclear myocardial perfusion imaging (1, 2). Cardiac MRI has been recognized as an accurate and reliable modality for the evaluation of cardiac anatomy and ventricular function. Moreover, stress first-pass perfusion and late gadolinium enhancement (LGE)-cardiac MRI can provide direct visualization of myocardial ischemia and myocardial infarction, respectively. In addition, coronary MR angiography (CMRA) has emerged as a possible noninvasive alternative for

visualizing the coronary arteries. The capability to perform comprehensive assessments of ventricular wall motion and myocardial ischemia and viability, as well as of the coronary anatomy, is a major strength of cardiac MRI (3). In addition, cardiac MRI does not expose patients to ionizing radiation (4, 5). Therefore, cardiac MRI is expected to play a pivotal role in the management of CAD and is becoming more widely used in our clinical practice.

Here, we review the relative merits of cardiac MRI for the diagnosis and evaluation of patients with known or suspected CAD, as compared with other noninvasive imaging modalities.

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Assessment of cardiac structure and function

Assessment of accurate LV global and regional systolic function is very important in diagnosis, risk stratification, and prediction of prognosis in CAD. Although transthoracic echocardiography is currently the primary imaging test for evaluating cardiac structure and function, owing to its widespread availability, it has several important limitations including substantial inter- and intra-observer variability, poor image quality in specific populations, and calculations of the cardiac volumes based on incomplete sampling (2, 6). Conversely, cine MRI, which is not limited by an imaging window or imaging plane, provides accurate and highly reproducible volumetric data independent of the geometric assumptions (1, 2). In addition, cine MRI has important advantages of high spatial and temporal resolution and excellent tissue contrast between the myocardium and blood pool, enables the evaluation of regional LV systolic function more precisely (7). The ability to accurately assess global and regional LV systolic function is one of the important advantages of cardiac MRI over CCTA or nuclear myocardial perfusion imaging.

The absence of regional wall motion abnormality was an insensitive marker of normal coronary arteries (8). However, cine MRI can be performed to examine regional myocardial function throughout dobutamine stress protocols in a similar manner to dobutamine stress echocardiography (9). Dobutamine, which increases myocardial oxygen demand, is a widely used pharmacological stressor in patients who are unable to exercise. In the presence of flow-limiting stenosis, high dose dobutamine stress protocol and results in demand/supply mismatch and deterioration of regional function. The safety and efficacy of dobutamine stress cardiac MRI have already been evaluated, and multiple large studies have demonstrated that the rates of major adverse events are similar to those observed during dobutamine stress echocardiography (approximately 1/1000) (10, 11). Owing to its excellent endocardial visualization, dobutamine stress cardiac MRI provides high accuracy for detecting CAD, with a sensitivity of 83-91% and specificity of 75-100% (2). In addition, the low-dose dobutamine stress protocol, which increases myocardial contractility in dysfunctional myocardium if there is sufficient contractile reserve, can be used for prediction of functional recovery of the left ventricular wall after coronary artery revascularization (2). Therefore, dobutamine stress cardiac MRI can be used to identify myocardial ischemia and viability, with high diagnostic accuracy and low inter-observer variability (2, 9).

There are increasing interests in myocardial deformation imaging which allows more direct quantification of myocardial contractility. Various MR techniques have been proposed to enable the quantification of myocardial deformation,

expressed as the strain, strain rate, twist, and torsion. Myocardial tissue tagging was initially developed and has been the gold standard in deformation imaging (12). However, quantitative analysis of tagging MRI is relatively laborious and time-consuming. Recently, feature tracking or tissue tracking technique was introduced which allows strain analysis using a cine-MRI as a part of routine cardiac MRI protocol in a similar manner to speckle tracking echocardiography (13). Since it does not require additional sequence acquisition, and post-processing analysis is rapid and semi-automated, it is expected to be more widely used in our daily clinical practice. However, further studies are still needed to evaluate the clinical utility of these novel imaging technologies.

Assessment of myocardial perfusion

Vasodilator stress myocardial perfusion single-photon emission computed tomography (SPECT) has been widely used to demonstrate reduced regional myocardial perfusion in patients with CAD. Myocardial perfusion MRI can also be performed with a vasodilator (adenosine or dipyridamole) to induce a perceptible difference in perfusion between the normal and ischemic myocardium. Perfusion MRI is commonly achieved using a T1-weighted sequence to visualize the first passage of a gadolinium contrast agent. Since the signal intensity correlates with the contrast concentration, perfusion MRI analysis can be performed in a quantitative, semi-quantitative, or qualitative fashion (14). Visual interpretation is most commonly performed to identify dark areas of hypoperfusion relative to the normally perfused myocardium (Fig. 1).

Since myocardial perfusion MRI has a high spatial resolution, it provides more accurate evaluation of myocardial ischemia, allowing detection of subendocardial ischemia in patients with mild-to-moderate CAD (15), as well as detection of diffuse subendocardial ischemia in patients with multivessel disease (balanced ischemia) (16), which might be missed by SPECT. Previous multicenter, multivendor head-to-head comparison trials have suggested that perfusion MRI is a valuable alternative to SPECT for the detection of significant anatomic CAD, with superior diagnostic performance, especially in multivessel disease (17-19). In a recent meta-analysis, myocardial perfusion MRI demonstrated a sensitivity of 89% and specificity of 87% for the diagnosis of hemodynamically significant CAD using a X-ray coronary angiography with fractional flow reserve as a reference standard on a per-patient level, which are similar to those of PET (84% and 87%, respectively) and superior to those of SPECT (74% and 79%, respectively) (20). In addition, vasodilator stress myocardial perfusion MRI provides prognostic value in patients with biomarker negative angina and

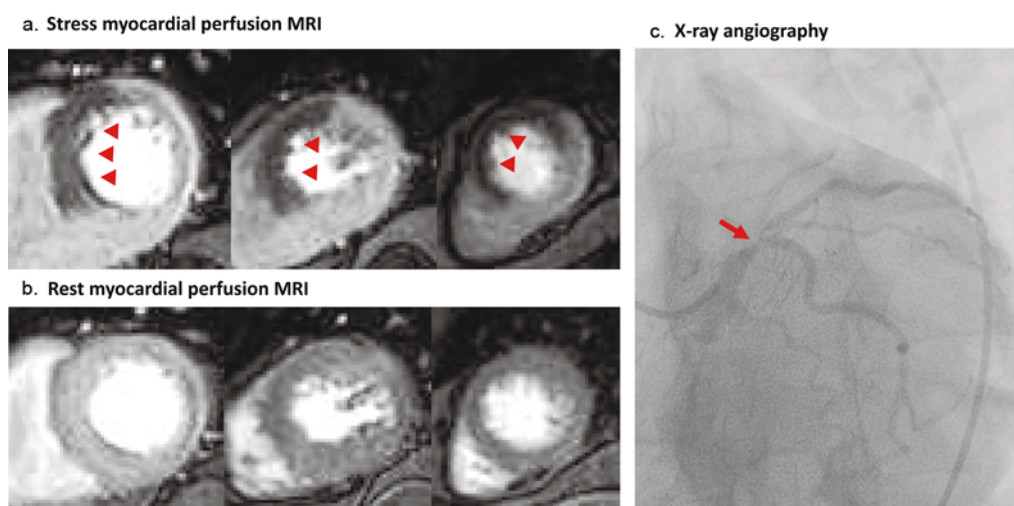


Fig. 1 Representative case of significant stenosis of the left main trifurcation and myocardial ischemia.

A 62-year-old man presented with chest pain. (a) Stress and (b) rest myocardial perfusion magnetic resonance imaging revealed severe ischemia (arrowheads) in the anterior and septal walls. (c) X-ray angiography demonstrated severe stenosis of the left main trifurcation (arrow), with significantly decreased flow of the left anterior descending artery.

reclassifies risk in patients with prior CAD (21, 22). Of course, to achieve the diagnostic and prognostic value of myocardial perfusion MRI demonstrated in previous studies, facilities capable of performing the stress testing, along with appropriate physician and staff training, are required.

Assessment of myocardial viability

LGE-MRI is a cardiac MRI technique that directly visualizes myocardial injury based on differences in the distribution of gadolinium, an extracellular agent. LGE-MR images are usually acquired 10-15 min after intravenous administration of gadolinium, when the gadolinium has washed out from the normal myocardium but remains in the intracellular spaces of acutely injured myocardium, distributed through the damaged cell membrane, and in chronic infarcted tissues, owing to their increased extracellular matrix (Fig. 2). With its extraordinary spatial resolution, LGE-MRI is more reliable in detecting subendocardial infarction compared to SPECT and allows accurate evaluation of the transmural extent of an infarct scar (23). Since the transmural extent of LGE is inversely related to the functional recovery after revascularization, LGE-MRI has been regarded as a gold standard to evaluate myocardial viability (24).

Moreover, the presence and extent of LGE have been reported to be independent predictors of poor prognosis in patients evaluated for ischemic heart disease. In patients without a prior myocardial infarction, LGE-MRI detects unrecognized MI that carries a high cardiac risk (25, 26). The presence of unrecognized MI detected by LGE-MRI was associated with unfavorable outcome comparable to recognized MI (27, 28). In patients with myocardial infarction, either acute or chronic, infarct size by LGE-MRI provides

superior prognostic value over left ventricular ejection fraction (29, 30). In acute myocardial infarction, LGE-MRI can also reveal the presence of microvascular obstruction that is a strong independent prognostic marker even after adjustment for the left ventricular ejection fraction and total absolute infarct size (29, 31).

LGE-MRI also can visualize peri-infarct zone (gray zone) surrounding the core infarct characterized by the presence of viable myocytes, which leads to potential multiple re-entry circuits that increase susceptibility to cardiac arrhythmia (32). In addition, when LGE-MRI was performed with T2-weighted MRI which can characterize area at risk, the myocardial salvage index can be calculated as the difference between the area at risk and the area at infarction. The myocardial salvage index predicts outcome in acute reperfused myocardial infarction (33).

Assessment of coronary anatomy

While CCTA is regarded as a reliable noninvasive alternative to invasive coronary angiography, CMRA is currently rarely used for the evaluation of CAD. The lower spatial resolution and long imaging time are major limitations of CMRA in comparison with CCTA (34). While CCTA can be acquired in only a few seconds at higher spatial resolution, CMRA images are typically acquired with a resolution of 1-1.5 mm and in an imaging time ranging from 5-15 minutes by using free-breathing respiratory-gated sequences (34). Although the gap between CMRA and CCTA is hard to overcome, CMRA has steadily evolved for the past decade. The imaging time of CMRA has been substantially reduced by using a 32-channel cardiac coil and a higher parallel imaging factor (35). A high-field-strength 3.0-T system has been

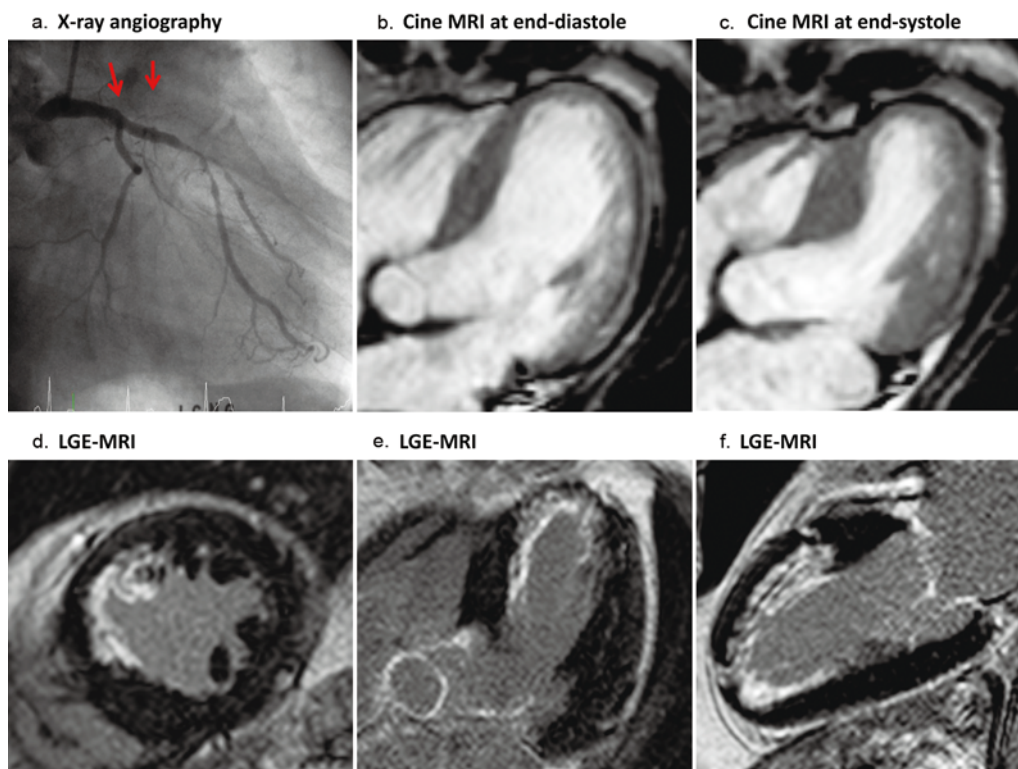


Fig. 2 Representative case of total occlusion of the left anterior descending artery (LAD) and myocardial infarction.

A 69-year-old man presented with chest pain. (a) X-ray angiography demonstrated chronic total occlusion in the ostium of the LAD (arrows). Cine magnetic resonance imaging (MRI) at (b) end-diastole and (c) end-systole demonstrated akinesia of the apical septal wall. (d-f) Late gadolinium enhancement-MRI showed subendocardial myocardial infarction in the LAD territory.

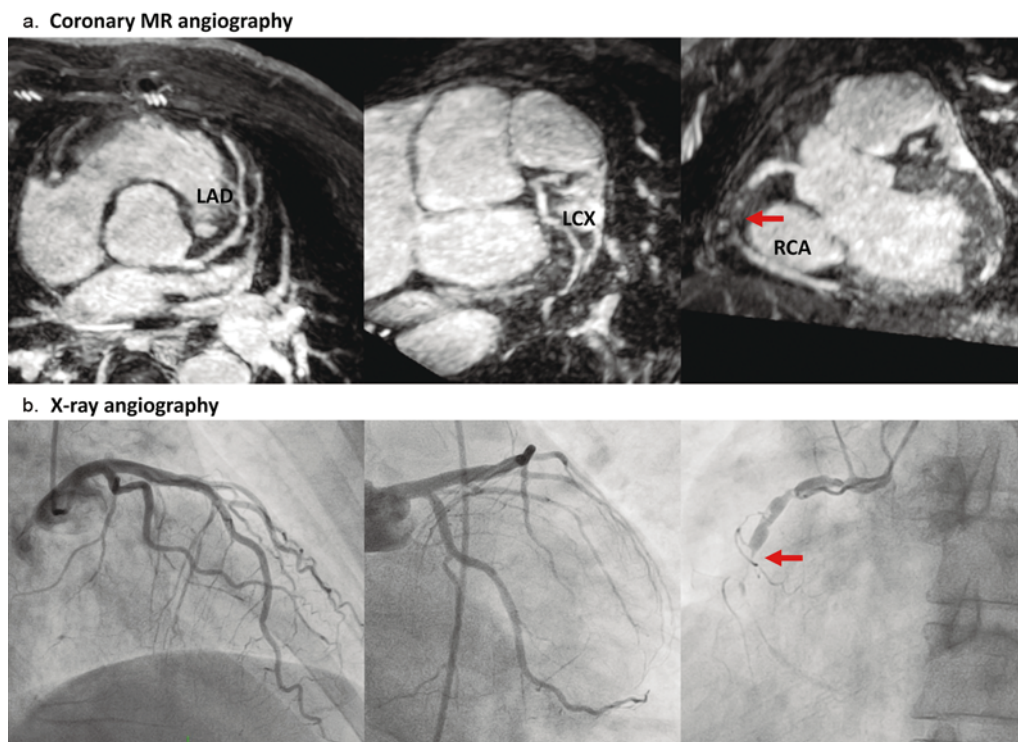


Fig. 3 Representative case of significant stenosis of the right coronary artery (RCA).

A 60-year-old man presented with chest pain.

a: Non-contrast-enhanced 3.0-T coronary magnetic resonance (MR) angiographic images (thin-section maximum intensity projection images) showed severe stenosis of the RCA (arrow).

b: Good agreement was observed between the coronary MR angiography and X-ray coronary angiography findings. LAD: left anterior descending artery, LCX: left circumflex artery, RCA: Right coronary artery.

Table 1 Advantage of cardiac MRI in diagnosis and evaluation of CAD

	Advantages	Applications	Comparison with other imaging modalities
Cine-MRI	<ul style="list-style-type: none"> • High temporal and spatial resolution • Excellent tissue contrast between myocardium and blood pool • Volumetric assessment independent to geometric assumption 	<ul style="list-style-type: none"> • Highly accurate and reproducible measure of LV volume and function • Low dose dobutamine stress test for assessing myocardial viability and high dose dobutamine stress test for assessing inducible myocardial ischemia in a similar manner to dobutamine stress echocardiography 	Echocardiography <ul style="list-style-type: none"> • Primary imaging test with wide availability, portability, and relatively low cost • Limited by poor image quality in specific population (ie. Lung disease or obesity) • Calculation of the cardiac volumes based on incomplete sampling
Stress/rest myocardial perfusion MRI	<ul style="list-style-type: none"> • High spatial resolution allowing detection of subendocardial ischemia, balanced ischemia by multivessel disease 	<ul style="list-style-type: none"> • First pass myocardial perfusion imaging with vasodilator stress (adenosine or dipyridamole) for assessing myocardial ischemia • Quantitative, semiquantitative, or qualitative analysis of myocardial perfusion 	Myocardial SPECT <ul style="list-style-type: none"> • Relatively low diagnostic accuracy due to low spatial resolution Myocardial PET <ul style="list-style-type: none"> • Higher diagnostic accuracy with quantitative analysis of myocardial perfusion
LGE-MRI	<ul style="list-style-type: none"> • Direct visualization of scar tissue • High spatial resolution 	<ul style="list-style-type: none"> • Detection and quantification of infarcted tissue • Evaluation of transmural extent of infarction for predicting functional recovery after revascularization 	Unique advantage of cardiac MRI
Coronary MRA	<ul style="list-style-type: none"> • Radiation free imaging • Absence of exposure to iodine contrast 	<ul style="list-style-type: none"> • Noninvasive coronary imaging as a part of comprehensive cardiac MRI study • Assessment of coronary arteries in young adults, or child. 	Coronary CTA <ul style="list-style-type: none"> • High spatial resolution and excellent diagnostic accuracy • Short imaging time • Exposure to radiation and iodine contrast

CAD: coronary artery disease, CTA: computed tomography angiography, MRA: magnetic resonance angiography, MRI: magnetic resonance imaging, PET: positron emission tomography, SPECT: single-photon emission computed tomography

shown to improve the signal-to-noise ratio of CMRA, resulting in diagnostic accuracy comparable to 64-slice CCTA (36). In a recent meta-analysis, the sensitivity and specificity of CMRA for the detection of significant CAD, as confirmed by invasive coronary angiography, were 89% and 72%, respectively (37). In this meta-analysis, the specificity using a 3T system (83%) was higher than that obtained using a 1.5T MRI machine (68%).

Despite its limitations, CMRA has several important advantages over CCTA. CMRA can be acquired without exposing the patients to ionizing radiation and without the need for an iodine contrast agent (34). In addition, CMRA can be performed without the use of β -blockers, even in patients with a high heart rate, since the temporal resolution of free-breathing CMRA can be flexibly determined by using imaging parameters (1, 34). Moreover, CMRA, in contrast to CCTA, allows evaluation of heavily calcified coronary arteries (34). Above all, the combination of CMRA with cine MRI, stress myocardial perfusion MRI, and LGE-MRI can provide a comprehensive evaluation of CAD.

Conclusion

Cardiac MRI is now recognized as a promising noninvasive method that can provide valuable diagnostic and prognostic information of known or suspected CAD. Due to its high spatial resolution, cardiac MRI allows accurate evaluation of myocardial ischemia and infarction without exposing the patient to ionizing radiation. Above all, cardiac MRI can provide comprehensive evaluation of ventricular function and myocardial perfusion and viability, as well as the coronary anatomy. Although the availability of cardiac MRI is currently limited, an increase in trained investigators and technologists, standardization of MRI protocols, and efforts to raise awareness of the value of cardiac MRI would increase the use of cardiac MRI in our clinical practice.

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Conflicts of interest

The authors have declared that no competing interest exists.

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