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Review Article
Cardiac Magnetic Resonance Imaging in the Diagnosis of Ischemic Heart Disease

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Abstract

Cardiac magnetic resonance imaging (CMRI) has become a routinely used modality for the diagnosis of ischemic heart disease (IHD) and can provide non-invasive evaluation of reperfusion therapy through a comprehensive evaluation of wall motion, global function, perfusion and viability. This paper was designed to update the reader on the current status of CMRI, with a special focus on the basic CMR sequences in IHD. The recent advances on the prognostic and diagnostic value and future directions in the CMR evaluation of IHD was also discussed. The CMRI is emerging as the most promising complementary imaging techniques in the primary diagnosis of coronary artery disease (CAD) and for coronary atherosclerotic disease detection. Also, CMRI can provide comprehensive evaluation of ventricular function and myocardial perfusion and viability, as well as the coronary anatomy. Although the availability of CMRI is currently limited, an increase in training investigators and technologists, standardization of MRI protocols and efforts to raise awareness of the value of CMRI would increase the use of CMRI in clinical practice.

Key words: Cardiac magnetic resonance imaging, coronary artery disease, coronary atherosclerotic disease, ischemic heart disease, myocardial perfusion, reperfusion therapy

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Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Ischemic heart disease (IHD) also known as coronary artery disease (CAD), refers to a group of diseases which includes stable and unstable angina, myocardial infarction (MI) and sudden cardiac death[1,2]. A common symptom is chest pain or discomfort which usually occurs with exercise or emotional stress, last less than a few minutes and improves with rest[3]. Imaging in CAD helps physicians to diagnose patients more precisely and to treat them more effectively. Although in many cases the diagnosis or the exclusion of stable CAD can be made on the basis of clinical evaluation. However, in numerous patients the tool, verifying the baseline clinical judgment is needed. Moreover, a physician needs information additional to clinical evaluation to make a decision about management strategy[4].

There is a constant need to improve the decision-making process in these situations. Among other imaging modalities, cardiac magnetic resonance imaging (CMRI) has provoked increasing interest in the potential clinical role in the non-invasive work-up of patients with suspected CAD and correct patient selection for these emerging imaging techniques[5]. In recent years, CMR has become a routinely used modality for the diagnosis of IHD and can provide non-invasive evaluation of reperfusion therapy through a comprehensive evaluation of wall motion, global function, perfusion and viability. In fact, CMR is widely considered the clinical gold standard for viability imaging by providing high resolution images of post-contrast gadolinium enhanced acquisitions that accurately depict the transmurality of MI, which is critical to guide re-vascularization therapy[6]. Thus, the growing number of patients undergoing CMR studies and CMR centers and the evidence for the use of CMR both in patients with stable CAD, as well as acute coronary syndrome (ACS) justify reviewing its capabilities[4,7].

Beside the facts mentioned, CMR has matured into a multipurpose non-invasive imaging tool for the assessment of IHD. The breadth of applications possible with CMR allows combined non-invasive assessment of myocardial perfusion, function and myocardial viability, which is a task that usually requires use of echocardiography and myocardial scintigraphy. As such, CMR currently holds a strong position in the non-invasive work-up of patients with CAD[8]. In addition, the distinct advantages of MRI over current conventional nuclear-based cardiac-imaging techniques, such as PET or myocardial scintigraphy, include its high spatial resolution and lack of exposure of the patient to ionizing radiation. Also, quantification of cardiac morphology and function by MRI is more accurate and image quality is more reproducible than in echocardiography, independent of the operator's experience and skill level or the patient's anatomy[8-12].

This paper updated the reader on the current status of CMRI, with a special focus on the basic CMR sequences in IHD. The recent advances on the prognostic and diagnostic value and future directions in the CMR evaluation of IHD was also discussed.

CURRENT STATUS OF CMRI AND THE BASIC CMR SEQUENCES IN IHD

CMR has emerged as a valuable tool in the assessment of patients with suspected CAD. The growing evidence supporting the use of CMR to diagnose the presence of CAD has led to the recognition of stress CMR as a method equal to well established methods of functional testing in the case of suspected CAD, namely stress echocardiography, nuclear imaging single photon emission computed tomography (SPECT) and positron emission tomography (PET) perfusion[8,13,14]. But the very first imaging modality in patients with suspected CAD should be transthoracic echocardiography and determining left ventricular ejection fraction (LVEF)[13]. The overall and final imaging strategy for the assessment of CAD and its sequel, however, has to be chosen based on the clinical background information and the intended question for further therapeutic decisions[8].

BASIC CMR PULSE SEQUENCES IN IHD

Currently available CMRI techniques are able to fulfill the aims of imaging in IHD patients: (i) On one hand, anatomic imaging with visualization of CAD and (ii) On the other hand, ischemia imaging with evaluation of the consequences of CAD of the heart, particularly myocardial perfusion and function and depiction of irreversible myocardial damage[15,16]. The viability protocol is the backbone of any CMR study, such that the sequences necessary for viability assessment are present in most protocols. These sequences include: (i) Cine imaging in long-axis (two-chamber, three-chamber and four-chamber) and short-axis orientations and (ii) Delayed enhancement imaging in the same planes to assess myocardial scar and determine viability[17].

CMR functional imaging: Electrocardiography (ECG) gated is acquired during breath holds, (i) Dynamic cine MRI balanced steady-state free precession (b-SSFP) sequences provide a non-invasive, accurate and reproducible alternative to

conventional echocardiography for calculating ventricular volumes and function and visualizing regional wall motion and contraction patterns. Thus, cine MRI should be considered as a fast and robust imaging modality for both daily clinical routine and research purposes. With techniques as real-time non-gated cine sequences (Fig. 1), problems like the presence of atrial fibrillation or the incapacity for breath holding are now mostly overcome[18,19].

(Ii) The myocardial tagging MRI techniques non-invasively creates tag or grid lines on the myocardium, allowing to analyze regional myocardial deformation 2 or 3 dimensionally throughout the cardiac cycle and to calculate myocardial strains (Fig. 2). A better characterization of the mechanisms of normal or impaired myocardial contraction is thus achieved, but due to the Elaborative post-processing, the clinical use of myocardial tagging MRI is currently limited[19,20].

CMR myocardial perfusion imaging: The most frequently used approach to assess myocardial perfusion with MRI is monitoring of the first pass of contrast medium through the heart, using a bolus injection of gadolinium in combination with ultra-fast cine MR sequences. As presented in Fig. 3, normally perfused myocardium enhances homogeneously, becoming bright, hypo-or non-perfused regions appear darker for a variable amount of time during/after first-pass are most intense in the sub-endocardium and typically respect coronary artery perfusion territories[19].

CMR edema imaging: Edema is visible on T_2-weighted MR sequences in infarcted myocardium as hyper-intense areas due to increased free water in the infarcted myocardium that changes tissue magnetization properties. Abnormalities are most evident in the acute and sub-acute phase of MI and slowly fade away due to processes of infarct healing with scar formation and resorption of infarct-related myocardial edema and inflammation. T_2-weighted MR sequences, equipped with inversion techniques to null the signal of fat and blood (will appear dark) (T_2-weighted short inversion time inversion recovery, T_2w-STIR MRI, triple inversion recovery sequences), are now most commonly used for edema imaging as shown[21-23] in Fig. 4.

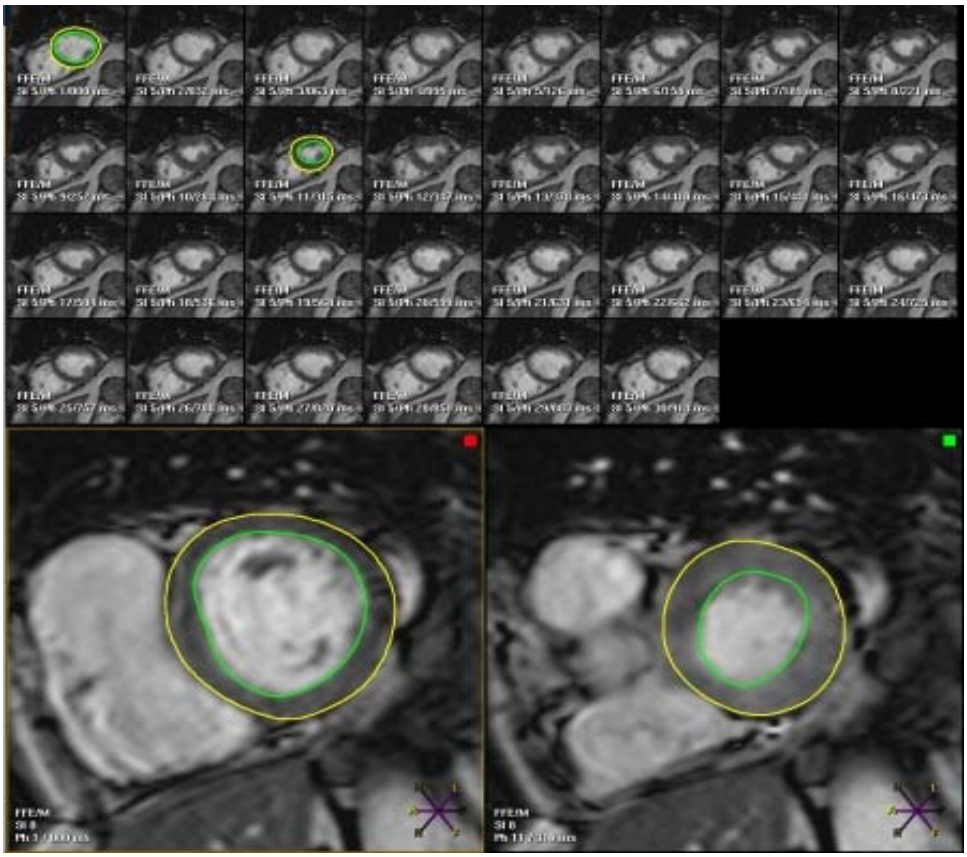

Fig. 1: Functional analysis of short axis cine MRI. End diastolic (ED) and end systolic (ES) time frames are defined and then the endo and epicardial borders are manually drawn for each slice[19]

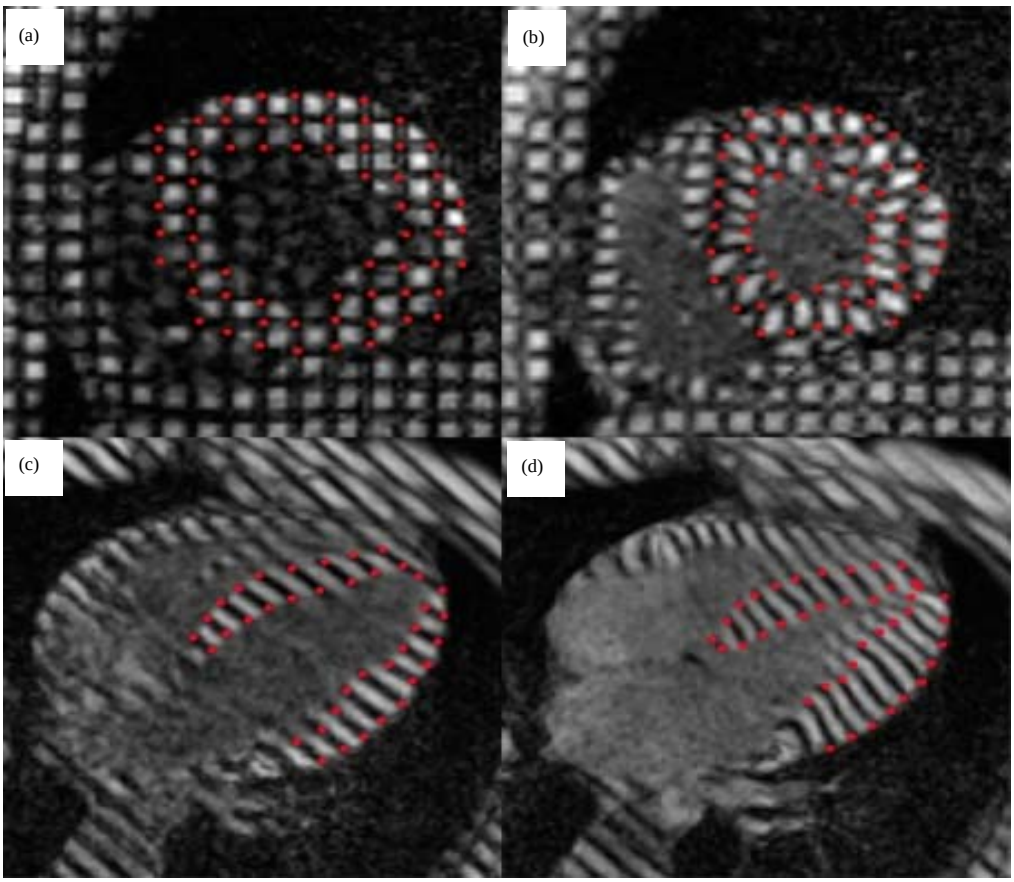

Fig. 2(a-d): MRI study with 2D tagging analysis (a,b) Tagging in cardiac short axis and (c,d) Horizontal long axis, ED (left) and ED time frame (right). Tracking of the grid intersections (indicated in red) on the short axis views and the intersections of the tags with the endo and epicardial border (indicated in red) on the long-axis views, allow analyzing the local myocardial deformation[19]

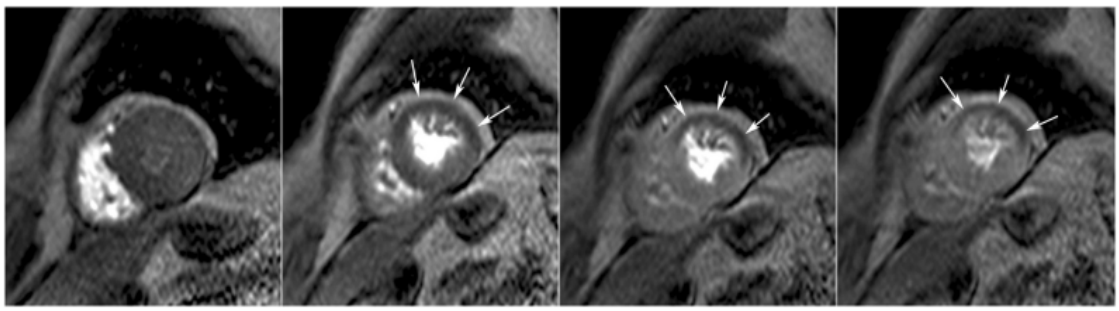

Fig. 3: MRI stress perfusion with suspected mid left anterior descending coronary artery (LAD) in-stent stenosis. Midventricular short-axis serial time frames of first pass perfusion during Dipyridamole vasodilatory stress show contrast successively enhancing the right, left chambers and myocardium (images from left to right). A transmural perfusion defect in the anterior and lateral walls is seen (arrows)[19]

CMR contrast enhanced imaging: Currently, in the routine clinical setting, contrast enhanced MRI (Ce-MRI) for MI imaging after gadolinium administration is done by an inversion recovery T_1-weighted sequence, which achieves an increased

contrast between normal and pathological tissue. Also, Ce-MRI is a robust, well-validated and accurate tool to depict myocardial necrosis in the acute setting of MI. This technique (Fig. 5) is nowadays routinely used to depict infarct-related myocardial scarring and is helpful to differentiate dilated cardiomyopathy from LV dysfunction related to CAD and to predict functional recovery post-coronary re-vascularization[19,24-26].

CMR stress perfusion imaging: The first pass of an intravenously injected gadolinium contrast agent during administration of a vasodilator is used by MRI perfusion studies to depict hemodynamically significant coronary artery stenosis as demonstrated in Fig. 6. This technique has been well validated, showing similar or better accuracies (a sensitivity of 91% and a specificity of 81%) when compared to routinely invasive techniques used such as SPECT imaging[19,27]. A relatively simple semi-quantitative method that has been validated against coronary flow reserve measurements is the assessment of the myocardial perfusion reserve (MPR) or MPR index. This index is defined as the ratio of regional myocardial blood flow after induced vasodilatation for that under resting conditions. As an MPR index cutoff value of 1.5 was able to distinguish between hemodynamically relevant and non-relevant coronary lesions with a sensitivity of 88% and specificity[28] of 90%.

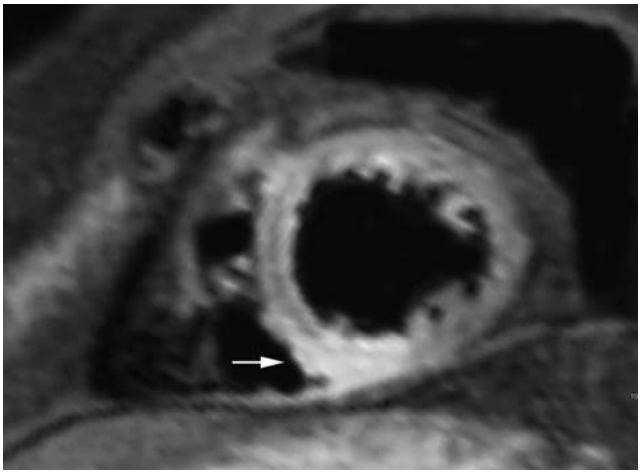

Fig. 4: Inferoseptal MI in a 47-year-old man imaged in the acute phase. On T_2w-STIR MRI, tissue edema is depicted as a homogeneous transmural area of hyper-intense signal located in the inferior and infero-septal left-ventricular wall (arrow)[23]

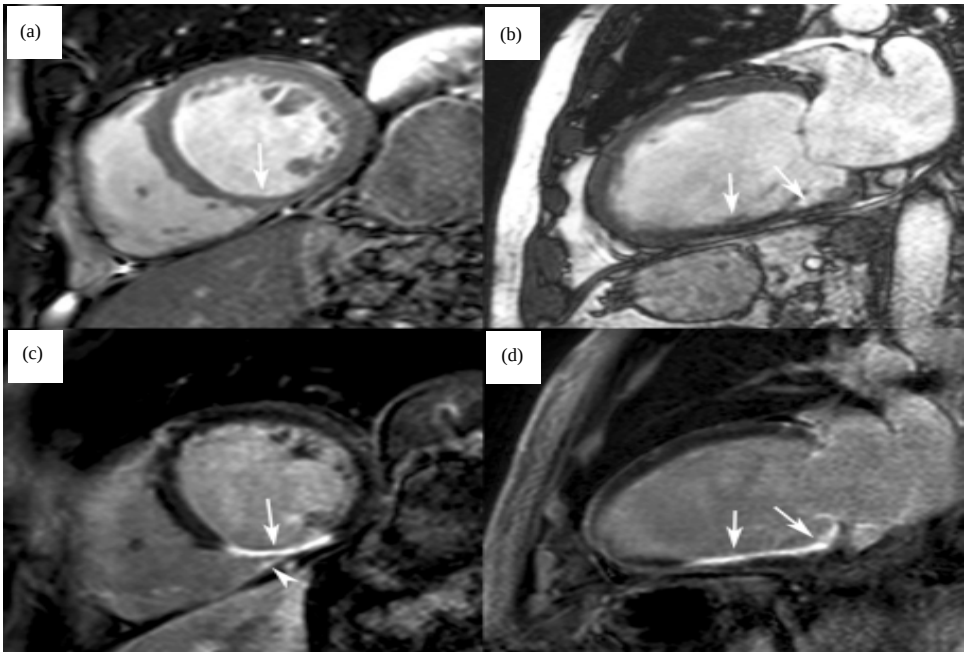

Fig. 5(a-d): A case diagnosed with dilated cardiomyopathy, (a) Still midventricular short-axis and (b) Vertical long-axis images of cine MRI show a remodeled, dilated LV and inferior wall thinning (arrows). Late Ce-MRI in the same imaging planes show transmural enhancement of the base and (c and d) Mid inferior wall and of the mid infero-medial RV suggests an old inferior MI with RV involvement (arrow head)[19]

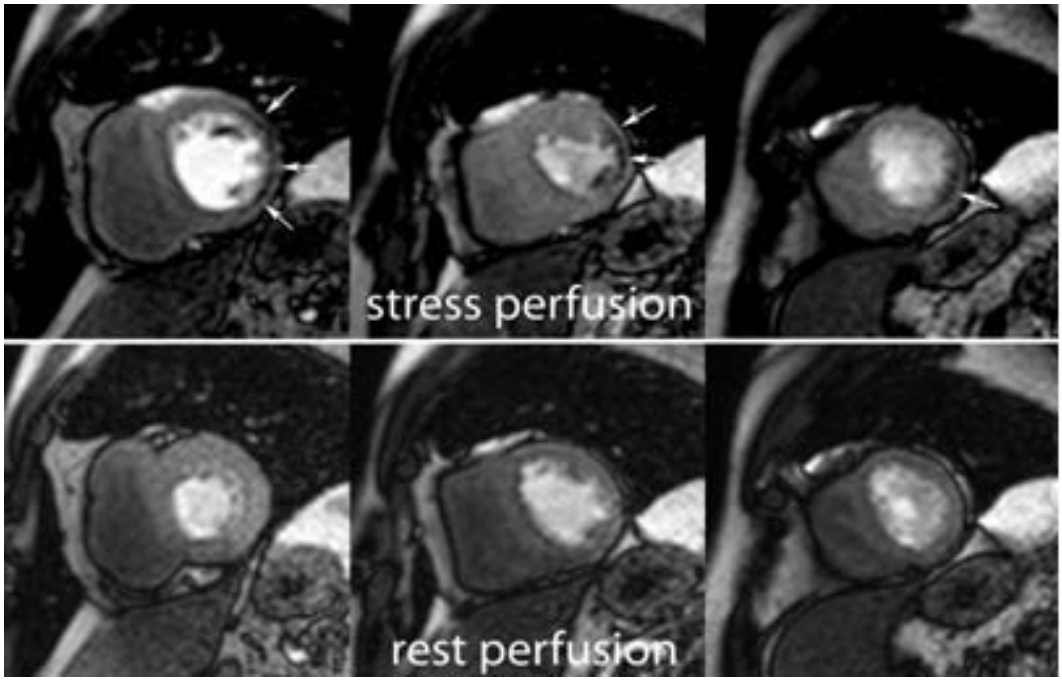

Fig. 6: CMR rest and stress perfusion imaging in a case with stable angina. Mid ventricular short-axis cardiac MRI images of first pass perfusion during rest (bottom) show no perfusion defects while during Dipyridamole vasodilatory stress (top) show a sub-endocardial perfusion defect in the lateral wall (arrows)[19]

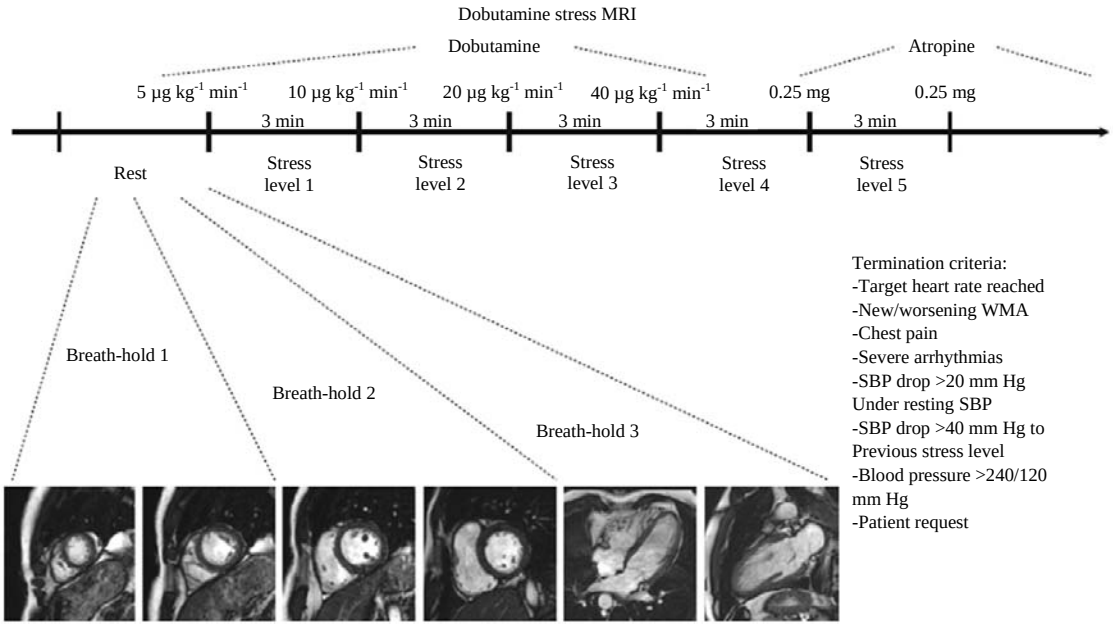

Fig. 7: Practical schematic for dobutamine stress MRI. For each stress level, 4 short-axis and two long axis cine studies are obtained in 3 consecutive breaths-hold periods. If termination criteria are not met at the highest Dobutamine dose, Atropine can be additionally administered[30]

CMR stress functional imaging: The CMR stress functional imaging is usually performed during Dobutamine administration. The protocol acquisition (Fig. 7) is started in resting conditions with cine MR images with a set of

standardized imaging planes through the ventricles. This approach allows the evaluation of regional contractility in all segments of the LV. In addition, the calculation of LV volumes and ejection fraction is done with a single breath-hold 3D cine MRI sequence encompassing the entire left ventricle[29,30].

With respect to adverse effects, studies have shown that high-dose functional stress imaging in an MR environment can be considered as safe and feasible in patients with suspected or known CAD. Also a higher accuracy (86.0 vs. 72.7%) of high-dose stress Dobutamine MRI compared to high-dose Dobutamine stress echocardiography in detecting patients with significant CAD[31]. Currently, the most commonly used approach for evaluating functional stress studies is a visual analysis of new or worsening wall motion abnormalities (WMAs) using a high-dose Dobutamine/Atropine regimen using a 16 or 17 segment classification system by the American heart association (AHA), yielding a good sensitivity (82-96%) and specificity (80-100%) for detection of significant CAD[32].

RECENT ADVANCES ON THE PROGNOSTIC AND DIAGNOSTIC VALUE AND THE FUTURE DIRECTIONS OF CMR EVALUATION OF IHD

The quest for successful MR coronary angiography (MRCA) started in the early 1990s. These techniques relied upon a combination of segmental acquisition of data in k-space (is the 2D or 3D Fourier transform of the MR image measured) to minimize cardiac motion and the use of a single breath-hold to minimize respiratory motion artifacts[33]. Only portions of the coronary arteries can be visualized within each breath-hold and the inconsistency of breath-hold position makes coronary artery imaging, even for experienced investigators in the field, a difficult task. Because of the severe limitations of the 2D breath hold approach, investigators have explored several alternatives to overcome these problems and improve image quality. They can be summarized as: (i) 3D imaging approaches, (ii) Techniques to suppress respiratory motion either by using navigators or acquisition during breath-hold and (iii) Use of intravascular contrast agents[30].

More recent improvements in MR imaging technology with stronger gradient systems, shorter rise times and more sophisticated ECG triggering devices have further contributed to current high-quality sub-millimeter 3D visualization of the coronary arteries. In addition, dynamic contrast-enhanced MR angiography (Ce-MRA), can now be used within very short breath-hold periods (7-23 sec) to study the aorta or the pulmonary arteries. Initial experience with extravascular MR contrast agents indicated that very high doses of gadolinium would be needed for 2D-breath-hold coronary MRA. With bolus arrival timing to catch the first pass of the gadolinium contrast agent, image quality improvements have been obtained from the 3D coronary MR angiography techniques by improving both the signal-to-noise ratio (SNR) and carrier-to-noise ratio (CNR)[30].

High field-strength 3 Tesla (3.0T) coronary MRA: The recent approval of 3.0T systems for clinical use has opened new perspectives for overcoming some of the limitations encountered in 1.5T systems, in particular, suboptimal SNR, which limits spatial resolution and the ability to visualize the distal and branch vessel coronary segments (Fig. 8)[6,34]. However, a number of potential adverse effects have been reported at higher field strengths, such as: (i) Susceptibility artifacts, reduced T_2* decay and increased T_1 radio frequency (RF) field distortions, (ii) At high field-strength, reliable ECG triggering becomes more challenging due to the amplified magneto-hydrodynamic effects and (iii) Flexibility of sequence design is less because of increased RF deposition[30]. However, these preliminary studies demonstrate that 3.0T coronary MR angiography is feasible and with further fine-tuning of the sequence 3.0T might become the preferred field-strength to study the coronary artery lumen and wall[30,34].

CMR in coronary blood flow assessment and bypass graft imaging: Although highly challenging, MR flow measurements can be performed in the small cardiac vessels (coronary arteries, coronary sinus) and coronary artery bypass graft (CABG) vessels (Fig. 9), during rest and during hyperemia using fast velocity encoded cine MR imaging techniques. Another way to assess coronary perfusion and myocardial blood flow is assessment of blood flow in the coronary sinus, which represents approximately 96% of the total myocardial blood flow. By measuring myocardial mass with cine MR imaging, the average coronary blood flow per gram of myocardial mass can be quantified by using non-invasive MR imaging[30,35]. To assure accurate coronary flow measurements with MR imaging, at least four important sources of error should be taken into consideration, such as: (i) Partial volume effects, (ii) Misalignment of flow axis and flowen coding gradients, (iii) Intra-voxel dispersion and (iv) Through and in-plane motion[36].

Future directions in the CMR evaluation of IHD: The future of cardiac imaging is dynamic. With ever increasing advances in

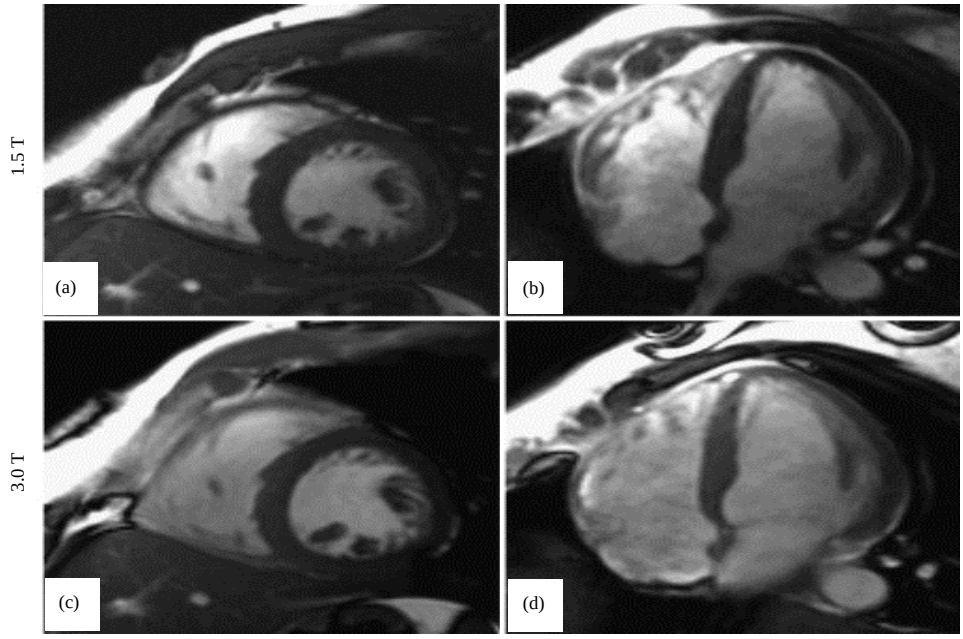

Fig. 8(a-d): Cardiac b-SSFP acquired at (a-b) 1.5T and (c-d) 3.0T with identical imaging parameters except of the flip angle of 60° (1.5T) and 45° (3.0T). The images were acquired in a short axis view (left column) and four chamber view (right column)[6]

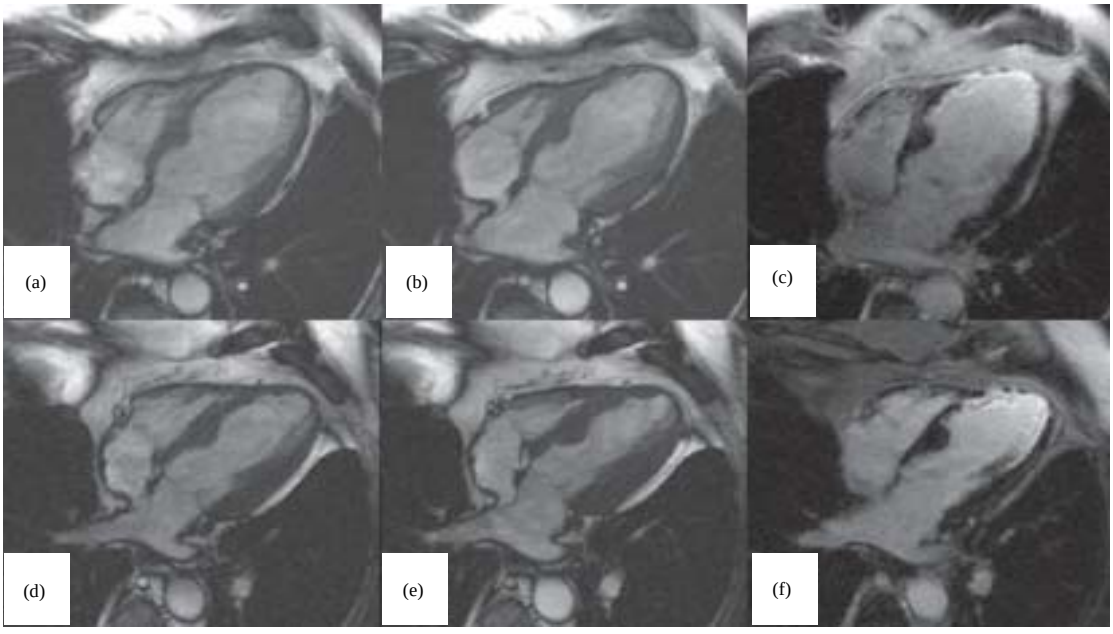

Fig. 9(a-f): MRI of a case before (top line) and after (bottom line) 3-fold CABG. (a) SSFP cine images in end diastole and (b) End systole reveal the severely impaired global LV function before surgery (EF 30%), (c) Ce-turbo fast, low angle shot (FLASH) image shows broad sub-endocardial late enhancement (bright signal) in the apical septum, thin LE in the lateral wall and transmural LE in the apex meaning chronic scar. The LV function after surgery, (d-e) No improvement in the apical septum and the apex, whereas the complete lateral wall improved and became normo-kinetic and (f) No changes in scar extent[36]

both hardware and software, CMRI will continue to evolve and improve. Increasing magnetic field strength, coupled with multi-phased array coils promise to improve CMR spatial resolution at present. With these continued advancements, CMR will continue to play an ever increasing role in the non-invasive hemodynamic evaluation of patients[37].

CONCLUSION

This study concluded that CMRI can give a complete assessment of ventricular function, myocardial perfusion and viability, as well as the coronary anatomy. CMRI widely available and is increasingly being applied in clinical routine by applying stress function and stress perfusion imaging for the detection of CAD. Although the availability of CMRI is limited at this time, but increase in training investigators and technologists, standardization of MRI protocols and awareness of the CMRI value would enhance the use of CMRI in clinical practice.

SIGNIFICANCE STATEMENT

The review focused on three different areas: (i) Update the reader on the current status of CMRI, with a special focus on the basic CMR sequences in IHD, (ii) The recent advances on the prognostic and diagnostic value of CMR in the evaluation of IHD and (iii) The future directions in the CMR evaluation of IHD. Thus, this review gave an additional insight for the researchers on how CMRI allows accurate evaluation of myocardial ischemia and infarction without exposing the patient to ionizing radiation. Also, the reduction of diagnostic invasive catheterization without angioplasty intervention, by a carefully selected approach using CMRI.

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