The Role of Cardiac MRI In Coronary Heart Disease Management

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ABSTRACT

Coronary artery disease is still the leading cause of mortality in the western countries (8). Many studies have been conducted to find what are the best investigation to be included in the diagnosis, risk assessment and to assess the effect of ischemic heart disease (including ACS) on the cardiac function as well as predict the response to treatment and the future possibility of recurrent disease.

CMR is now a crucial part of the diagnosis of heart disease especially the coronary artery disease (CAD) for many reasons:

1. It makes an early diagnosis which in turn means early intervention and less incidence of some of the complications of CAD.
2. As the CMR examination do not expose patients to radiation, it can be used repetitively without harming the patients.
3. Since CAD is a chronic disease, the role of CMR in monitoring CAD patients regularly over many decades is highly valuable.

In this dissertation, the specific role of CMR in the management of ischemic heart disease is studied in details by looking at many published articles. These reports focused on the performance of CMR in comparison to others methods of diagnosis. Some of these studies demonstrate the capability of CMR to diagnose CAD with both high sensitivity and specificity (52,10) which could be comparable to other modalities like X-ray angiography (52), CT scan (89,90) and SPECT (80,81) and others.

Although the current role of CMR in the diagnosis of CDA is limited, In comparison to other tests like CT, SPECT, and others. This review has proved that CMR is an accurate diagnostic tool and has a comparable sensitivity and specificity to all other tests with the exclusion of CT scan, which has better performance (89).

Keywords: Cardiac, MRI, Coronary, Heart, Disease

1. INTRODUCTION

Coronary artery atherosclerosis is the major reason of coronary artery disease (CAD), in this condition atherosclerotic changes are existing inside the walls of the coronary arteries. CAD is considered to have a progressive course which generally arises in childhood and reveals clinically in the middle to late adulthood (6).

The term atherosclerosis has a Greek origin and literally means a focal buildup of lipid and thickening of arterial intima (i.e., sclerosis). Atherosclerosis is a pathology of large and medium-sized muscular arteries, and the following are the main characteristic features (6):

1. Endothelial dysfunction
2. Secular inflammation
3. Buildup of lipids, cholesterol, calcium, and cellular debris within the intima of the vessel wall
The most important results of atherosclerosis are the following (6):

1. Plaque formation.
2. Vascular remodeling.
3. Acute and chronic luminal blockage.
5. Oxygen supply to target organs is diminished

Pathophysiology:
Ischemic heart disease (IHD) is most commonly caused by Vascular endothelium includes single cellular layer. As soon as an injury occurred, a sequence of protective events (which are the natural hemorrhage prevention measures after external trauma) create a platelet plug over the uncovered area of arterial endothelium, similar to the thrombolytic processes of aggregation and thrombus formation. Thus, atherosclerotic plaques are formed, a process of macrophage cell reaction evolve this process. Lipid core plaques may increase in size and eventually cause vascular stenosis or remain entirely inside the vessel wall. Some plaques become stable and calcify with time, and other may breach liberating an extremely thrombogenic material into the arterial lumen. They may form platelet emboli on the ulcerated crater at the site of the plaque. The variable symptoms and signs, depending on the location of the plaque, and the onset of the event. All these events constitute the term acute coronary syndromes (ACS). It covers a spectrum ranging from sudden death to unstable angina (14). Myocardial injury either acute or chronic, localized to the endocardium, or transmural. Both clinical and radiographic presentation is different between acute and chronic (14).

In chronic IHD, the pathological atherosclerotic process starts early in life during the second and third decades (14) and sometimes remain undetected until causing first exercise-induced, following by rest symptoms. The effect of prior myocardial infarction and its pathophysiologic consequences characterize the radiographic findings of these patients. The imaging study of patients with IHD is a good tool providing clinically significant information regarding the extent and severity of coronary artery pathology, if there are any chronic changes, what is the effect of superimposed acute ischemic events on this subclinical process (14).

Epidemiology:
Despite the reduction in the mortality associated with IHD has shown a decline in the recent decades, because of the improvement in therapeutic strategies (e.g., thrombolytic agents and early revascularization), it represents the leading cause of adults death in the developed countries and the prevalence will continue to rise (59). IHD is expected to be the number one cause of death by 2020 (60). Type II diabetes, physical inactivity, and obesity are contributing factors.

Over the last few decades, MRI has become a major contributor in the clinical, preclinical diagnosis and assessment of prognosis of IHD (61). CMR help to extend our knowledge of the pathophysiology and the detection of obstructive coronary artery disease (56).

Imaging study of ischemic heart disease:
There are three roles of imaging in IHD patients:

1. Visualization of CAD
2. Evaluation of the consequences of CAD on the heart, in particular, the impact on myocardial perfusion and function
3. The depiction of irreversible myocardial damage.

A. Plain X-ray
There are some limitations which result in the low sensitivity of plain x-ray film in the detection of coronary arterial calcium like the bony thoracic spine which is underlying the proximal coronary arterial tree. Coronary calcium could be seen as a small triangular area on the mid-left heart border of the (PA) chest film. The absence of coronary calcification on the x-ray does not exclude coronary calcification. Left ventricular configuration can be identified in plain PA film of some patients with left ventricular ischemia (15). This includes an increase in the curvature of the left ventricular contour and aortic arch segments of the left heart border, between which are sandwiched normal left atrial appendage and main pulmonary artery segments, this can help to identify patients with subclinical heart disease (14). Signs of elevated pulmonary venous pressure are found in some patients with IHD. Chronic left ventricular ischemia may result in ventricular dilatation and mitral incompetence, causing left atrial and ventricular dilatation (16,17). In acute myocardial infarction, the most common radiographic abnormalities in these patients result from dramatic increases in left atrial pressure (18), acute myocardial infarction may result in pulmonary edema, present as diffuse, bilateral, fluffy pulmonary infiltrates. The cardiac radiographic appearance in the first acute myocardial infarction has prognostic value.

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Normal cardiac size may associate with better outcome (19). Left ventricular myocardial aneurysms may occur after myocardial infarction (20,21) between 2 weeks and two years after the attack (22). Ventricular aneurysms present as distortion of the left ventricular portion or as linear calcification.

B. Transthoracic echocardiography (TTE)

Is a valuable test in the diagnosis of acute MI, particularly in patients with inconclusive clinical history and ECG. The abnormal motion in the wall corresponding to the distribution of coronary artery is the most common finding (24,25,26). However, a similar finding could be seen in areas of old infarction (30,31), so that, it diagnoses acute MI with moderate certainty, as it cannot differentiate between acute MI, ischemia or old pathology (27,18,29). Nevertheless, the lack of abnormal segmental wall motion provides a high negative predictive value (29). If normal wall thickness and reflectivity is preserved, this suggests an acute injury.

TTE is valuable to detect complications of acute MI like acute mitral regurgitation which associates with a worse prognosis (31). Follow-up TTE is a good way for detection of post-MI progressive chamber dilatation and global systolic function deterioration (32), in addition, echocardiography may demonstrate VSD after MI (33,34).

Echocardiography is a diagnostic test for intracardiac thrombi after MI (35). A high mortality may associate with intracavitary thrombus (34).

TTE has been used for assessment of myocardial viability after MI. Detection of hypokinesia or akinesia which may disappear after low-dose dobutamine is highly suggestive of possible functional improvement and vice versa (36,37). Segments show initial functional recovery with low-dose dobutamine infusion, but later worsening of function occur with higher dobutamine doses commonly are associated with substantial arterial stenosis.

C. Nuclear Medicine

Over the last few years, nuclear cardiac imaging role has progressed rapidly from just diagnosis to complete assessment of coronary artery disease including myocardial functional capacity, cardiac risk stratification, evaluate the existence of viable myocardium and the identification of patients who need and get benefits from myocardial revascularization (38,39).

Nuclear cardiac imaging tends to depend more on the use of pharmacological stress rather than exercise induced stress to check the coronary response. Myocardial perfusion studies are sensitive to CAD (40). Furthermore, it is used to investigate for artery restenosis after PCI (40), or CABG.

In patients with acute coronary syndromes, nuclear perfusion imaging is used to detect the hypoperfusion (41) and to evaluate the response to the reperfusion therapy by estimation of the persistence perfusion abnormality (42).

Dual-tracer positron emission tomography (PET) scanning can differentiate between viable and dead muscle. Despite having less flow, viable myocardium shows normal to increased metabolic activity (43).

Computed Tomography in IHD

The use of cardiac CT scan is increasingly becoming valuable in the assessment of patients with IHD; the early CT scanners demonstrated acute myocardial infarction as an area of lower attenuation in comparison to normal enhanced myocardium. Infarction area may also be seen as a delayed hyper-enhanced region (44). These can aid in measuring the infarction size (45). After 2-6 months, myocardial wall thinning is usually identified (46,47). Ct scan is currently used to measure the total calcified plaque burden on the coronary tree (48). Such measurement can help to estimate coronary artery disease risk (49).

D. Cardiac Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) is used to image the brain and other organs in the body and has become broadly accessible as a diagnostic technique of cardiovascular disease. The first ECG-gated magnetic resonance (MR) images of the heart were acquired more than 25 years ago, and initially used to assess the cardiac morphology and motion. With developments of late gadolinium enhanced (LGE) MRI and myocardial perfusion MRI, the application of MRI in ischemic heart disease (IHD) has been considerably expanded in the past ten years. Because MRI has high spatial resolution and excellent image contrast, subendocardial infarction, and myocardial ischemia can be clearly visualized (Wu and Lima, 2003).
Also, the use of MRI reduce ionizing radiation exposure which is an essential part of other diagnostic tests like conventional angiography, also, it does not require the administration of iodinated contrast medium, which is possibly nephrotoxic(Wu and Lima, 2003). Coronary MR Angiography. (MRA) Is rapidly evolving and has emerged as a possible alternative to multidetector-row computed tomography (MDCT) for Noninvasive visualization of coronary artery disease (CAD). In this dissertation, we will demonstrate the usefulness of MRI for the diagnosis and risk stratification of patients with IHD.

**Definition**
Cardiac magnetic resonance imaging (CMR) is the usage of magnetic resonance (MR) modalities to acquire images of the heart. In CMR, a strong magnetic field that orients the protons of hydrogen atoms is subjected to the tissues; thus, they rotate in a uniform mode. After that, hydrogen atoms are exposed to a radio signal, called the pulse sequence, which briefly alters their orientation. After the radio signal, the protons return to their original precession designs and generate a signal that is captured to produce images. Tissue composition influences the resulting signal patterns by determining the time needed to recover to their orderly precession, so it is specific to the tissue composition (9).

**How CMR Can Detect Ischemia**
Since disease states may affect tissue conformation, a different signal is provided by the diseased tissue which allows the determination of normal and disease states. By developing ECG-gating, CMR could create both static and motion images of the heart. Furthermore, imaging can be obtained during both cardiac rest and stress state. Finally, contrast agents can be utilized to refine differences in cellular and tissue composition or function (9).

Temporary or permanent impairment of myocardial contractility is one of the direct consequences of IHD including not only the ischemic zone but also it may affect the Pregnant portion of one ventricle or both, and it may reduce ventricular performance. MRI offers a noninvasive and precise means to have a good view of regional wall motion and contraction patterns, making it attractive imaging modality in daily clinical assessment, and novel therapies evaluation. It also can be used to study long-term effects of IHD like ventricular remodeling (62).

For functional analysis, CMR can assess the pattern of circumferential or longitudinal wall motion and the degree of wall thickening (58).

Although cardiac function can be evaluated in resting conditions, in patients with CAD, myocardial contractility needs to be assessed under stress conditions which either be physical or pharmacological stress. The primary goal for stress test is to find any significant stenosis and to check for viability

Adding late Gd imaging enables to depict myocardial infarction whether new or old healed one. For example, dysfunctional myocardium no or only mild myocardial scarring at LGE-MRI is highly probable to be viable, while extensive scarring is most likely to be non-viable tissue with low probability of getting recovery after revascularization (63).

**Equipment**
CMR test is commonly accomplished by commercially manufactured MRI machines which provided with specialized software to obtain cardiac images.

1.5 Tesla machines are commonly utilized, but some health institutions adopt machines with stronger magnetic fields. For perfusion imaging, power injectors are ideal. Some Specialized monitoring equipment should be provided (9).

**Technique**
There are three mainstays techniques of clinical CMR despite the many different techniques used in the MRI systems (6).

1. **Spin echo imaging**: Spin echo imaging depicts the tissue structures of the heart as bright and the blood pool as dark (black blood approach). The spin echo method is mainly used for anatomical imaging of the heart (2).

2. **Gradient echo imaging**: it produces images in which the blood pool looks bright and the myocardium dark (bright blood approach). This technique is very beneficial to evaluate left and right ventricular sizes and function, ventricular mass, intracardiac shunts, valvular functions, and to detect intracardiac masses.

3. **Flow velocity encoding** is a technique directly measures blood flow and is helpful in measuring the severity of valvular pathologies such as regurgitation and
stenosis, the size of a shunt, and the severity of arterial stenosis \(^{(3)}\).

**Gating**

The real-time MRI method has both lower temporal and spatial resolution \(^{(5)}\). Therefore, cardiac gating (in which data is acquired during many heart cycle) is used for CMR to optimize spatial resolution. In the presence of atrial fibrillation, ECG gating could be used to ensure ideal image quality \(^{(5)}\).

Although breath-holding is used in most CMR imaging to minimize motion artifact, in longer image acquisitions and to ensure higher and better resolution imaging of coronary artery, respiratory gating in addition to cardiac gating may be required \(^{(7)}\). It can be done by using the navigator approach (by following the diaphragm) or respiratory bellows (including wrapping an elastic band around the chest) to track respiratory movement \(^{(7,8)}\).

**Cine Imaging**

The evaluation of the regional and global function of the left and right ventricles by CMR is based on a cine data set placed in the short axis of the left ventricle which covers the heart in 10 to 12 consecutive 2-dimensional slices \(^{(65)}\). Alternatively, 3-dimensional cine data sets can cover the heart entirely in one breath-hold \(^{(66)}\).

CMR offers not only a high tissue contrast but also imaging planes which can be identified clearly and reproducibly. Therefore, CMR is the most precise imaging modality for the evaluation of global ventricular volumes and function \(^{(67)}\). Furthermore, we can assess regional contractile function directly by visual interpretation of cine loops or by wall motion and thickness measurement \(^{(68)}\).

Following acute MI, cine CMR with low-dose dobutamine can be used to assess viability \(^{(69)}\). High-dose dobutamine stress CMR has high predictive value in identifying LV wall motion abnormalities due to coronary stenosis \(^{(70)}\).

**First-Pass Myocardial Perfusion**

In this test, data acquired under stress induced by intravenous vasodilator (most commonly with adenosine) which defines regions with under perfusion due to MI. Subendocardial ischemia can be diagnosed due to the high spatial resolution of CMR. Furthermore, in ACS, myocardial perfusion CMR imaging can show ischemia and microvascular obstruction.

**Gadolinium Contrast Techniques**

Late gadolinium enhancement (LGE) can demonstrate fibrosis and permanent myocardial damage in both acute and chronic myocardial infarction \(^{(6)}\).

The proper role of this diagnostic tool in the evaluation of patients with suspected or known coronary artery disease remains to be determined.

LGE can demonstrate both acute and chronic MI with the assessment of the location and the extent of infarction \(^{(12,13,14)}\). Infarct sizing could be precisely identified, with minimal inter-observer and intra-observer variability \(^{(14)}\). 10 to 20 minutes after intravenous injection of 0.1 to 0.2 mmol/kg of gadolinium chelate, Imaging can typically be performed \(^{(1)}\). The microvascular obstruction could be detected by CMR \(^{(15,16)}\) it can be seen that the extent of microvascular obstruction and infarct size increases substantially over the first 48 hours after an MI \(^{(15)}\). LGE can evaluate myocardial viability. Areas showing enhancement at least 10 minutes after gadolinium-based contrast injection are most commonly regions of myocardial necrosis and irreversible myocardial injury; while viable regions fail to enhance \(^{(18,19)}\).

**Stress CMR**

High-dose dobutamine stress MRI may also be performed to detect ischemia as inducible wall motion abnormalities \(^{(74)}\). High-dose dobutamine should be administered at a maximum of four stress levels if starting at a dose of 10 μg/kg/min, and at a maximum of five stress levels if starting at a dose of 5 μg/kg/min at 3 to 5 minutes per level. Dosing should not be above 40 μg/kg/min. No more than 1 mg of atropine at the highest dobutamine dose should be administered to achieve a submaximal target heart rate \(^{(73)}\).

Dobutamine stress may be performed in the MRI environment safely. However, for the administration of dobutamine at high levels (>10 μg/kg/min), a separate satellite monitors workstation in addition and adjacent to the scanning console in the control room for real-time monitoring of WMAs while scanning is going on is highly recommended for safe practice. Images should be vigorously monitored by a physician and assessed for induced wall motion abnormality at each increment of dobutamine as the images are acquired. The physician should observe regional wall motion in the long and short axis at each stress level.
and the examination should be stopped if new regional WMAs are seen. The physician should be prepared to treat any induced ischemia or arrhythmia with medications, including beta blockers and nitrates. An external cardiac defibrillator should also be readily available. Perfusion MRI with gadolinium can be performed at peak dobutamine stress and may provide additional diagnostic information (75). Lower dose dobutamine (at levels of 5 and then 10 μg/kg/min) can be administered to determine myocardial viability through qualitative and quantitative assessment of myocardial thickening and improvement in wall motion.

**Technical Aspects of Cardiac Magnetic Resonance Pulse Sequences**

In CMR, technical difficulties which can be caused by respiratory motion, blood flow and cardiac motion could be overcome by using a range of strategies. So, data collection in a synchronized cardiac cycle (gating) is needed, and thus electrodes placement should be done in a careful manner to get a reliable electrocardiographic signal. Fortunately, advances in gating technology have allowed reliable cardiac gating in almost all patients in 1.5-T and even 3-T scanners.

**Role of CMR in ACS Detection of ACS**

CMR plays an effective role in low-risk ACS patients or when other medical problems interfere with cardiac catheterization. In addition, as a noninvasive test, it may be preferred initially (71) for early changes detection after ACS, CMR is helpful in patients with cardiac chest pain without MI. CMR is also valuable in differentiating acute and chronic MI. This can be accomplished by using LGT with T2-weighted imaging and will outline acute MI associated edema. In patients with negative cardiac enzymes and no ECG abnormalities, CMR can detect changes which could occur before any changes in cardiac enzymes. CMR can also be used in the patients with delayed presentations when cardiac biomarkers returned to normal, while findings on CMR can be persevered for several weeks (72).

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**Box 1 Indications for cardiovascular magnetic resonance in ischemic heart disease (72)**

1. Assessment of global ventricular (left and right) function and myocardial mass
2. Detection of coronary artery disease
   - Regional left ventricular function at rest and during dobutamine stress
   - Assessment of myocardial perfusion
   - Coronary angiography for anomalous coronary artery origins
   - Coronary angiography for bypass graft patency (class II evidence)
   - Coronary angiography for coronary artery disease (class III evidence)
3. Acute and chronic myocardial infarction (MI)
   - Detection and assessment/Myocardial viability
   - Ventricular septal defect/Mitral regurgitation (acute MI)
   - Ventricular Thrombus

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**CMR to assess myocardial viability**

After ischemic events, the dysfunctional myocardium -which is viable- may present in one of the two closely related pathophysiological states. These are myocardial hibernation and stunning. The chance of contractile recovery after reperfusion is high in the viable myocardium. In stunning, the ischemic injury is followed by a loss of myocardium in spite of the sufficient perfusion. While the hibernating myocardium shows a reduction of cellular metabolism due to the sustained decline in perfusion which may worsen with longer time of low perfusion (82). The exact structural changes remain controversial (83). So, that, precise and prompt recognition of viable myocardium is considered to be an increasingly important in both prognosis and treatment of CAD. Scintigraphy techniques and stress echocardiography were the main guides of diagnosis until recently (84). The CMR has an emerging clinical role of assessment of viable myocardium which has two important prognostic considerations (84).

First, viable myocardium which is treated medically is a herald of additional nonfatal ischemic events with higher mortality. In patients with viable myocardium, there is 4-folds annual mortality rate in patients treated medically in comparison to those treated with successful revascularization (85). Second, differentiation between viable and nonviable...
myocardium can help the patients to avoid the unnecessary revascularization when they may not be beneficial. CMR has a diagnostic value in the evaluation of viability by assessment of several markers of proven importance. These include myocardial scar burden (86), coronary perfusion (87) and contractile reserve (88) by CMR.

**Guidelines:**
These guidelines are issued by the American Heart Association which has scientific statement on noninvasive coronary artery imaging in addition to the 2010 Expert Consensus Document on CCTA (93)

- Neither CCTA nor CMRI should be used in screening of coronary disease in patients who have no signs nor symptoms suggestive of coronary artery disease.
- Noninvasive coronary angiography is reasonable for symptomatic patients who are at intermediate risk for coronary artery disease after initial risk stratification, including patients with equivocal stress test results. Diagnostic accuracy currently favors CCTA over CMRI for these patients.
- CCTA is NOT recommended in patients with either a very low pretest likelihood of coronary stenosis or a high pretest likelihood of coronary stenosis. Concerns about radiation exposure limit the use of CCTA in patients with very low likelihood of coronary disease. Patients with a high likelihood of coronary artery disease are likely to require invasive coronary angiography and intervention.
- The usefulness of CCTA is reduced in patients with pronounced coronary calcification.
- CMRI or CCTA is suggested to evaluate suspected or known congenital or acquired coronary anomalies, particularly to establish the proximal course relative to the great vessels of coronary arteries with abnormal origin. CMRI is preferred in these younger patients to avoid radiation exposure and in patients with contraindications to iodinated contrast or beta blockers.

2. **METHODS**

**Rationale for study**
Coronary artery disease is a major reason of death in the western world (6). Despite being the gold standard as the diagnostic and therapeutic test, conventional x-ray angiography is an invasive test. It is associated with exposure to ionizing radiation. The risk is shared with other non-invasive investigation like CT scan and SPECT. CMR represents the exceptional chance to diagnose CA stenosis non-invasively and to assess myocardium viability without the need to expose the patient to the ionizing radiation. Since it offers an excellent temporal and spatial resolution, it can evaluate the myocardial perfusion. The more multiplane properties of CMR allow better assessment of the anatomy. Also, its use can help to avoid the iodine-containing contrast. Many studies have been conducted to evaluate its role as a first-line investigation in comparison to other tests. The aim of this dissertation is to assess these studies to evaluate the possibility of making MRI a routine test in CAD.

**Search Strategy**
A systemic search for articles has been done in open ATHENS including all the resources using the keywords ‘cardiac magnetic resonance’, ‘CMR’, ‘ischemic heart disease’, ‘angiography.’ The initial search results are 566 articles; I considered all studies published in English evaluating the role of CMR including CMRA in the assessment of patients with CAD and comparing its value to other invasive and non-invasive imaging study of the coronary arteries. Studies were chosen regardless of the technique used for CMR. Duplicates were excluded manually. Unrelated articles were ignored after checking the titles and the abstracts. Finally, a thorough evaluation was conducted on the studies have been chosen regarding their relation to the topic, results, and outcomes. Studies include both primary and secondary assessment of CAD are involved.

A. **Inclusion Criteria:**
- English only
- Human only
- Research paper about the use of CMR in CAD

B. **Exclusion Criteria:**
- Other Original research about ischemic heart disease
- Other original research about MRI in other condition
• Non-human based study
• Research in other languages

3. ANALYSIS
Many studies have been conducted to assess the diagnostic role of CMR in patients with known or suspected CAD. Some of them compared CMR to other tests like the conventional angiogram, CT scan, ECG and SPECT, others evaluate its role in myocardium viability assessment following MI.

CMR versus Conventional X-RAY Angiography
One study was published in BMJ heart 1993 to assess the role of MRI in CAD diagnosis [52] funded by the heart association. In which 26 subjects are involved but only 22 had been imaged successfully. Seven had undergone previous x-ray contrast coronary angiography, normal coronaries have been found in two and an isolated occluded left anterior descending artery in three. The other two had bypass grafting of the coronary artery. MRI performed with gradient echoes and a segmented k-space technique; complete images were acquired in 16 cardiac cycles with breath holding and fat suppression. Two expert observers reviewed each image and measured the diameter and length of each artery. The seven angiograms had been reviewed by an experienced observer blinded to the results of MRI. They found:

1. The left main stem (95%), left anterior descending (91%), and right coronary arteries (95%) were identified in nearly all subjects, but identification of the left circumflex artery was more difficult (76%).

2. In 12 healthy men, the total coronary area, defined as the sum of the areas of the proximal arteries was 309 mm² (range 19.4-57.2), and the total coronary area to body surface area ratio was 16.4 mm².

3. Observer variation for measurement of the diameter of the proximal arteries was 7% for the left main stem, 12% for the left anterior descending artery, 11% for the right coronary artery, and 18% for the left circumflex artery.

4. There was clear similarity between the magnetic resonance and conventional coronary images.

5. The insertion of the bypass graft distal to the left anterior descending artery occlusion was identified and compared with conventional angiography.

6. The patients with occlusion of a coronary artery had diagnostic images, and the insertion of vein grafts was clearly seen.

This study demonstrates the satisfactory performance of CMR in the assessment of patients with stable angina in comparison to the conventional angiogram. It showed that both have high sensitivity and specificity. The authors used a clear measurement for all coronary arteries which were approximately similar to those obtained by conventional angiogram. It also demonstrate how CMR can be used in the evaluation of patients with CABG.

There are some limitations in this study. The small number of patients included in the study is the major one. Furthermore, only a few patients had undergone conventional angiography making the comparison between CMR and angiogram unfair. Consequently, in addition to the absence of clear statistical data, the small sample of patients made the results less convincing.

Another study has been conducted to assess Cardiac magnetic resonance perfusion imaging role for the functional assessment of coronary artery disease in comparison with coronary angiography and fractional flow reserve [10]. It depended on the measurement of FFR which represents the ratio of maximal coronary blood flow when stenosis was existing to the maximum blood flow if no epicardial obstructions were present [54]. In which 79 Patients underwent coronary angiography to detect CAD or to assess the progress of previous one. Of those only 50 patients were having the inclusion criteria. Exclusion criteria included contraindications to CMR, unsuitable to pharmacological agents in us and ACS within the previous 30 days of these 50 patients; seven had to be excluded due to technical reasons or claustrophobia. The remaining 43 patients were involved in the study. Clinical features like [hypertension, NIDD, angina class, family history of CAD] were identified. They underwent CMR and CA within four weeks. FFR was measured if angiography showed a coronary stenosis of 50–99%.

All perfusion territories were classified as normal, intermediate, or severe, according to the coronary angiogram and FFR measurements:

• Normal if CA showed no significant stenosis (less than 50%).
• Intermediate if a stenosis of more than 50% and an FFR more than 0.75.

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- Severe when lesions of less than 50% and an FFR less than 0.75 or a total occlusion. Normal and intermediate results were considered negative and severe results as positive. Normal angiography was noted in (23%) perfusion territories. Angiographic stenosis of 50% was present in (36%) cases. Fifty-three (41%) perfusion territories revealed an angiographic stenosis 50%. Stenosis was located at LAD (38%), LCx (32%), and RCA (29%). 58% of lesions were proximal and 42% distal. The result showed that the Sensitivity of CMR for ischemic CAD detection was approximately equal to the reported sensitivities of usually used imaging. CMRI shows good correlation with the invasive FFR functional assessment of coronary stenosis with sensitivity 88% and a specificity of 90%.

In these studies, there are many positive points including the detailed explanation of data on the diagnostic accuracy of CMR especially regarding the exact site of the stenosis in term of the level and the segment involved. These absolutely will have a positive effect on the management of patients with CAD as the exact localization can aid the decision about how to deal with patients. Another good point in this study is the detailed explanation of the CMR techniques that have been used. These can be used in further studies and in real life. Furthermore, these studies include interpretation of results in correlation with the most important risk factors of CAD which include smoking, male sex, diabetes and family history. By this way, CMR can be considered as a valuable test in the risk stratification and primary prevention of ischemic heart disease. Since subjects involved are both with and without CAD, in the subject-level analysis, So that specificity could be estimated in this study accurately. In the previous two studies, although there are some limitations of being non-randomized, non-controlled studies in addition to the small number of patients included, but they highlighted to some extent the significant role of MRI in evaluation on CAD.

**CMR versus ECG And Troponin in Emergency Situation**

A large, prospective observational clinical trial was conducted by the National Heart, Lung, and Blood Institute in Bethesda with the aim of evaluation of CMR in the detecting of ACS in the emergency unit published in 2003. 161 consecutive patients had been included. Patients with STEMI were excluded. Within 12 hours of onset of symptoms, a non-stress MRI was conducted. After chest pain resolution and patients stabilization, MRI was performed.

**Inclusion criteria:**
- ≥ 30 minutes of chest pain likely to be myocardial ischemia
- within 12 hours before ED presentation
- >21 years of age
- Weight <270 lb.

**Exclusion criteria**
- Patients with ST-elevation MI.
- pregnant women
- Severe congestive heart failure that is unable to lie flat.
- MRI contraindications including any metallic implant

The end point of this study is the CMR to be considered as a true positive if it shows a significant stenosis in the territory of Coronary vessels. The CMR scan was performed at rest (not stress). After lesion localization, a gadolinium-based contrast had been injected to all patients. Followed by evaluation of left ventricular function with cine CMR. Finally, MI regions were assessed by delayed hyperenhancement image.

ACS patients should satisfy the guidelines of the American College of Cardiology and the American Heart Association which include:

**Probable ACS:**
- Resting chest pain compatible with myocardial ischemia of ≥30 minutes duration within 12 hours of ED presentation.
- NSTEMI required abnormal serial troponin-I (≥1.96 µg/dL) with a temporal pattern consistent with acute MI and any clinical evidence of coronary artery disease.

**Confirmation of unstable angina:**

A 70% epicardial coronary stenosis or true positive abnormal stress testing performed during the index hospitalization or subsequent 6-8 weeks follow-up period. The CMR showed a sensitivity and specificity of 84% and 85%, respectively for ACS detecting. It also had more sensitivity than ECG (p<0.001) and peak troponin-I (p<0.001) for ischemia detection. It was more specific than electrocardiogram (p<0.001). A nonstress CMR is suitable for patients presenting with
catheterization within 24–48 hours after the MR examination. Finding of 50% or more stenosis in a major epicardial coronary artery or the major branches was considered to be a significant stenosis.

The overall sensitivity, specificity, and diagnostic accuracy for the detection of coronary artery stenosis (50%) were 90%, 71%, and 84%, respectively. Negative and positive predictive values were 76%, and 88%, respectively.

The main conclusion of this trial is that myocardial stress perfusion CMR has an accuracy ranging between 84%–86% so help identify significant coronary artery stenosis. The main merit of this trial is that patient population consisted of a cohort which includes a high number of hypertensive patients, others with a history of preceding interventions, and previous myocardial infarction, subsequently, a high specificity can be obtained. The large number enrolled also improved the accuracy, but the limited use of only one technique which is the stress CMR without using other techniques may be a source of debate.

**CMRI Versus SPECT**

The diagnostic performance of cardiac MRI especially the perfusion study could be compared to SPECT, and it may be superior. Many studies evaluate the role of MRI in comparison to nuclear studies. In 40 patients, Sakuma et al. \(^{(80)}\) compared perfusion MRI to SPECT, followed by X-ray angiography. The study showed a comparable sensitivity and specificity for CMR and SPECT, MRI had a sensitivity of 87-90% and specificity of 85% when coronary angiography was the reference. More precisely, for patients having significant stenosis in at least single CA the sensitivity was 81.0% for MRI and 81.0% for SPECT. Similarly, the specificity in diagnosing patients with significant coronary artery stenosis was 68.4% for MRI and 63.2% for SPECT. Regarding the value of stress first-pass contrast-enhanced CMR in stenosis detection, the sensitivity and specificity were 69.7% and 87.6%, respectively.

Another study conducted by Ishida et al. \(^{(81)}\) which demonstrated a better diagnostic value for perfusion MRI than SPECT. In this study, 104 subjects were enrolled, and First-pass contrast-enhanced MR was performed in 104 patients at rest and stress X-ray angiography was conducted in all patients. Stress perfusion (SPECT) was acquired in 69 patients, the study concluded the sensitivity of CMR imaging for...
predicting significant stenosis in one coronary artery was 90% while it was 82% with SPECT. The sensitivities of MR imaging for identification of one, two and three vessel stenosis were 85%, 96%, and 100% respectively. Corresponding SPECT sensitivities were 73%, 88% and 100%, respectively.

There are some limitations in the first study including the retrospective analysis of the results and the limited number of subjects with a high prevalence of CDA. This may interfere with an accurate determination of both the sensitivity and specificity in predicting CDA. There were several limitations in the second study mainly the high prevalence of CDA within the small number of patients with no significant CD stenosis precluded a reliable prediction of specificity of CMR and SPECT in myocardial ischemia diagnosis.

Role of Cardiac Magnetic Resonance Imaging in the Assessment of Myocardial Viability

Many studies have been conducted to demonstrate the utility of MRI in predicting functional recovery in patients with acute MI in one study (91), a group of 24 patients with first myocardial infarction have been involved. They underwent DE-MRI within a week after the acute attack, they found that the best predictor of global improvement after 2 to 3 months was the extent of myocardium dysfunction with or without 25% hyperenhancement.

Another study was done by Gerber et al. (92). In which 20 patients were enrolled, the main conclusion was that the sensitivity of absence of hyper enhancement in dysfunctional segments was 82% in the prediction of contractile recovery.

In contrast, another study, conducted by Kramer et al. (93) showed that areas of hyper enhancement revealed contractile and functional improvement. They enrolled 23 patients in the first 4 days after their first MI and reperfusion. Low-dose dobutamine MRI was done, followed by contrast-enhanced MRI, to assess functional recovery at 3 months. In this study, the hyper enhancement was found to exist even in viable segments. They also reported that the lack of first-pass hypo-enhancement confirm a good prognosis for contractile recovery. Contradicted by Gerber et al. study results (92) which showed that the absence of hyperenhancement had a sensitivity and accuracy of 82% and 74%, respectively, in predicting functional recovery.

All these three studies included a clear code of conduction in term of the techniques used and the timing and dose of dobutamine administered, so that they can be a base for more future studies. However, A limited number of patients had been enrolled in these studies which interfere with its predictive value. Furthermore, there is some heterogeneity between these studies in term of interpretation of their findings which might be the basis for their variable results.

CMR versus CT scan

Many studies have been conducted over the last few years with the purpose of directly comparing the diagnostic performance of magnetic resonance imaging and multi-slice CT for the non-invasive recognition of coronary artery stenosis. While CT angiography is an anatomical method for CAD detection, CMR can evaluate ischemia and myocardial scar and is especially efficient in the assessment of the functionally significant CAD and in guiding management. Both these modalities emerged as effective noninvasive diagnostic modalities for CDA; nevertheless, MRI — unlike CT — does not expose patients neither to ionizing radiation nor to iodinated contrast agent.

A prospective study (89) compare the value of low-dose computed tomography coronary angiography and CMR and combinations for the detection of significant coronary stenosis in Forty-three consecutive patients with a known or suspected CAD. After catheter, coronary angiography has been conducted, they underwent CTCA and cardiac CMR. The sensitivity and specificity of CTCA for the detection of significant CAD were 100 and 92.9 respectively. While For CMR, sensitivity, specificity was 89.7 and 100 respectively. When they are compared to the coronary angiography as a reference, CTCA has better performance than CMR regarding the sensitivity and NPV; however, CMR shows higher specificity and PPV than low-dose CTCA (89).

Another prospective study was conducted with the same aim (90) involved performing MRI and CT followed by elective X-ray angiography in one hundred twenty patients with known or suspected CAD.

The diagnostic values of both modalities for significant CA stenosis were comparable. In the patient-based analysis, both MRI and CT angiography have similar diagnostic accuracy with 83% versus 87%, sensitivity of 87% versus 90%, and specificity of 77% versus 83% respectively.

So, that MRI and 64-slice CT angiography equally detect significant CAD in patients who suspected or known to have a CDA. However, CT angiography
offers a better trend toward higher diagnostic performance.

These studies performed prospectively, and a large number of patients have been enrolled, this can be counted as a positive point.

These studies were performed in patients with high prevalence of CAD and with clinical indications for cardiac catheterization. Thus, findings of both studies might not necessarily be suitable for patients having less severe CAD. The lack of clear explanation of the techniques used may limit these studies value as a reference for further study.

4. DISCUSSION

Coronary artery disease (CAD) is the main cause of death in the western world, and its prevalence is continuously increasing (1). The conventional coronary angiography represents the gold standard for the diagnosis of obstructive CAD as it offers the chance for intervention when it is mandatory in addition to high sensitivity and specificity (52), however, there are many disadvantages as it is invasive procedure associated with many risks especially the risk of ionizing radiation. Despite being a diagnostic and therapeutic procedure, a substantial number of these procedures are done only for diagnostic purposes without the need for intervention. Thus, finding a noninvasive, low-risk, and cost-effective substitute for conventional coronary angiography would be a beneficial important advancement in the diagnosis of CAD.

CMR has some advantages over x-ray angiography and CT scan includes the lack of exposure to ionizing radiation and iodinated contrast media. These features make further follow-up studies much easier and allow performing CMR in both younger patients and those with renal impairment (10).

CMR &CMR angiography are progressively becoming a favorable alternative to conventional invasive angiography. During the last period, it has been studied passionately. Some of these studies demonstrate the capability of CMR to diagnose CAD with both high sensitivity and specificity (10,52) which could be comparable to other modalities like X-ray angiography (52), CT scan (89,90), SPECT (80,81) and others.

In patients with intermediate or high possibility of having CAD

CMRA can detect approximately three-quarters of significant stenosis [more than 50%] in the visible segments of the main coronary arteries with a specificity of 86% (52). Coronary magnetic resonance angiography demonstrated an excellent diagnostic performance in all epicardial vessels except the left circumflex coronary artery. Probably caused by its close relationship with the accompanying vein and the adjacent left atrium and ventricle blood pools, in addition to its lower signal due to the greater distance from the MRI receiving coil (52).

In populations with high prevalence of coronary arteries stenosis

CMRA shows very good diagnostic value in all vessels except the left circumflex coronary artery. Across those populations, CMRA showed general high sensitivity for diagnosing those with CAD. Most of the published reports concerned with the diagnostic performance of CMRA in ischemic heart disease are heterogeneous not only regarding their study design but also their analytic methodologies. For instance, the assessment of CAD has been done in different manners, as some study analyzed the results according to subjects, other concern with the findings according to the segments involved. Furthermore, most of these studies did not assess the distal segments of coronary arteries, so that its diagnostic value is lower in the evaluation of distal vessel lesions. Despite the technical improvement, its use is limited to the proximal segments. This could be sufficient in some patients when the stenosis presents in the proximal segments and need a surgical intervention. Even in the proximal coronary arteries evaluation, only 80% (52) can be evaluated correctly. This may interfere with the wide use of CMR as alternative to conventional x-ray angiography.

Most of the studies included stated that the radiologists who interpret the CMR images were blinded to both patient’s history and X-ray angiography results while there was less clarity whether the clinicians who interpret the x-ray angiography were blinded or not. The experience differences between people who participate in these studies may be an important limitation. Finally, there was some difference in the definition of coronary stenosis used in X-ray angiography to make the diagnosis; this may have an impact on both sensitivity and specificity of these studies.

In comparison to SPECT, CMR is considerably more sensitive for all types of infarction (80,82) with better sensitivity for non-Q wave infarction (80). Both studies showed higher sensitivity for CMR than SPECT but relatively similar specificity. These studies are

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controlled non-randomized with limited number involved.
Cardiovascular magnetic resonance is involved in the management of acute coronary syndromes. In this situation, CMR help to diagnose important differential diagnoses (11). Cardiovascular magnetic resonance allocates exactly the various tissue components in acute myocardial infarction such as necrosis, microvascular obstruction (MVO), haemorrhage, and edema, i.e. area at risk (11). Both the sensitivity and specificity of CMR are higher than that of ECG while troponin has lower sensitivity but higher specificity (65).

Stress CMR was also assessed in comparison to x-ray angiography (55). The study demonstrated CMR sensitivity to be 90% which is relatively acceptable, but the study is not convincing as the evaluation was done for only dobutamine-induced stress CMR with no other techniques. Many studies compare CMR to CT as each of these tests is done invasively. There was heterogeneity between these trials as they used variable techniques. The results interpretation was also a matter of debate. Therefore, the final conclusions of these studies were different to some extent (89,90). The sensitivity and specificity of CMR are lower than those of CT scan (89) while some studies showed the reverse (90). Despite that CMR still offers the chance of an ionizing radiation free field with no need to use iodine containing contrast. In the case of coronary artery calcification, which reduces specificity in other diagnostic tests, is not noticeable on CMRI images (90). Consequently, recognition of coronary arteries stenosis by CMRI is more reliable than CCTA in profoundly calcified coronary segments (89,90). In addition, even though CMR could not achieve an excellent reliability in diagnosis of coronary arteries disease (like CT scan), it is the favorite imaging modality to assess the effect of ischemia on myocardial perfusion, function and myocardial integrity (57).

The assessment of myocardial viability following MI is a crucial emerging role for CMR. This can be assessed depending on the different levels of enhancement following gadolinium administration. Some trials consider the lack of hyper enhancement as a good marker of the non-viable myocardium (91,92). Others showed a better response to revascularization treatment when there is no hypo-enhancement in first pass images. Whether viable or not is an important factor which determines the possibility of response to revascularization therapy and can assist in deciding whether to do the revascularization or to depend on the conservative medical treatment (86).

5. LIMITATIONS

The main limitations in this dissertation are the limited number of relatively good quality studies which could be used as a baseline in further future trials which aim to promote the diagnostic performance of CMR in ischemic heart disease. Most of the available data are a single center trial which conducted by a certain brand equipment, and this may be a source of debate as the results may be on behalf of specific brand or center.

The use of CMR in ischemic heart disease may have several drawbacks including:

- The procedure needs the operators to have advance skills, the methods are presently manufacturer specific, and the whole acquisition may be time-consuming.
- There are many contraindications to CMRI which interfere with its diagnostic performance such as certain implanted foreign bodies or medical device that is metallic in consistency or includes an electrical circuitry (e.g., pacemakers, implantable cardioverter-defibrillators). Coronary artery stent is excepted, they are not a contraindication to MRI, but it may affect image quality.
- Some patients may have irregular heart rhythms, or they are unable to hold their breathing (to perform a breath-holding images), or having an irregular pattern of respiration (free breathing approaches). All these will associate with poor image quality (6).
- Compared to CCTA, the spatial resolution of CMRI is lower, but the temporal resolution is more flexible (5).
- The cost effectiveness is the main limiting factor to the widespread application of CMR in many purposes including the investigation of patients with CDA.

6. CONCLUSION

CMR has reasonably high sensitivity with acceptable negative predictive value in the exclusion of significant coronary artery stenosis. Coronary magnetic resonance angiography has a role in the diagnosis of significant multivessel CAD in patients
planned to undergo a diagnostic catheterization. CMR has a superior spatial resolution which aids the distinction between subendocardial and transmural MI. Despite the fact that CMR could not achieve an excellent reliability in diagnosis of coronary arteries disease (like CT scan), it is the favorite imaging modality to assess the effect of ischemia on myocardial perfusion, function and myocardial integrity\(^{(57)}\). If we use comprehensive MRI method, all this information can be acquired in a single exam lasting not more than 30–45 min\(^{(56)}\). Magnetic resonance spectroscopy has become a standard test in experimental cardiology to study cardiac metabolism such as cardiac high-energy phosphate metabolites ATP and phosphocreatine in patients with IHD\(^{(58)}\). In comparison to x-ray angiography, both the sensitivity and specificity vary according to the type of scan but in general, values usually more than 80%. Thus, 2 out of 10 patients with the disease would be missed otherwise its diagnostic performance.

My suggestions are to conduct additional large, multicentre studies in patients with varying levels of CAD risk to assess the diagnostic accuracy of cardiac MRI and its value compared to X-ray angiography and others. More rigorous reporting of future clinical research on coronary artery imaging technologies should be encouraged. The cost effectiveness of CMR should be evaluated and compared to others with the aim of making CMR accessible and feasible test.

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