



The role of Cardiac Magnetic Resonance in Patients post ST-Elevation Myocardial Infarction

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Abbreviations

CAD- Coronary artery disease

CMR - Cardiac magnetic resonance

LV - Left ventricle

LVEF - Left ventricular ejection fraction

IMH - Intramyocardial haemorrhage

MI - Myocardial infarction

MVO - Microvascular obstruction

NSTEMI - Non- ST-segment elevation myocardial infarction

STEMI - ST-segment elevation myocardial infarction

STIR - Short tau inversion recovery

Take Home Messages

- Cardiac magnetic resonance provides insights into infarct size and pathology
- More work needs to be done to determine the patient groups in whom CMR will have the greatest cost-effectiveness.
- The biggest breakthrough of the past decade has been in the quantification and discrimination of reversible and irreversible myocardial injury, and novel infarct characteristics e.g. microvascular obstruction and intramyocardial haemorrhage.

Introduction

Coronary artery disease (CAD) is the most common worldwide cause of adult mortality, with a one year mortality of approximately 10% (1). In Europe, 1 in 6 men and 1 in 7 women will die of myocardial infarction (MI) (1). In the UK in 2012, CAD caused 73,680 deaths and was an important cause of premature death (12%, <75 years) (2). Whilst MI death rates are falling (2), risk assessment in individual patients post-MI remains problematic (3,4). Increasing numbers of acute ST-elevation myocardial infarction (STEMI) survivors have residual infarct pathology that predisposes them to the subsequent development of LV dysfunction and heart failure, which remain the major causes of death post-MI (5). In fact, despite improved early survival after an acute STEMI, the incidence of heart failure in the longer term has increased to 32% (1990-1999) from 10% twenty years earlier (5,6), making the case for accurate risk stratification of patients post-STEMI all the more important.

Advantages and Disadvantages of Cardiac Magnetic Resonance (CMR)

CMR has superior accuracy and precision when compared with echocardiography (7,8), and uses nuclear magnetic resonance, i.e. the electromagnetic radiation emitted by protons when placed in a magnetic field.

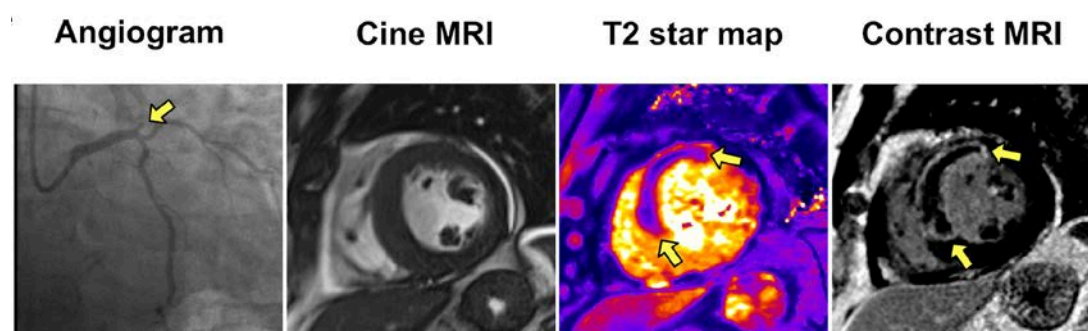
CMR has a number of advantages. The lack of ionising radiation makes it useful in young people and those requiring serial follow-up. It is the gold standard technique for accurate assessment of LV volumes and function and therefore lends itself to clinical trial use. CMR produces high spatial resolution imaging with excellent soft tissue contrast (9,10) despite the structures being close to bone or air (lungs), unlike echocardiography. Views are less likely to be foreshortened, or acquired off-axis, especially short axis views when compared with transthoracic echocardiography. However, examination times are longer with CMR than with echocardiography or computed tomography, and CMR has lower temporal resolution than echocardiography. CMR is unsuitable for claustrophobic patients, and because the

patient is isolated from direct care this makes CMR unsuitable for haemodynamically unstable patients. Patients with intra-cranial and intra ocular ferromagnetic objects, cochlear implants and certain cardiac pacemakers and leads are contra-indicated (11). A number of studies have investigated and confirmed the safety of CMR in patients with STEMI (12,13) and non-ST elevation MI (NSTEMI) (14).

Risk Stratification with Cardiac Magnetic Resonance

A number of studies have described the utility of CMR to identify patients at risk of adverse LV remodelling and major adverse cardiac events (MACE) (see figure 1 for examples).

Figure 1. What happens within an infarct? Insights from Cardiac Magnetic Resonance



Cardiac Magnetic Resonance Imaging obtained from a 52 year old man with a history of current hypertension. The symptom-to-balloon time was 1.4 hours. The coronary angiogram revealed a proximal occlusion of the left anterior descending artery (yellow arrow, A). Two days later, CMR disclosed an extensive wall-motion abnormality in the antero-septal walls on cine imaging (B- end-diastolic image), in keeping with the echo report. Intramyocardial hemorrhage was revealed by T2* mapping (yellow arrows, C) and transmural infarction of the antero-septal walls of the left ventricle (LV) (yellow arrows, D) associated with microvascular obstruction revealed by late gadolinium enhancement. The initial infarct size was 38.9% and the LVEF and LV end-diastolic volume indexed to body surface area (LVEDVi) were

48.5% and 90.2 ml/m², respectively. Six months later, infarct size was 26.7% of LV mass and the LVEDVi was 127 ml/m². This is in-keeping with an >20% in LVEDVi, i.e. adverse remodeling. This patient went on to have an unplanned admission for heart failure treatment on day 493 of follow-up.

Left Ventricular Function

The practice guidelines for ST-elevation MI (STEMI) issued by the European Society of Cardiology (1) allocate echocardiography with a class 1, level of evidence B indication for risk stratification based on assessment of infarct size and resting left ventricular function. CMR imaging has a class 2a, level of evidence C, i.e., indicated when echocardiography is not feasible, whereas routine computed tomography is not recommended (class 3, level of evidence C). The infarct territory is inferred by the presence of a wall-motion abnormality (15) and the standard assessment of left ventricular (LV) function post MI consists of estimating the LV ejection fraction (LVEF) and wall motion scoring. However echocardiography does not directly reveal MI pathology and LVEF may be normal even in STEMI survivors despite marked reductions in regional contractility (16,17).

Volumes and mass are assessed on analysis of a stack of short-axis steady-state free precession cine slices (breath-held or free breathing) which produce high spatial resolution images with excellent myocardium-blood contrast. In a meta-analysis of 25,497 STEMI patients, LVEF by CMR was an independent predictor of MACE (18).

Myocardial strain

Strain is defined as the deformation of an object relative to its original length (19,20). Strain reflects myocardial deformation and is more closely linked with myocyte metabolism and contractility than LVEF (19). There are several techniques for assessing myocardial strain with CMR including bespoke strain methods such as myocardial tagging (21) and displacement encoding with stimulated echoes (22–24).

Recently there has been a surge in publications utilising cine-derived strain (25–29) based on optical flow (26) or deformable image registration methods (27).

Retrospective cine strain imaging has appeal in routine clinical practice given the current drive for time-efficient imaging, reduced scanning times and patient comfort as it obviates the need for additional breath-hold scans by utilising cine imaging traditionally acquired to calculate LVEF and volumes to derive strain.

Myocardial strain has been reported to be a predictor of adverse remodelling in the longer term (30–32). A number of studies have reported peak systolic strain to be an independent predictor of MACE (33–37).

Area-at-risk

The area-at-risk refers to the edematous myocardium subtended by the infarct-related artery that would have fully infarcted following STEMI if reperfusion had not taken place. Prompt revascularization interferes, salvaging jeopardized myocardium. Myocardial salvage is calculated by subtracting the final infarct size on contrast-enhanced CMR (3 to 6 months post-MI) from the initial area-at-risk and predicts the likelihood of functional recovery (38). There are a number of different techniques used to quantify the area-at-risk including 2-weighted short tau inversion recovery (STIR) black blood sequences, as well as newer techniques such as T1 and T2 mapping (39–41). The area-at-risk and myocardial salvage have prognostic utility for adverse LV remodeling (42,43) as well as MACE (44,45)

Infarct Size

One of the strengths of CMR is the ability to infer the mass or volume of acute infarction through the use of gadolinium chelate contrast agents and the use of late gadolinium enhancement imaging (46). Late gadolinium enhancement is the result of gadolinium entering disrupted cell membranes (in acute MI) or from reduced washout from increased extracellular space within a chronic infarct. The infarcted region appears as 'enhanced', whilst normal myocardium appears 'nulled'.

There is a strong evidence base that infarct size quantified by late gadolinium enhancement is an independent risk factor for adverse remodelling (47,48) and MACE (49–51). There is still debate on the optimal timing of the assessment of infarct size, which if assessed early, may be over-estimated due to oedema(52). The generally agreed consensus is three to seven days post MI (53,54).

Microvascular obstruction and Intramyocardial haemorrhage

Despite restoration of epicardial artery patency, myocardial perfusion remains compromised in up to 50% of STEMI, resulting in persistent myocardial ischemia and infarction (55). This 'no-reflow' phenomenon is associated with larger post-infarction myocardial necrosis, which is a major adverse predictor of outcomes in STEMI patients (56,57).

The motivation of emergency coronary angioplasty has extended from achieving epicardial coronary artery patency alone, towards preserving the integrity of the coronary microvasculature bed. Traditionally, no-reflow was hypothesized to result from microvascular obstruction (MVO) due to the distal embolization of epicardial thrombotic and atheromatous debris. However, irreversible microvascular injury and subsequent intramyocardial hemorrhage (IMH) are now also thought to be important contributing factors.

MVO is traditionally quantified as present/ absent or quantified in grams or % LV mass as a hypointense core within an infarct on late gadolinium enhancement. MVO is dynamic and peaks at 3 days post-MI, is stable up to 10 days post MI and resolves by 6 months (53). The presence of MVO within an infarct is predictive of adverse remodeling (58,59) and confers an adverse prognosis (57,60,61).

For the assessment of IMH, CMR is considered to be the gold-standard method. T2 or T2* CMR techniques identify hemorrhage through a signal drop due to the paramagnetic effects of iron-containing hemoglobin. The standardized imaging protocol for the assessment of IMH is debated, as is the timing of image acquisition

post-reperfusion. T2* is more specific in detecting IMH in comparison to T2-weighted imaging because the paramagnetic effects of hemoglobin products are stronger on T2* than T2, resulting in greater signal depletion within the infarct core (62,63). IMH is an independent predictor of adverse LV remodeling (58,64) as well as MACE (64,65).

An argument in favor of cardiac magnetic resonance

There is currently a discrepancy in the availability of CMR through UK wide health boards, despite increasing indications and subsequent demand for CMR exams (66). CMR plays an important role in the risk stratification of STEMI patients, especially those with anterior MI(67), low LVEF and sub-optimal echo windows(1). CMR gives the clinician insights into the pathophysiology of infarcted, salvaged and remote myocardium. This modality also identifies patients who require stringent follow-up, including optimization of medical therapy to prevent adverse LV remodeling and heart failure as well as for the consideration of primary prevention implantable cardioverter defibrillator therapy. There is a requirement for large, multi-centre studies to demonstrate that CMR-led care has utility in risk-stratification of patients post-STEMI when compared to usual care, and through optimization of medical management this translates into a reduction of adverse LV remodeling and MACE. In my opinion, the presence of adverse markers such as microvascular obstruction, intramyocardial hemorrhage is clinically relevant as it will identify at-risk patients who might benefit from more intensive evidence-based interventions (pharmacological and non-pharmacological) in order to reduce their increased risk of major adverse cardiac events.

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