Cardiovascular magnetic resonance imaging assessment of outcomes in acute myocardial infarction

Jamal N Khan, Gerry P McCann

Jamal N Khan, Gerry P McCann, Department of Cardiovascular Sciences, University of Leicester and the NIHR Leicester Cardiovascular Biomedical Research Unit, University Hospitals of Leicester NHS Trust, Glenfield Hospital, Leicester LE3 9QP, United Kingdom

Author contributions: Khan JN wrote the manuscript; McCann GP critically reviewed and edited the manuscript.

Conflict-of-interest statement: There are no relevant conflicts of interests for the authors with respect to this manuscript or with respect to any manuscripts that the authors may be asked to review.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/

Manuscript source: Invited manuscript

Correspondence to: Dr. Jamal N Khan, MBChB, PhD, BMedSci, Clinical Research Fellow in Cardiovascular Sciences, Department of Cardiovascular Sciences, University of Leicester and the NIHR Leicester Cardiovascular Biomedical Research Unit, University Hospitals of Leicester NHS Trust, Glenfield Hospital, Groby Road, Leicester LE3 9QP, United Kingdom. jk211@le.ac.uk Telephone: +44-0116-2044746

Received: October 15, 2016
Peer-review started: October 19, 2016
First decision: November 30, 2016
Revised: December 2, 2016
Accepted: January 2, 2017
Article in press: January 3, 2017
Published online: February 26, 2017

Abstract
Cardiovascular magnetic resonance (CMR) imaging uniquely characterizes myocardial and microvascular injury in acute myocardial infarction (AMI), providing powerful surrogate markers of outcomes. The last 10 years have seen an exponential increase in AMI studies utilizing CMR based endpoints. This article provides a contemporary, comprehensive review of the powerful role of CMR imaging in the assessment of outcomes in AMI. The theory, assessment techniques, chronology, importance in predicting left ventricular function and remodelling, and prognostic value of each CMR surrogate marker is described in detail. Major studies illustrating the importance of the markers are summarized, providing an up to date review of the literature base in CMR imaging in AMI.

Key words: Myocardial infarction; Infarct; Cardiovascular magnetic resonance; Left ventricular remodelling; Prognosis

© The Author(s) 2017. Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Cardiovascular magnetic resonance (CMR) imaging uniquely characterizes myocardial and microvascular injury in acute myocardial infarction (AMI). Contrast-enhanced CMR offers robust, validated and reproducible surrogate markers, providing an accurate representation of pathophysiology, assessment of myocardial function and injury, and predictive value for medium to long-term LV function, remodelling and prognosis following primary percutaneous coronary intervention for STEMI. These qualities significantly increase the statistical power of studies using CMR endpoints and has resulted in an exponential increase in AMI studies utilizing CMR based endpoints. An understanding of the role of CMR in the assessment of outcomes in AMI is of key importance not only to interventional and imaging cardiologists, but to the cardiology community as a whole.

Khan JN, McCann GP. Cardiovascular magnetic resonance imaging assessment of outcomes in acute myocardial infarction. World J Cardiol 2017; 9(2): 109-133  Available from: URL: http://www.
INTRODUCTION
Cardiovascular magnetic resonance (CMR) imaging uniquely characterises myocardial and microvascular injury in acute myocardial infarction (AMI), providing powerful surrogate markers of outcomes. The last 10 years have seen an exponential increase in studies utilising CMR based endpoints in patients with AMI undergoing primary percutaneous intervention. This article provides a contemporary, comprehensive review of the powerful role of CMR imaging in the assessment of outcomes in AMI. The theory, assessment techniques, chronology, importance in predicting left ventricular function and remodelling, and prognostic value of each CMR surrogate marker is described in detail. Major studies illustrating the importance of the markers are summarised, providing an up to date review of the literature base in CMR imaging in AMI.

MARKERS OF OUTCOMES FOLLOWING PRIMARY PERCUTANEOUS CORONARY INTERVENTION IN AMI
Prognostic studies using clinical outcomes, in particular mortality require large sample sizes. Surrogate biomarkers of outcome are directly measured alternative endpoints used as a substitute for biological processes and clinical outcomes[1,2]. CMR imaging uniquely characterises myocardial and microvascular injury in AMI due to its accuracy, reliability and validity (Figure 1)[2-4]. This significantly increases the statistical power of studies, allowing sample size requirements to be reduced. CMR data are used as a substitute for biological processes and clinical outcomes including infarct size (IS), microvascular obstruction (MVO), intramyocardial haemorrhage (IMH) and myocardial salvage [non-infarcted proportion of ischaemic area at risk (AAR)] [26,27]. Anterior STEMI results in larger IS and lower LVEF due to the greater ischaemic AAR[28].

LV EJECTION FRACTION AND VOLUMES IN AMI
Background
In the medium-term following STEMI, LV end-diastolic volume (LVEDV) increases, LV end-systolic volume (LVESV) decreases[5-7] and there can be compensatory hypertrophy of remote myocardium[8,9] in order to preserve stroke volume and ejection fraction (LVEF). Adverse remodelling results from an inability of the heart to maintain geometry post MI in the context of large infarcts and increased wall stresses[10,11]. An increase in LVEDVI > 20%[12,13] and increase in LVESVI > 15%[14] at follow-up are the most commonly used criteria for adverse remodelling.

CMR assessment of LV volumes and ejection fraction
CMR is the gold standard modality for the assessment of ventricular function and volumes. It has higher spatial resolution than single-photon emission computed tomography (SPECT) (approximately 1.8 mm × 1.8 mm × 8 mm vs 10 mm × 10 mm × 10 mm)[15], and suffers from little subjectivity or reliance on patient body habitus[16].

Volumes and mass are assessed on analysis of a 3D cine stack of short-axis biventricular contiguous slices. Modern cine sequences use breath-hold, electrocardiographic-gated, segmented steady-state free precession (SSFP) to produce high spatial resolution images with excellent myocardium-blood contrast. Regional systolic function can alternatively be assessed using wall motion scoring[17].

CMR studies have demonstrated that recovery of LVEF occurs relatively early post STEMI. Ripa showed that improvement in LVEF and systolic wall thickening occurred by 1 mo, with no further change at 6 mo[5]. The majority of improvement in LVEF occurred between day 2 and 1 wk in the study by Mather[18], with a final increase by 3 mo. Beek showed that 55% of segments with initially impaired systolic wall thickness improved at 13-wk[19]. Ganame et al[20] and Dall’Armelina et al[21] however showed that LVEF underwent no significant change by 6 and 12 mo post PPCI respectively. This may be because their subjects sustained less myocardial damage, represented by relatively preserved LVEF and thus lower potential for improvement[21].

Volumetric changes occur more slowly. Ripa et al[5] showed a continued increase in LVEDV and reduction in LVESV until 6 mo. Engblom et al[7] demonstrated similar sequelae to 12-mo. Ganame showed progressive significant changes in LVEDV and LVESV and resulting LV sphericity at all timepoints to 12 mo[20]. These studies have important implications for optimising timing of follow-up CMR studies assessing remodelling.

The degree of impairment of LVEF and changes in volume depend on a number of CMR-based markers including infarct size (IS)[22], microvascular obstruction (MVO)[23-26], intramyocardial haemorrhage (IMH)[27] and myocardial salvage [non-infarcted proportion of ischaemic area at risk (AAR)] [26,27]. Anterior STEMI results in larger IS and lower LVEF due to the greater ischaemic AAR[28].

Prognostic importance of LVEF and volumes in AMI
Norris et al[28] and White et al[30] first illustrated the prognostic importance of LVEF (strongest independent predictor of survival at 3.5 years) and LVESV (only independent predictor of long-term mortality at 6 years) respectively, using invasive ventriculography. Burns first demonstrated the prognostic importance of LVEF and LV volumes and their strong correlation with each other, using radionuclide analysis[31].

A large evidence base has emerged for the prognostic impact of impaired systolic function based on reduced CMR-derived LVEF (Table 1).

In addition to LVEF-based global systolic function, Bodet demonstrated that the number of dysfunctional segments on CMR at 1-wk post STEMI was an independent predictor of combined MACE at a median follow-up of 553 d[30]. The evidence base for the prognostic importance of LV volumes is largely historical, based on large echocardiographic
and radionuclide studies, demonstrating the negative prognostic impact of ventricular dilatation and remodelling as summarised in Table 2.

### Table 2: Studies illustrating the prognostic importance of left ventricular volumes and adverse left ventricular remodelling in acute myocardial infarction

| Ref.          | Year | n   | Modality | Main findings                                                                 | Follow-up |
|---------------|------|-----|----------|-------------------------------------------------------------------------------|-----------|
| Ahn et al[^13] | 2013 | 135 | Echo     | Adverse LV remodelling (> 20% inc. LVEDV) at 6 mo was IP for 3 yr MACE. MACE rate approximately 25% in patients with adverse LV remodelling was approximately 6% in non-remodelled patients | 981 d     |
| Hombach et al[^6] | 2005 | 110 | CMR      | Baseline LVEDV was IP for MACE (P = 0.038)                                     | 225 d     |
| St John Sutton et al[^49] | 2003 | 512 | Echo     | Percentage change in LV area (surrogate for LV volume) between baseline echo and follow-up at 12 mo was IP for ventricular ectopy and VT | 24 mo     |
| Billongese et al[^2] | 2002 | 284 | Echo     | Baseline LVESV was IP for cardiac death and MACE. Components of MACE higher in patients with adverse remodelling (> 20% inc. LVEDV: Mortality 14% vs 5%, MACE 18% vs 10%) | 5 yr      |
| Otterstad et al[^40] | 2001 | 712 | Echo     | Increase in LVEDV between acute scan at 7 d and echo at 3 mo strongest IP for MACE | 24 mo     |
| St John Sutton et al[^49] | 1994 | 512 | Echo     | LV end-diastolic area (RR 1.1) and LV end-systolic area (RR 1.1) on baseline echo, and % change in LV area at 12 mo echo (RR 1.35) were strongest IPs for MACE | 12 mo     |
| White et al[^41] | 1987 | 605 | LV gram  | LVEDV at LV gram at 4 wk was strongest IP of long-term mortality (P < 0.0003) | 78 mo     |

MACE: Major adverse cardiovascular events; IP: Independent predictor; LVEDV: Left ventricular end-diastolic volume; LVESV: Left ventricular end-systolic volume; Modality: Modality of LV volume assessment (CMR: Cardiovascular MRI; Echo: Echocardiography; LV gram: LV contrast angiography).
Recently, left ventricular global performance index has been proposed as a CMR marker of cardiac performance, incorporating LVEF, LV volumes and mass. It has been assessed in one study in STEMI and correlated strongly with IS, MSI, MVO and IMH extent, and had incremental prognostic value to LVEF in predicting 12-mo MACE\(^\text{[42]}\). Further work is needed to investigate its prognostic value in STEMI.

### MYOCARDIAL STRAIN IN AMI

CMR-measured myocardial strain (tissue deformity) is the gold standard non-invasive measure of systolic and diastolic myocardial function\(^\text{[43]}\). Circumferential strain (Ecc) describes shortening of fibres (contraction) in a short-axis plane tangential to the epicardium; longitudinal strain (Ell) describes shortening in the long axis, and radial strain (Err) describes lengthening (thickening) of fibres towards the centre of the ventricle. Torsion is wringing of the ventricle caused by clockwise rotation at the base, and anticlockwise at the apex.

Strain offers greater accuracy in detecting myocardial dysfunction compared with global (LVEF) and regional (visual wall-motion scoring, segmental wall thickening)\(^\text{[44]}\) measures.

### CMR assessment of myocardial strain

In 1989, Axel et al\(^\text{[45]}\) developed a T1 spoiled gradient echo sequence, creating “tags” formed by saturation of thin myocardial lines running in perpendicular directions in-plane to form a myocardial grid. These lines act as tissue markers, tracking myocardial deformation as shown in Figure 2. Peak systolic strain and peak diastolic strain rate (relaxation rate of strain) provide very sensitive measures of systolic and diastolic function respectively. Its accuracy has been validated on comparison with sonomicrometry\(^\text{[46,47]}\). Harmonic Phase Analysis (HARP) is currently the most widely used CMR strain method\(^\text{[48]}\).

Feature tracking (FT) has been introduced as an alternative method to tagging for assessing strain on CMR. FT tracks anatomical features of interest along contour lines on routinely acquired SSFP cine images analogous to echocardiographic Speckle Tracking, obviating the need for additional tagging sequences\(^\text{[49]}\). FT-derived strain has been compared to tagging in acute STEMI and shown greater feasibility, accuracy and observer agreement\(^\text{[50]}\) and remains an exciting prospect.

### CMR LV strain as a predictor of LV function and remodelling in AMI

Strain could improve our understanding of the mechanics underlying LV dysfunction associated with prognostic CMR surrogate markers of myocardial damage in STEMI (e.g., MVO, IMH, oedema).

Systolic function is also in remote (non-infarcted) segments, and LV mechanics outside of the infarct zone are also affected during infarction and contribute to remodelling\(^\text{[44,51,53]}\). MVO had the highest predictive value for persistent dysfunction on circumferential strain at 7-mo post STEMI and may result in systolic dysfunction due to direct mechanical effects (myocardial stiffness)\(^\text{[53]}\). Baseline segmental circumferential strain was the strongest predictor of segmental functional recovery at 3-mo in a model containing infarct transmurality and MVO\(^\text{[54]}\). FT-derived global circumferential strain assessed acutely post PPCI was recently shown to correlated strongly with

![Figure 2 Cardiovascular magnetic resonance assessment of strain using tissue tagging. Cine SSFP images in end-diastole (A) and end-systole (C), with corresponding Spatial Modulation of Motion (SPAMM) tagged images (B and D). Grid lines (tags) are visible and contours drawn at 3 myocardial levels [green (epicardial), red (mid myocardial), yellow (endocardial)] allow tracking of myocardial motion and strain (circumferential), here using Harmonic Phase Analysis.](image)
molecules (Figure 3). Infarct can be visualised on T1-weighted imaging approximately 10 min after intravenous contrast administration, known as LGE imaging. In acute infarct, LGE results from gadolinium entering ruptured cell membranes. In chronic infarction, LGE results from increased extracellular space due to collagen deposition and prolonged washout due to reduced capillary density within myocardium [60,63]. Gadolinium shortens T1, causing infarcted myocardium to appear bright, and normal myocardium to appear black (Figure 4) [63,64]. Normal myocardium is progressively nulled using the appropriate inversion time to provide optimal contrast between infarct and normal myocardium.

Typically, a high spatial resolution of approximately 1.4 mm × 1.6 mm × 6–8 mm is achieved15. IS is typically expressed as a percentage of total LV mass. Delineation of infarct can be performed visually (manual quantification)6,8,22, however most groups use semi-automated methods to reduce observer variability. These include enhancing myocardium exceeding a predefined signal intensity (SI) threshold, typically > 2–6 standard deviations above that of remote (non-infarcted) myocardium16,64. Currently, the semi-automated full-width at half-maximum (FWHM) method is commonly used66–70, defining infarct as myocardium with SI > 50% of the peak SI in the infarct core. Amado demonstrated that FWHM had the highest interobserver agreement and closest correlation with TTC-stained infarct in a dog model of acute infarction (r² = 0.94), compared with standard

Table 3  Studies illustrating the prognostic importance of left ventricular strain in acute myocardial infarction

| Ref.      | Year | n   | Modality | Main findings                                                                 | Follow-up |
|-----------|------|-----|----------|-------------------------------------------------------------------------------|-----------|
| Ersbøll et al64 | 2014 | 1048 | TTE      | (E-prime divided by peak early diastolic strain rate) strongest IP of MACE and death | 29 mo     |
| Ersbøll et al67 | 2013 | 849  | TTE      | GLS was IP of MACE                                                            | 30 mo     |
| Hung et al66 | 2010 | 610  | TTE      | GLS and strain-rate, and GCS and strain-rate IP’s for MACE in model with WMS, LVEF | 25 mo     |
| Antoni et al64 | 2010 | 659  | TTE      | GLS (HR 1.2) was IP of mortality. LVEF, wall-motion score and Tissue Doppler mitral valve inflow not | 21 mo     |

TTE: Transthoracic echocardiography; GLS: Global longitudinal strain; MACE: Major adverse cardiovascular events; IP: Independent predictor; HR: Hazard ratio; LVEF: Left ventricular ejection fraction.

![Figure 3 Mechanism of late gadolinium enhancement.](image)

**Figure 3 Mechanism of late gadolinium enhancement.** Gadolinium is extracellular: A: In normal myocardium, gadolinium washes out approximately 10 min post administration and there is no late gadolinium enhancement (LGE); B: In acute infarct, gadolinium (yellow stars) enters ruptured cell membranes and causes LGE; C: In chronic infarct, LGE results from increased extracellular space due to fibrotic scar deposition.

**Prognostic importance of LV strain in AMI**

The evidence base for the prognostic importance of LV strain post STEMI is currently based on echocardiographic studies demonstrating that global longitudinal predicts medium and long-term using Speckle Tracking analysis as summarised in Table 3.

**INFARCT SIZE IN AMI**

**Background**

The “ischaemic cascade” is the sequence of pathophysiological effects developing immediately following coronary occlusion. Aerobic respiration loses efficiency resulting in cellular oedema. With increasing ischaemic time, cell membranes rupture. Following healing, necrotic cells are replaced by extracellular collagen deposition (scar). The acute and chronic phases are characterised by increased myocardial extracellular volume60–62.

**CMR assessment of IS in AMI**

Gadolinium contrast agents are large extracellular molecules (Figure 3). Infarct can be visualised on T1-weighted imaging approximately 10 min after intravenous contrast administration, known as LGE imaging.

In acute infarct, LGE results from gadolinium entering ruptured cell membranes. In chronic infarction, LGE results from increased extracellular space due to collagen deposition and prolonged washout due to reduced capillary density within myocardium60,63. Gadolinium shortens T1, causing infarcted myocardium to appear bright, and normal myocardium to appear black (Figure 4)63,64. Normal myocardium is progressively nulled using the appropriate inversion time to provide optimal contrast between infarct and normal myocardium.

Typically, a high spatial resolution of approximately 1.4 mm × 1.6 mm × 6–8 mm is achieved15. IS is typically expressed as a percentage of total LV mass. Delineation of infarct can be performed visually (manual quantification)6,8,22, however most groups use semi-automated methods to reduce observer variability. These include enhancing myocardium exceeding a predefined signal intensity (SI) threshold, typically > 2–6 standard deviations above that of remote (non-infarcted) myocardium16,64. Currently, the semi-automated full-width at half-maximum (FWHM) method is commonly used66–70, defining infarct as myocardium with SI > 50% of the peak SI in the infarct core. Amado demonstrated that FWHM had the highest interobserver agreement and closest correlation with TTC-stained infarct in a dog model of acute infarction (r² = 0.94), compared with standard
deviation methods\textsuperscript{[66]}. This may be because FWHM is less prone to IS overestimation in the presence of oedema, and partial volume effects giving rise to intermediate signal intensities\textsuperscript{[18,71]}. Comparing techniques in STEMI patients showed that FWHM quantification had the lowest intraobserver and interobserver variability, and greatest agreement with LVEF\textsuperscript{[72]}.

CMR measurement of IS on LGE is well validated\textsuperscript{[63,64]}. Kim demonstrated that IS in dog myocardium on ex-vivo CMR corresponded closely with IS derived from tetrazolium (TTC) staining (r = 0.99)\textsuperscript{[15,64]}. LGE has higher sensitivity for infarct detection compared with SPECT. In an experimental model of MI, CMR LGE detected 92% of all segments with subendocardial infarction (< 50% transmurality) compared with only 28% with SPECT\textsuperscript{[15]}. In patients with MI, SPECT only detects approximately 50% of the infarcts seen on LGE. The superior sensitivity is due to the increased spatial resolution and reproducibility of CMR\textsuperscript{[60]}.

Since gadolinium is distributed throughout the extracellular space, gadolinium contrast agents are not specific to necrosis. Acutely, the area of LGE detects not only necrotic cells but also the increased (oedematous) interstitium surrounding viable cells, and thus can overestimate true IS. Studies of IS chronology in humans corroborate this (Table 4). Indeed, severely dysfunctional segments with minimal myocardial salvage early post STEMI can show significant functional improvement at follow-up\textsuperscript{[72]}.

The majority of IS reduction occurs relatively early post STEMI, particularly by 1 wk. Indeed IS assessed at 1 wk has been shown to closely correlate with final IS\textsuperscript{[7,9,18]}. Overestimation of necrosis by LGE-derived IS early post STEMI is due to a combination of oedema, infarct resorption and partial volume effects. Oedema results in an overestimation of LGE IS due to increased extracellular water content and thus volume of distribution of contrast agent\textsuperscript{[66,75]}

Infarct resorption results from the healing process where collagenous scar tissue is produced to provide stability and tensile strength to necrotic myocardium\textsuperscript{[7,21]}. This was confirmed in a canine model where a 3.4-fold decrease in infarct volume was seen between day 3 and 8-wk post infarct on ex-vivo LGE and TTC-stained slices\textsuperscript{[64]}. The degree of infarct resorption has been shown to be proportional to initial IS (r = 0.65) and presence of LV remodelling (r = 0.41)\textsuperscript{[10]}. The greater degree of infarct resorption relative to total myocardial

---

**Table 4 Temporal changes in cardiovascular magnetic resonance-derived infarct size in acute myocardial infarction**

| Ref.         | Year | n   | CMR times post STEMI | Relative LGE IS reduction | LGE method | Main findings                                                                 |
|--------------|------|-----|----------------------|---------------------------|------------|-------------------------------------------------------------------------------|
| Carrick et al\textsuperscript{[65]} | 2016 | 50  | 30 d → 3 d → 10 d → 7 mo | 26%                       | Automated  | Significant decrease d3 to d10 (20% ± 13% to 14% ± 10% LV mass).             |
| Dall’Amergina et al\textsuperscript{[66]} | 2011 | 50  | 30 d → 6 mo           | 22% > 2SD                  | Automated  | IS reduced at times from 27% ± 15% LV mass 24 h post PPCI, to 21% ± 11% at 6 mo |
| Mather et al\textsuperscript{[67]}   | 2011 | 50  | 48 d → 1 wk → 30 d → 3 mo | 37% > 2SD                  | Manual     | 27% IS drop between d2 and d7 post PPCI, no change at 3 mo                   |
| Ganame et al\textsuperscript{[68]}   | 2011 | 50  | 58 d → 4 mo → 12 mo → 4 mo | 45% Manual                |            | 33% decrease IS d3 and 4 mo then no further decrease at 12 mo                |
| Ibrahim et al\textsuperscript{[69]}  | 2010 | 50  | 17 d → 1 wk → 1 mo → 6 mo | 37% Manual                |            | 34% reduction in IS from d2 to 1 wk, then no further change at 1 and 6 mo    |
| Engblom et al\textsuperscript{[70]}  | 2009 | 50  | 22 d → 1 wk → 12 mo → 40% | Automated                |            | 28% reduction in IS between d1 and 1 wk                                      |
| Ripa et al\textsuperscript{[71]}     | 2007 | 50  | 58 d → 2 d → 1 mo → 6 mo | 30% Manual                |            | 14% % reduction in IS from d2 to 1 mo                                         |
| Hombach et al\textsuperscript{[72]}  | 2005 | 110 | 6 d → 9 mo           | 28% Manual                |            | 28% reduction in IS from d6 to 9 mo                                          |

LGE method: SD: Standard deviations; Total LGE IS Overest: Relative overestimation of final IS (last timepoint) on acute CMR; CMR: Cardiovascular magnetic resonance; LGE: Late gadolinium enhancement; IS: Infarct size; PPCI: Primary percutaneous coronary intervention.

---

**Figure 4** Late gadolinium enhancement of acute infarct. Infarct appears white (enhanced) in the inferior wall, with unaffected myocardium black (nulled). A: 2-chamber long-axis view; B: Short-axis view, mid ventricular level. The posteromedial papillary muscle is also infarcted in the short-axis view.
mass and volume results in an inability to maintain LV geometry in light of mechanical stresses post STEMI, resulting in adverse LV remodelling and sphericity\cite{10,70}.

Factors known to affect IS include AAR extent\cite{77,79}, collateral flow to the AAR\cite{79,80}, MVO\cite{81}; time to reperfusion\cite{82} and hyperglycaemia\cite{63}.

**CMR IS as a predictor of LV function and remodelling in AMI**

**Segmental function:** Kim illustrated in stable patients awaiting revascularisation, that LGE transmurality strongly predicted recovery of systolic function in dysfunctional segments. Only 2% of segments with > 75% transmurality improved after revascularisation\cite{84}. Segmental extent of LGE has also been shown to negatively predict functional recovery in dysfunctional segments following PPCI for acute STEMI, as summarised in Table 5.

**Global function:** IS is a powerful independent predictor of global LV function and adverse LV remodelling in the medium to long-term post STEMI as summarised in Table 6.

**Prognostic importance of CMR-derived IS in AMI**

The goal of STEMI management is early reperfusion in order to minimise IS and thus maximise myocardial salvage\cite{85}. There is a strong evidence base for the prognostic importance of CMR-derived IS post STEMI, as summarised in Table 7. IS strongly predicts medium to long-term clinical outcomes.

---

**Table 5 Cardiovascular magnetic resonance studies illustrating importance of segmental late gadolinium enhancement extent and functional recovery in acute myocardial infarction**

| Ref. | Year | n | LGE method | Cutoff (LGE) | Main findings | Time of CMR 1 | Time of CMR 2 |
|------|------|---|------------|-------------|---------------|--------------|--------------|
| Khan et al\cite{10} | 2016 | 135 | Manual | IS strongest IP of LVR in model with LVEF and MI location | 7 d | 6 mo |
| Wong et al\cite{11} | 2014 | 45 | FWHM | IS IP of LVR in model incl. LVEF, IS, LV vols, MVO | 6 d | 189 d |
| Natale et al\cite{12} | 2011 | 64 | > 2SD | IS IP of LVEF in model with MVO, troponins | 2 d | 6 mo |
| Engblom et al\cite{13} | 2008 | 98 | Manual | IS strongest IP of LV (> > MVO, AAR, Troponin-I) | 7 d | 6 mo |
| Shapiro et al\cite{14} | 2007 | 214 | > 2SD | Extent of transmural necrosis (no. segments > 50% TEE) | 7 d | 6 mo |
| Kitagawa et al\cite{15} | 2007 | 18 | 50% TEE | Inverse relationship between TEE and functional recovery. 31% segments > 50% TEE still improved | 5 d | 39 wk |
| Janssen et al\cite{16} | 2006 | 67 | Manual | Inverse relationship between TEE and functional recovery on WMS at 12w (51%-75%: 39% segments improved, 76%+: 21% improved) | 4 d | 12 wk |
| Motoyasu et al\cite{17} | 2004 | 23 | 50% TEE | Inverse relationship between SEE and functional recovery on SWT | 25 d | 24 wk |
| Beek et al\cite{18} | 2003 | 36 | 50% TEE | Inverse relationship between SEE and functional recovery on WMS | 7 d | 13 wk |

WMS: Wall motion scoring; SWT: Systolic wall thickening; TEE: Transmural extent of enhancement; SEE: Segmental extent of enhancement; SD: Standard deviations.

**Table 6 Cardiovascular magnetic resonance studies illustrating importance of infarct size on left ventricular function and remodelling in acute myocardial infarction**

| Ref. | Year | n | LGE method | Main findings | Time post STEMI of predictive CMR | Follow-up |
|------|------|---|------------|---------------|-------------------------------|----------|
| Ahn et al\cite{19} | 2013 | 135 | Manual | IS strongest IP of LVR in model with LVEF and MI | 7 d | 6 mo |
| Husser et al\cite{20} | 2012 | 304 | > 2SD | IS IP of LVR in model incl. LVEF, IS, LV vols, MVO | 6 d | 189 d |
| Mommeneu et al\cite{21} | 2012 | 118 | > 2SD | No. segments > 50% transmurality IP for LVR | 6 d | 6 mo |
| Ezekowicz et al\cite{22} | 2010 | 64 | Manual | IS strongest IP of LVEF in model with MVO, troponins | 7 d | 3 mo |
| Ganame et al\cite{23} | 2009 | 98 | Manual | IS strongest IP of LV (> > MVO, AAR, Troponin-I) | 2 d | 6 mo |
| Bodi et al\cite{24} | 2009 | 214 | > 2SD | Extent of transmural necrosis (no. segments > 50% TEE) | 7 d | 6 mo |
| Wu et al\cite{25} | 2008 | 122 | Manual | IS extent only IP for LVEF and LVR | 2 d | 4 mo |
| Hornbach et al\cite{26} | 2005 | 110 | Manual | IS extent IP of LVR in model with MVO, % transmurality | 6 d | 225 d |

IS: Infarct size; IP: Independent predictor; LVR: LV remodelling; LVEDVI: Left-ventricular end-diastolic volume index; LVEDVI: Left-ventricular end-systolic volume index; LVEF: Left ventricular ejection fraction; MVO: Microvascular obstruction; SD: Standard deviation.
MVO IN AMI

Background

Despite prompt IRA recanalization, perfusion of the microcirculatory bed does not always ensue. Histopathological studies have demonstrated that the infarct core (endocardial) perishes first as necrosis spreads transmurally towards the epicardium. This is known as the "wavefront theory"[100]. At the infarct core, necrosis occurs rapidly with myocardial and capillary endothelial cells perishing simultaneously. Capillaries can become obstructed by cellular debris, resulting in non-perfusion of the infarct core, despite IRA patency[100]. This is known as MVO and can be indicated at angiography, as "no reflow"[101].

CMR assessment of MVO in AMI

Three CMR methods demonstrate MVO (Figure 5). MVO extent is typically expressed as a percentage of LV mass: (1) Qualitative first-pass rest perfusion. A modified version involves quantification of myocardial blood flow (SI-time curve) and time to 50% of maximal SI[102,103], (2) Hypoperfusion on inversion recovery images between 1-3 min post contrast. A fixed inversion time of approximately 440 ms nulls MVO and retains intermediate signal in normal myocardium. This is known as "early MVO (E-MVO)"[28,104]; and (3) Hypointensity within infarct core on LGE due to absence contrast perfusion, known as "late MVO (L-MVO)". L-MVO occurs in up to 60% of patients on CMR within the first week post STEMI[5,6,18,20]. This is the preferred method of MVO demonstration in contemporary clinical practice and research.

L-MVO extent is maximal at 48 h post infarct[8,18], and then decreases. It exists for at least 1 wk, and for up to 1 mo[8,18] and then resolves in the medium-term in humans (Table 8). Animal models corroborate these findings[105,106].

The extent of MVO on CMR has been shown to correlate with IS[82,94,107,108], oedema, IMH, TIMI-flow post PCI[35,109] and time to reperfusion[35,82,110].

CMR MVO as a predictor of LV function and remodelling in AMI

L-MVO is a strong independent predictor of medium-term LV function and adverse remodelling (Table 9). It

---

**Table 7** Cardiovascular magnetic resonance studies illustrating the prognostic importance of infarct in acute myocardial infarction

| Ref.          | Year | n   | LGE method | Main findings                                                                 | CMR timepoint | Follow-up |
|--------------|------|-----|------------|------------------------------------------------------------------------------|---------------|----------|
| Husser et al[94] | 2013 | 250 | > 2SD      | Extent of transmural infarction (no. of segments > 50% transmurality)         | 7 d           | 163 wk   |
| Izquierdo et al[95] | 2013 | 440 | > 2SD      | IS was IP for AACEs (arrhythmic cardiac events: Sudden death, VT, VF, ICD shock) in model including LVEF, hypertension | 7 d           | 123 wk   |
| Eitel et al[94] | 2011 | 208 | > 5SD      | IS was IP of MACE at 19 mo in model including MVO, LVEF, MII, Killip, TIMI post-PPCI | 3 d           | 18.5 mo  |
| Miszalski-Jamka et al[96] | 2010 | 77  | Manual     | LV transmurality index IP (HR 1.03) and IS (HR 1.03) IPs for MACE in a model containing RVEF and RV IS | “3-5 d”       | 1150 d   |
| Larose et al[97] | 2010 | 103 | FWHM       | IS strongest IP for MACE (HR 1.36) in model containing LVEF, CK, LGE > 23% had HR 6.1 for MACE | 4.5 h         | 2 yr     |
| Bodi et al[98] | 2009 | 214 | > 2SD      | Extent of transmural infarction (no. of segments > 50% transmurality)         | 7 d           | 553 d    |
| Wu et al[99] | 2008 | 122 | Manual     | IS only IP of 2 yr MACE in model containing LVEF, LVESVI                      | 2 d           | 538 d    |

LGE: Late gadolinium enhancement; FWHM: Full-width half-maximum; SD: Standard deviations; MACE: Major adverse cardiovascular events; LVEF: Left ventricular ejection fraction; PPCI: Primary percutaneous coronary intervention; LGE method (LGE quantification method): SD: Standard deviations; FWHM: Full-width half-maximum.

---

Figure 5  Early and late microvascular obstruction on cardiovascular magnetic resonance. A: Early gadolinium imaging at 1-min post contrast with hypoperfusion in anteroseptal, anterior and anterolateral segments, consistent with early MVO (E-MVO, *); B: Corresponding late gadolinium image showing transmural infarction with a hypointense late MVO core (L-MVO, **) co-localising with E-MVO. MVO: Microvascular obstruction.
is likely that this is because L-MVO reflects more severe microvascular and myocardial damage than E-MVO. In most studies demonstrating the independent predictive value of L-MVO on LV function and remodelling, E-MVO was not a predictor. L-MVO was a predictor independent of baseline IS. Monocyte recruitment, crucial in cellular debris removal and scar formation, is impaired in areas of L-MVO in rat myocardium and may contribute to the adverse remodelling.

Table 8 Temporal changes in cardiovascular magnetic resonance late microvascular obstruction in acute myocardial infarction

| Ref.          | Year | a     | CMR timepoints | LGE method | Main findings                                                                 |
|---------------|------|-------|----------------|------------|--------------------------------------------------------------------------------|
| Carrick et al  | 2016| 30    | 8 h → 3 d → 10 d → 7 mo | Auto       | L-MVO in 20%, peaked early at 8 h and stable at d3. Decreased by d10, absent at 7 mo |
| Mather et al   | 2011| 48    | 2 d → 1 wk → 30 d → 3 mo | > 2SD      | L-MVO in 60%, peak at d2. Decrease at subsequent points. L-MVO absent at 3 mo    |
| Ganame et al   | 2011| 58    | 3 d → 4 mo → 12 mo | Manual     | L-MVO in 64%. L-MVO absent at 4 mo                                             |
| Ripa et al     | 2007| 58    | 2 d → 6 mo | Manual     | L-MVO in 42%. L-MVO absent at 6 mo                                             |
| Hombach et al  | 2005| 110   | 6 d → 9 mo | Manual     | 46% had L-MVO (2.8% LV mass, 16% of IS) on acute CMR. L-MVO absent at 6 mo |

MVO: Microvascular obstruction; LGE method: SD: Standard deviations; IS: Infarct size; LV: Left ventricle; CMR: Cardiovascular magnetic resonance.

Table 9 Cardiovascular magnetic resonance studies illustrating the importance of late microvascular obstruction on left ventricular function and remodelling in acute myocardial infarction

| Ref.          | Year | a     | LGE method | Main findings                                                                 | Time post STEMI of predictive CMR | Follow-up |
|---------------|------|-------|------------|--------------------------------------------------------------------------------|-----------------------------------|----------|
| Kadamby et al  | 2013| 39    | > 2SD      | L-MVO only IP of impaired infarct strain. Model with IS, TIMI flow, diabetes, transmurality | 3 d                               | 3 mo     |
| Wong et al    | 2012| 40    | Manual     | L-MVO extent only IP for LVEF at 3 mo in model including E-MVO, IS and myocardial blood flow on perfusion | 3 d                               | 3 mo     |
| Ezekowitz et al | 2010| 64    | Manual     | L-MVO extent was IP of LVEF in model with IS and NT-proBNP                     | 7 d                               | 4 mo     |
| Weir et al    | 2010| 100   | Manual     | L-MVO extent was IP of LVEF in model with IS and NT-proBNP                     | 4 d                               | 6 mo     |
| Ganame et al  | 2009| 98    | Manual     | L-MVO extent was IP of LVR in model with IS, troponin-1, TTR                  | 2 d                               | 6 mo     |
| Nijveldt et al | 2008| 60    | Manual     | L-MVO presence strongest IP of LVEF change and LVR in model with TTR, IS, LVEF, E-MVO | 5 d                               | 4 mo     |
| Hombach et al | 2005| 110   | Manual     | L-MVO extent IP for LVR in model with baseline IS, infarct transmurality       | 6 d                               | 225 d    |

MVO: Microvascular obstruction; IS: Infarct size; IP: Independent predictor; TTR: Time to revascularisation; LVR: Left ventricular remodelling; LVEF: Left ventricular ejection fraction; LVEDVI: Left-ventricular end diastolic volume index; LVESVI: Left-ventricular end systolic volume index.

**Prognostic importance of CMR MVO in AMI**

An increasing evidence base demonstrates the strong medium-term prognostic value of L-MVO following STEMI, independent of IS and LVEF (Table 10). The 2 studies featuring both L-MVO and E-MVO showed that L-MVO was a stronger prognostic indicator. Regenfus et al demonstrated that L-MVO was the strongest IP of long-term combined MACE at 6 years follow-up in a model including CMR-assessed LVEF and IS (HR 3.9), providing incremental prognostic value over traditional CMR markers of myocardial damage. A meta-analysis (8 studies, n = 1025) demonstrated that L-MVO presence was the strongest independent predictor of medium-term combined MACE (HR 3.7) and cardiovascular death (HR 13.2) at 2 years independent of IS and LV volumes.

The strong adverse prognostic value of L-MVO may be due to its negative effects on LV function, wall thickness and stiffness, and remodelling, and subsequent risk of heart failure and arrhythmias.

**IMH IN AMI**

**Background**

IMH is a reperfusion injury occurring when restored blood flow into damaged capillaries extravasates erythrocytes into myocardium. CMR-derived IMH was first described in reperfused canine myocardium on ex vivo T2-weighted spin-echo (T2w-TSE) imaging with excellent agreement with histology (r = 0.96 for IMH extent). CMR assessment of IMH in AMI

**Paramagnetic haemoglobin breakdown products shorten T2 relaxation times.** IMH is seen as hypointense zones within hyperintense oedematous myocardium on T2w-TSE sequences. It shows good histological correlation in canine myocardium (ex vivo MRI, r = 0.96) and in an human autopsy case series (in vivo MRI, r = 0.97).
T2w-TSE was present in 33% of patients, with maximal extent at 48 h post PPCI and progressively resolution by 3 mo. Carrick et al.[74] recently demonstrated that the incidence and extent of IMH on T2* increased between 8 h and 3 d post PPCI. Its extent was significantly lower at 10 d and was seen in only 13% of patients at 7 mo. The authors also found that MVO was present in all patients with IMH, and its extent peaked earlier at 8 h suggesting that IMH is an ensuing reperfusion injury in regions of MVO.

CMR IMH as a predictor of LV function and remodelling in AMI

There is a small evidence base demonstrating that IMH is a strong univariate predictor of medium-term impaired LV function and remodelling, however multivariate analysis reveals mixed results, with some studies suggesting no incremental predictive value of IMH over MVO and IS (Table 11).

| Ref.          | Year | n     | LGE method | Main findings                                                                 | Time of prognostic CMR post STEMI | Follow-up |
|--------------|------|-------|-------------|-------------------------------------------------------------------------------|----------------------------------|-----------|
| Regenfus et al[117] | 2015 | 249   | Manual      | L-MVO extent strongest IP for MACE in model including IS, LVEF, TIMI pre and post PPCI and no. diseased vessels | 3.7 d                             | 72 mo     |
| Eitel et al[119] | 2014 | 738   | > 5SD       | Largest multicentre study of L-MVO in PPCI. L-MVO > 1.4% LVM and TIMI risk score only IPs of combined MACE. Adding L-MVO to model with clinical predictors, LVEF and IS increased c-statistic | 7 d                               | 6 mo      |
| de Waha et al[120] | 2012 | 438   | Manual      | L-MVO extent IP for combined MACE in model including IS, LV volumes (only other IP was LVEF). L-MVO/IS strongest IP in model including L-MVO extent, LVEF, IS, LV volumes | 3 d                               | 19 mo     |
| de Waha et al[121] | 2010 | 438   | Manual      | Presence and extent of L-MVO were strongest IPs for MACE and mortality in models with IS, LVEF, ST-res, TIMI-flow post PCI. E-MVO was not an IP | 3 d                               | 19 mo     |
| Cochet et al[122] | 2009 | 184   | Manual      | L-MVO strongest IP for MACE, in models including GRACE score, IS, LVEF. L-MVO stronger IP than E-MVO (OR 8.7 vs 2.5) | “3-7 d”                           | 12 mo     |
| Bruder et al[123] | 2008 | 143   | Manual      | Only extent of L-MVO > 0.5% LV mass was IP for MACE; model included IS, LVEF, age, DM, sex | 4.5 d                             | 12 mo     |
| Hombach et al[124] | 2005 | 110   | Manual      | L-MVO IP for MACE (P = 0.04) in model including LV end-diastolic volume and LVEF | 6 d                              | 268 d     |

MVO: Microvascular obstruction; LVEF: Left ventricular ejection fraction; IS: Infarct size; PCI: Percutaneous coronary intervention; MACE: Major adverse cardiovascular events; IP: Independent predictor.

**Figure 6** Intramyocardial haemorrhage on cardiovascular magnetic resonance. A: T2-weighted spin-echo image with hypointensity corresponding with IMH within the hyperintense oedematous region in the inferior wall (red arrow); B: Corresponding LGE image showing co-localisation of IMH and L-MVO (yellow arrow). IMH: Intramyocardial haemorrhage; LGE: Late gadolinium enhancement; MVO: Microvascular obstruction.

IMH occurs exclusively in areas of L-MVO (r$^2$ for co-localisation approximately 0.9) (Figure 6)\textsuperscript{[25,33,125,126]}.

Newer sequences based on direct quantification of T2 and T2*\textsuperscript{[74,126-129]} allow IMH to be quantified without the limitations of T2w-TSE imaging. Initial studies have been promising and shown that these sequences are reproducible and appear more sensitive and accurate than T2w-TSE for IMH detection\textsuperscript{[126,130,131]}. O’Regan et al\textsuperscript{[126]} showed that T2* had 100% sensitivity for IMH detection compared to 90% for T2w-TSE, where the “gold standard” was co-localisation with L-MVO. In canines, T2* in haemorrhagic infarcts closely correlates with iron levels on spectrometry, and T2*-detected IMH co-localises with iron deposition on Perl’s staining\textsuperscript{[122]} and extravasated erythrocytes on Haematoxylin-Eosin staining\textsuperscript{[128]}. In pigs, regions of IMH on T2* imaging showed vessel degeneration and iron deposition\textsuperscript{[8]}.

There is a paucity of data on temporal changes in CMR-detected IMH. Mather et al\textsuperscript{[128]} showed that IMH on T2w-TSE was present in 33% of patients, with maximal extent at 48 h post PPCI and progressively resolution by 3 mo. Carrick et al\textsuperscript{[74]} recently demonstrated that the incidence and extent of IMH on T2* increased between 8 h and 3 d post PPCI. Its extent was significantly lower at 10 d and was seen in only 13% of patients at 7 mo. The authors also found that MVO was present in all patients with IMH, and its extent peaked earlier at 8 h suggesting that IMH is an ensuing reperfusion injury in regions of MVO.
Prognostic importance of CMR IMH in AMI

Multivariate analyses including IMH as a prognostic indicator also show mixed results. Amabile et al. demonstrated that IMH on T2w-TSE at 4 d post STEMI was the strongest independent predictor of MACE at 1-year (HR 2.8) in a model including LVEF, ST-resolution and L-MVO. Husser et al. showed that only LVEF and IMH extent on T2w-TSE independently predicted MACE at 140 wk follow-up in a model containing LV volumes, AAR, IS and L-MVO. However IMH and MVO extent showed strong correlation (r = 0.95) and adding T2w imaging to a model containing LGE and cine imaging did not improve the predictive power for MACE, supporting a strong concordance of IMH and MVO. Eitel et al. demonstrated that IMH presence on T2w-TSE and LVEF < 53% were the only CMR independent predictors of MACE at 6 mo in a model with lone MVO. Carrick et al. recently demonstrated that IMH on T2* mapping was the strongest independent predictor of cardiac death and heart failure hospitalisation at 830 d follow-up. In their multivariate model, L-MVO was not a predictor suggesting that IMH reflects extreme microvascular injury.

Regional water content. T2w-TSE sequences illustrate oedema as hyperintensity and are currently the mainstay of CMR oedema imaging. Most commonly used is the black-blood T2-weighted short-tau inversion-recovery sequence (T2w-STIR). This uses two initial inversion pulses to null moving blood. This is followed by a third inversion pulse, which nulls tissues with short T1 times (fat) to provide high contrast between blood (nulled) and myocardium. T2w imaging of myocardial oedema is well-validated in animal studies assessing myocardial water content on histological assessment and fluorescent microspheres. T2w imaging of myocardial oedema is therefore a strong predictor of cardiac function and remodeling in acute myocardial infarction.

ISCHAEMIC AAR AND MYOCARDIAL SALVAGE IN AMI

Background

Oedema is seen in acute cardiac inflammation. In STEMI, it signifies reversible myocardial injury in the ischaemic cascade. The area of oedematous myocardium defines the ischaemic AAR supplied by the occluded IRA.

CMR assessment of AAR and MSI in AMI

The T2 (transverse) relaxation time is increased by regional water content. T2w-TSE sequences illustrate oedema as hyperintensity and are currently the mainstay of CMR oedema imaging. Most commonly used is the black-blood T2-weighted short-tau inversion-recovery sequence (T2w-STIR). This uses two initial inversion pulses to null moving blood. This is followed by a third inversion pulse, which nulls tissues with short T1 times (fat) to provide high contrast between blood (nulled) and myocardium. T2w imaging of myocardial oedema is therefore a strong predictor of cardiac function and remodeling in acute myocardial infarction.

Regional water content. T2w-TSE sequences illustrate oedema as hyperintensity and are currently the mainstay of CMR oedema imaging. Most commonly used is the black-blood T2-weighted short-tau inversion-recovery sequence (T2w-STIR). This uses two initial inversion pulses to null moving blood. This is followed by a third inversion pulse, which nulls tissues with short T1 times (fat) to provide high contrast between blood (nulled) and myocardium. T2w imaging of myocardial oedema is therefore a strong predictor of cardiac function and remodeling in acute myocardial infarction.

However T2w-TSE imaging has inherent disadvantages that can compromise image quality and oedema detection. Upto 30% of datasets are non-analysable in studies. New T2w sequences have been studied, with encouraging results (Figure 7).

The aim of prompt reperfusion is to limit IS by minimizing the conversion of reversibly injured myocardial cells (AAR) into necrotic, infarcted tissue (IS). Anterior STEMI typically results in larger IS due to the larger coronary bed supplied by the left anterior descending artery. Hence a more accurate assessment of revascularisation strategies can be provided by adjusting IS for the AAR. The resulting myocardial salvage index (MSI) defines the proportion of reversibly injured tissue (AAR) that does not progress to infarction (IS, Equation 1, Figure 8). MSI is expressed as percentage of the initial AAR (0% is no salvage, 100% is complete salvage (aborted

References

Table 1: Cardiovascular magnetic resonance studies illustrating the importance of intramyocardial haemorrhage on left ventricular function and remodelling in acute myocardial infarction

| Ref. | Year | n | IMH CMR method | Main findings | CMR time post MI | Mean/median F/U CMR |
|------|------|---|---------------|--------------|------------------|---------------------|
| Carrick et al. | 2016 | 245 | T2* | IMH strongest IP for LVR. IMH associated with lower LVEF and greater volumes | 3 d | 7 mo |
| Kidambi et al. | 2013 | 39 | T2w-TSE and T2* | IMH associated with attenuation of follow-up infarct strain | 3 d | 3 mo |
| Husser et al. | 2012 | 304 | T2w-TSE | IMH strongest IP for LVR in model with LVEF, IS, LV vol, L-MVO | 6 d | 189 d |
| Mather et al. | 2011 | 48 | T2w-TSE and T2* | IMH was a univariate predictor of LVEF. | 2 d | 3 mo |
| Beek et al. | 2010 | 45 | T2w-TSE | IMH was an independent predictor of LV MEP. | 5 d | 4 mo |
| Bekkers et al. | 2010 | 90 | T2w-TSE | Acute MSI and LVEF increase at follow-up lowest if IMH present. But IMH no prognostic significance beyond baseline LVEF and MVO in predicting final LVEF | 5 d | 103 d |
| O’Regan et al. | 2010 | 50 | T2* | IMH presence univariate predictor of LVEF and LV volumes. However only IS independently predicted LVEF | 3 d | N/A |
| Garana et al. | 2009 | 98 | T2w-TSE | IMH extent strongest IP of LVR in model with IS, E-MVO, Troponin-I, AAR, TTR, IS | 2 d | 4 mo |
Disadvantages of T2w TSE for oedema assessment
- Relatively long breath-hold
- Artefacts from poor breath-holding and arrhythmias
- Low contrast to noise ratio as relatively small changes in T2 with oedema (CNR 2.9 STIR AAR vs CNR 19 LGE IS)
- "Slow-flow" artefact with potential for false positives in areas of hypokinesia
- Signal inhomogeneities from phased-array coils
- Signal loss at inferolateral wall due to cardiac motion and unwanted nulling of myocardium (false negative)

Alternative sequences studied in small series
1. Non-contrast T1w as oedema increases T1 too (distinguishes acute from chronic MI well)
2. Bright blood TSE (double inversion; less motion artefact than STIR, better accuracy); recently single-shot version of sequence showed higher CNR, intra-observer agreement and accuracy (AUC 0.86) than STIR for AAR
3. SSFP (good image quality, correlates with STIR, short scan as SSFP used for AAR and LV function)
4. Hybrid of SSFP/TSE ("ACUT2E": Better CNR than STIR; high CNR of SSFP and oedema-specific T2w)
5. T2 quantification and production of T2 maps (as higher T2 in oedema; accurately defined oedema; faster acquisition than STIR; more robust, with on effect of slow-flow, through-plane motion or coil related SI differences); higher intraobserver agreement
6. Endocardial surface length of infarction (ESL): Proposes that endocardial circumferential length of infarct occurs early and correlates with AAR as infarct extends transmurally (surrogate for AAR); underestimates AAR compared with STIR
7. DWI: DWI is T2w and sensitive to water content. Was not possible to non-contrast T1w as oedema increases T1 too (distinguishes acute from chronic MI well)

Figure 7 Alternative sequences to dark-blood T2-weighted turbo spin-echo for visualising oedema. Left: Inherent disadvantages of T2w-TSE[5,154-157]. Right: Sequences compared with T2w-TSE: (1) Non-contrast T1w; (2) Bright blood TSE; (3) SSFP; (4) Hybrid of SSFP/TSE; (5) T2 quantification; (6) Endocardial surface length of infarction; (7) DWI: DWI is T2w and sensitive to water content. Was not possible to differentiate oedema from cleared cellular debris. Studies of temporal changes in AAR and MSI in humans are summarised in Table 12. Correct timing of oedema imaging is crucial in accurate calculation of AAR and MSI.

The near-resolution of oedema by 6 mo[5,18,21,91,138] allows distinction between acute and chronic infarcts when combined with LGE imaging.

STEMI[157].

Equation 1: Myocardial salvage index (MSI, %) = 100 × [(AAR-IS)/(AAR)].

Desch showed excellent intraobserver and interobserver agreement for MSI assessment using T2w-STIR and LGE (coefficients of variation approximately 5.0%) and excellent test-retest reproducibility in a study of 20 acute STEMI patients[158].

Other determinants of AAR include TTR[91,130,159-162], extent of collateralised IRA territory flow[158,159,163], TIMI-flow pre PCI, LAD IRA and diabetes[91].

Studies of the chronology of oedema suggest that it occurs very early in the ischaemic cascade. Abdel-Aty confirmed the presence of transmural oedema in canines on in-vivo T2w imaging at 28 min post LAD occlusion at which point LGE and troponin release were absent, indicating reversible injury[164]. Fernández-Jiménez et al[165] however recently demonstrated a bimodal pattern of AAR extent in pigs with T2-mapping CMR and histological water quantification. They showed peak values at 2 h thought to be a direct result of reperfusion, followed by a return to baseline at 2 d and then progressive increase towards peak values at 7 d, with the latter peak felt due to water replacement of cleared cellular debris. Studies of temporal changes in AAR and MSI in humans are summarised in Table 12. Correct timing of oedema imaging is crucial in accurate calculation of AAR and MSI.

The near-resolution of oedema by 6 mo[5,18,21,91,138] allows distinction between acute and chronic infarcts when combined with LGE imaging.

CMR MSI as a predictor of LV function and remodelling in AMI
Myocardial salvage is a strong univariate predictor of medium-term LV function[14,166,167] and adverse LV remodelling post STEMI[14,27,91,161]. Multivariate analysis demonstrates mixed results. MSI independently predicted LV remodelling in the work of Mather[131] (Table 13), However MSI was not a predictor once IS was added into multivariate models in studies by Monmeneu[91] and Masci[14]. This, in conjunction with the correlation between MSI and IS, and AAR and IS[26] questions whether MSI and IS are truly independent of each other in predicting LV remodelling and prognosis post STEMI. It could be argued that since MSI adjusts IS for the extent of AAR, it may have less inherent variability than IS. Since up to 30% of AAR datasets have been deemed non-diagnostic in previous studies[24,143,144], this may impact on the robustness of MSI quantification whereas IS datasets are exceptionally rarely excluded based on image quality. It is not clear currently whether IS or MSI is the better measure of revascularisation success post PPCI.

Prognostic importance of CMR MSI in AMI
Historically, the prognostic value of MSI was demonstrated using SPECT. Ndrepapa first showed that MSI was the strongest independent predictor of 6-mo mortality[168]. MSI was an independent prognostic indicator in the medium term post STEMI in two studies. Although both studies were from the same patient cohort, they have both been
quences. This can lead to subjectivity and dependence upon optimal nulling of normal myocardium and thus potential for error. In addition, commonly used T2w-TSE sequences suffer from non-diagnostic image quality in up to 30% of patients \[24,143,144\].

T1, T2 and T2* quantification present an exciting and complementary approach to LGE and T2w imaging. Developed by Messroghli et al. \[169\] in 2003, their use in MI research has accelerated over the last 5 years. They allow not only the location and extent of infarction, oedema, MVO and IMH to be determined from subsequent parametric myocardial maps, but also the severity of these pathologies to be assessed through the magnitude included in Table 14 due to their differing primary findings.

### Table 12 Temporal changes in cardiovascular magnetic resonance-derived area at risk and myocardial salvage index in acute myocardial infarction

| Ref.                  | Year | n  | CMR timepoints post STEMI | AAR, IS method | Main findings                                                                 |
|-----------------------|------|----|--------------------------|----------------|-----------------------------------------------------------------------------|
| Mather et al. \[18\]  | 2011 | 48 | > 2SD STIR, > 2SD LGE    | AAR reduction at successive timepoints, 1-3 mo (-75%). No change MSI at d2 or 1 wk as IS and AAR decreased proportionally |
| Dall’Armelina et al. \[21\] | 2011 | 30 | > 2SD T2p-BB, > 2SD LGE  | AAR at all timepoints. AAR stable in 1st week, correlated with 1 wk SPECT. Decrease by 1 mo (10% LVM), nearly gone by 6 mo |
| Carlson et al. \[138\] | 2009 | 16 | Manual STIR, and LGE     | AAR at all timepoints. AAR stable in 1st week, correlated with 1 wk SPECT. Decrease by 1 mo (10% LVM), nearly gone by 6 mo |
| Ripa et al. \[5\]    | 2007 | 58 | Manual STIR, and LGE     | AAR at all timepoints. AAR stable in 1st week, correlated with 1 wk SPECT. Decrease by 1 mo (10% LVM), nearly gone by 6 mo |

AAR: Area at risk; MSI: Myocardial salvage index; AAR, LGE method: SD: Standard deviations; STIR: T2-weighted short-tau inversion recovery imaging; T2p-SS-BB: T2-prepared single-shot bright-blood; 3T: 3.0 tesla field strength; IS: Infarct size.

T1, T2 AND T2* QUANTIFICATION AND MAPPING IN AMI

The current mainstay of LGE and T2w techniques for the detection of infarct and oedema rely on semi-quantitative threshold-based quantification methods using arbitrary SI cut-offs compared to user-defined regions of interest, automated algorithms or are based on manual planimetry. There is currently no consensus on the optimal quantification method for IS or AAR using these sequences. This can lead to subjectivity and dependence upon optimal nulling of normal myocardium and thus potential for error. In addition, commonly used T2w-TSE sequences suffer from non-diagnostic image quality in up to 30% of patients \[24,143,144\].
of values obtained\textsuperscript{170,171}. These methods are not reliant on reference regions of interest and do not suffer from T2w-TSE artefacts.

**T1 mapping (longitudinal relaxation)**

T1 relaxation curves allow calculation of the T1 time (time taken for recovery of 63% of longitudinal magnetization). The currently used curve-fitting sequences used include MOLLI (Modified Look-Locker Inversion Recovery), SHMOLLI (Shortened MOLLI), SASHA (SAturation recovery single-Shot Acquisition) and SAPPHIRE (SAturation Pulse Prepared Heart rate independent Inversion REcover). Messroghli showed that this technique had high test-retest reproducibility\textsuperscript{175}, was stable within the range of heart rates commonly seen in clinical practice and showed comparable sensitivity for IS quantification compared with LGE\textsuperscript{169,170,173,174}. Infarcted and oedematous myocardium demonstrate prolonged pre-contrast T1 values and reduced post-contrast T1 values compared with normal myocardium, allowing infarct visualisation and quantification\textsuperscript{169,170,173,174}. Messroghli showed that this technique had high test-retest reproducibility\textsuperscript{175}, was stable within the range of heart rates commonly seen in clinical practice and showed comparable sensitivity for IS quantification compared with LGE\textsuperscript{169,170,173,174}. T1 values within in the infarct core were recently shown to demonstrate a strong inverse correlation with L-MVO extent, incidence of LV remodelling and all-cause mortality at 2.5 years\textsuperscript{177}.

**T2 mapping (transverse relaxation)**

T2w images are generated using a T2-SSFP sequence with log-transformed curve-fitting T2 quantification, with different T2 preparation (TE) times. T2 mapping has shown excellent reproducibility and no effect of slow-flow, through-plane movement, SI loss, or effects of coil SI inhomogeneities\textsuperscript{151,178}. T2 mapping accurately assessed oedema in 96% of patients (good image quality in 100%), whereas T2w-STIR detected oedema in only 67% of patients (15% non-diagnostic 15%)\textsuperscript{151}. High observer agreement and close agreement between T1 ($r = 0.94$) and T2 maps ($r = 0.96$), and fluorescent microspheres for AAR detection was seen in canine myocardium\textsuperscript{179}.

**T2* mapping (transverse relaxation in presence of field inhomogeneities)**

T2* mapping allows visualisation and quantification of IMH due to the presence of paramagnetic haemoglobin breakdown products. A cut-off value of < 20 ms has been used to define the presence of IMH\textsuperscript{180}. Although the evidence base for T2* mapping in assessing IMH is currently limited, O'Regan demonstrated that it has greater sensitivity than T2w-STIR imaging (100% vs 90%) for IMH. Kali showed good correlation between in-vivo T2* and histological assessment of IMH and iron levels in canine myocardium\textsuperscript{127,128}. T2* mapping may improve the specificity of IMH detected on CMR\textsuperscript{151}.

T1, T2 and T2* surrogate markers hold promise for improving the accuracy of detection of infarct, oedema and IMH respectively, and further improving statistical power of STEMI studies. However, due to the importance

---

**Table 13** Cardiovascular magnetic resonance studies showing the importance of myocardial salvage index on left ventricular function and remodelling in acute myocardial infarction

| Ref. | Year | n | AAR, IS method | Main findings | CMR timepoint post STEMI | Follow-up |
|------|------|---|----------------|---------------|--------------------------|-----------|
| Mather et al\textsuperscript{169} | 2011 | 48 | > 2SD STIR, > 2SD LGE | MSI was IP for LVR (OR 0.95) in model including LV volumes, LVEF, IS, IMH, MVO | 2 d | 3 mo |
| Mornmeneu et al\textsuperscript{169} | 2012 | 118 | > 2SD STIR, > 2SD LGE | MSI univariate predictor of LVR and final LVEF. However not IP of LVR in model with LYESV, IS, no. transmural segs | 6 d | 6 mo |
| Masci et al\textsuperscript{169} | 2011 | 260 | > 2SD STIR, > 5SD LGE | MSI strong univariate predictor of LVR and final LVEF. However not IP in model including IS, MVO | 1 wk | 4 mo |
| Masci et al\textsuperscript{169} | 2010 | 137 | > 2SD STIR, > 5SD LGE | MSI strongest IP for LVR. However IS and MSI ($r = -0.72$) and IS and AAR ($r = 0.85$) correlated | 1 wk | 4 mo |

IS: Infarct size; IP: Independent predictor; LVR: Left ventricular remodelling; MVO: Microvascular obstruction; LVEF: Left ventricular ejection fraction; LYESV: Left-ventricular end systolic volume index; STIR: T2-weighted short-tau inversion-recovery; LGE: Late gadolinium enhancement.

**Table 14** Cardiovascular magnetic resonance studies illustrating the prognostic importance of myocardial salvage index in acute myocardial infarction

| Ref. | Year | n | AAR, IS method | Main findings | CMR timepoint post STEMI | Follow-up |
|------|------|---|----------------|---------------|--------------------------|-----------|
| Eitel et al\textsuperscript{34} | 2011 | 208 | > 2SD STIR, > 5SD LGE | MSI was only CMR-based IP of mortality in model with age, IS, MVO, LVEF, TIMI-post PCI, diabetes, age (IS not IP). MSI not IP of MACE (only IS, LVEF, age were) | 3 d | 19 mo |
| Eitel et al\textsuperscript{34} | 2010 | 208 | > 2SD STIR, > 5SD LGE | MSI was only IP for MACE and mortality in model including LVEF, MVO, IS, ST-resolution and TIMI-grade post PCI | 3 d | 6 mo |

IS: Infarct size; PCI: Percutaneous coronary intervention; MACE: Major adverse cardiovascular events; IP: Independent predictor; MVO: Microvascular obstruction; LVEF: Left ventricular ejection fraction.
of protocol standardisation, these techniques are rarely used in multicentre studies at present.

**RIGHT VENTRICULAR INVOLVEMENT IN AMI**

**CMR assessment of right ventricular infarction in AMI**

CMR is the gold standard imaging modality for the assessment of right ventricular (RV) volumes, function, oedema and infarction (RVI) [182]. CMR identifies RVI with greater sensitivity than echocardiography, ECG (V4s ST-segment elevation) and clinical examination [183,184] and demonstrates RV L-MVO [185,186]. There is good interobserver and intraobserver agreement for the identification of RV oedema ($\kappa = 0.62$, $\kappa = 0.62$, respectively) and very good agreement for RVI ($\kappa = 0.70$, $\kappa = 0.70$, respectively) [181].

The high MSI in RVI often > 90% [187,188] is thought to be due to the relatively low RV nutrient needs, direct endocardial oxygen diffusion and good collateral blood supply [188,189].

**Prognostic importance of CMR-derived right ventricular infarction in AMI**

RVI confers adverse short-term prognosis, with a large meta-analysis ($n = 7136$) demonstrating that RVI on CMR assessment of outcomes in AMI [187,188]. Shah demonstrated the prognostic importance of right ventricular infarction on imaging, where RVEF < 38% predicted 30-d mortality and in-hospital MACE [190]. Right ventricular infarction is a strong independent predictor of 1-year mortality [191].

### Table 15 Cardiovascular magnetic resonance studies illustrating the prognostic importance of right ventricular infarction in acute myocardial infarction

| Ref. | Year | n  | RV LGE analysis method | Main findings | CMR timepoint post STEMI | Follow-up |
|------|------|----|------------------------|---------------|--------------------------|----------|
| Jensen et al [96] | 2010 | 50 | Manual | RVI only IP of MACE in model with age, sex, LVEF, LV IS | 3 d | 32 mo |
| Miszalski-Jamka et al [96] | 2010 | 99 | Manual | RVEF (HR 1.46) and RVI extent (HR 1.50) IP for MACE | “3-5 d” | 1150 d |
| Grothoff et al [95] | 2012 | 450 | Manual | RVI was IP of MACE (HR 6.70) | “1-4 d” | 20 mo |

MACE: Major adverse cardiovascular events; IP: Independent predictor; HR: Hazard ratio; RV: Right ventricle; LVEF: Left ventricular ejection fraction; LGE: Late gadolinium enhancement; IS: Infarct size; RVI: Right ventricular infarction.

### Table 16 Key studies illustrating the independent predictive value of cardiovascular magnetic resonance markers for left ventricular remodelling

| CMR marker | Ref. | Year | n  | CMR quantification | Main findings | Acute CMR time | Follow-up CMR time |
|------------|------|------|----|--------------------|---------------|----------------|-------------------|
| IS         | Husser et al [100] | 2016 | 26 | 2SD                | IS extent IP for LVR in model with LVEF, LV volumes, MVO | 6 d | 189 d |
| IS         | Memonneu et al [102] | 2012 | 118 | Manual            | RVI extent IP of MACE in model with age, sex, LVEF, LV IS | 3 d | 7 mo |
| IS         | Wu et al [104] | 2008 | 122 | Manual            | IS extent IP of LVR in model with age, sex, LVEF, LV IS | 2 d | 4 mo |
| IS         | Hombach et al [94] | 2005 | 110 | Manual            | IS extent IP of LVR in model with age, sex, LVEF, LV IS | 6 d | 225 d |
| L-MVO      | Wit et al [106] | 2010 | 100 | Manual            | RVI extent of LVR in model with TIMI post PCI, E-MVO, IS | 4 d | 6 mo |
| L-MVO      | Hombach et al [94] | 2005 | 110 | Manual            | L-MVO extent IP of LVR in model with baseline IS, infarct transmurality | 6 d | 225 d |
| IMH        | Carrick et al [107] | 2016 | 245 | T2*               | IMH strongest IP of LVR in model with patient/angio characteristics, LVEDVI | 6 d | 189 d |
| IMH        | Husser et al [100] | 2010 | 304 | T2w-TSE           | IMH strongest IP of LVR in model with LVEF, IS, LV volumes, L-MVO | 6 d | 6 mo |
| MSI        | Memonneu et al [102] | 2012 | 118 | Manual            | MSI univariate but not IP of LVR in model with baseline IS, LVEF, LV ESI, segments > 50% | 6 d | 6 mo |
| MSI        | Masci et al [104] | 2011 | 260 | 2SD LCR/STIR      | MSI univariate predictor of LVR and final LVEF. However not IP of either | 1 wk | 4 mo |
| MSI        | Masci et al [104] | 2010 | 137 | > 5SD LGE         | MSI strongest IP for LVEF. However IS, MSi and IS and AAR correlated | 1 wk | 4 mo |
| T1         | Carrick et al [107] | 2016 | 300 | T1 map, 2SD STIR, 5SD LGE | Infarct core native T1 inverse relationship with LVR (OR 0.91 per 10 ms T1) | 2 d | 6 mo |

Criteria: Individual studies with $n \geq 100$ and follow-up CMR $\geq 3$ mo post-PPCI. IS: Infarct size; L-MVO: Late microvascular obstruction; IMH: Intramyocardial haemorrhage; MSI: Myocardial salvage index; SD: Standard deviations; STIR: T2-weighted short-tau inversion recovery; LGE: Late gadolinium enhancement; IP: Independent predictor; LV: Left ventricular; LVEF: Left ventricular ejection fraction; AAR: Area at risk; LVEDVI: Left ventricular end-diastolic volume; CMR: Cardiovascular magnetic resonance.
Table 17  Key studies illustrating the independent predictive value of cardiovascular magnetic resonance markers for prognosis

| CMR marker | Ref. | Year | n | CMR quantification | Main findings | Acute CMR time | Follow-up |
|------------|------|------|---|--------------------|---------------|----------------|------------|
| IS         | Husser et al[9] | 2013 | 250 | > 2SD | Extent of transmural infarction was only IP for MACE | 7 d | 163 wk |
| IS         | Lequierdo et al[10] | 2014 | 440 | > 2SD | IS was IP for arrhythmic cardiac events in model including LVEF, hypertension | 7 d | 123 wk |
| IS         | Eitel et al[11] | 2011 | 206 | > 5SD | IS was IP of MACE in model with MVO, LVEF, MI, Killip, TIMI flow post-PPCI | 3 d | 18.5 mo |
| IS         | Larose et al[12] | 2010 | 106 | FWHM | L-MVO strongest IP for MACE in model with LVEF, CK, LGE > 23% for MACE | 4.5 h | 2 yr |
| IS         | Bodi et al[13] | 2009 | 214 | > 2SD | Extent of transmural infarction (no. of segments > 50% transmurality) IP for MACE | 7 d | 533 d |
| IS         | Wu et al[14] | 2008 | 122 | Manual | IS only IP of 2 yr MACE in model containing LVEF, LVESVI (HR 1.06) | 2 d | 538 d |
| L-MVO      | Rengerfus et al[15] | 2015 | 249 | Manual | MVO extent strongest IP for MACE in model with IS, LVEF, TIMI and no. vessels | 3.7 d | 72 mo |
| L-MVO      | Eitel et al[16] | 2014 | 738 | > 5SD | L-MVO > 1.4% LVM IP of MACE in model with LVEDVI, LVEF, clinical markers | 7 d | 6 mo |
| L-MVO      | de Waha et al[17] | 2012 | 438 | Manual | L-MVO extent IP for MACE in model with IS, LV volumes. L-MVO/IS strongest IP | 3 d | 19 mo |
| L-MVO      | de Waha et al[18] | 2010 | 438 | Manual | L-MVO strongest IP of MACE/mortality in model with IS, LVEF, STR, TIMI post | 3 d | 19 mo |
| L-MVO      | Cochet et al[19] | 2009 | 184 | Manual | L-MVO strongest IP for MACE in model with GRACE, IS, LVEF. "3-7 d" | 3 d | 12 mo |
| L-MVO      | Brader et al[20] | 2008 | 413 | Manual | L-MVO extent > 0.5% LV mass IP for MACE in model with IS, LVEF, age, DM, sex | 4.5 d | 12 mo |
| L-MVO      | Hombach et al[21] | 2005 | 110 | Manual | L-MVO IP for MACE (P = 0.04) in model with LV end-diastolic volume and LVEF | 6 d | 268 d |
| IMH        | Carrick et al[22] | 2016 | 245 | T2* | IMH strongest IP of CV death and HF. Multivariate model, L-MVO not predictor | 3 d | 830 d |
| IMH        | Amabile et al[23] | 2012 | 114 | T2w-TSE | IMH presence was strongest predictor of MACE in model with MVO, LVEF, STR | 4 d | 12 mo |
| IMH        | Husser et al[24] | 2012 | 304 | T2w-TSE | IMH IP for MACE in model with AAR, IS, L-MVO. T2w: No inc. value with LGE | 6 d | 140 wk |
| IMH        | Eitel et al[25] | 2011 | 346 | T2w-TSE | IMH IP of MACE in model with L-MVO. T2w inc. value with LGE | 3 d | 6 mo |
| MSI        | Eitel et al[26] | 2011 | 208 | > 2SD/> 5SD | MSI only CMR IP of mortality in model with age, IS, MVO, LVEF, TIMI post, IS | 3 d | 19 mo |
| MSI        | Eitel et al[27] | 2010 | 208 | > 2SD/> 5SD | MSI only IP for MACE/mortality in model with LVEF, MVO, IS, STR, TIMI post | 3 d | 6 mo |
| TI         | Carrick et al[28] | 2016 | 300 | T1 map, > 2SD | Infarct core T1 inverse association with risk of mortality and heart failure hospitalisation, in model with LVEF, infarct T2, IMH. Similar prognostic as L-MVO | 2 d | 2.5 yr |

Criteria: Individual studies with n ≥ 100 and follow-up CMR ≥ 6 mo follow-up. IS: Infarct size; L-MVO: Late microvascular obstruction; IMH: Intramyocardial haemorrhage; MSI: Myocardial salvage index; SD: Standard deviations; TIMI: T2-weighted short-tau inversion recovery; LGE: Late gadolinium enhancement; IP: Independent predictor; LV: Left ventricular; LVEF: Left ventricular ejection fraction; AAR: Area at risk; LVEDVI: Left ventricular end-diastolic volume; CK: Creatine kinase; T2w-TSE: T2-weighted turbo spin echo; MACE: Major adverse cardiovascular events; CV: Cardiovascular.

WHEN IS THE OPTIMAL TIME TO PERFORM CMR ASSESSMENT IN MI?

In acute STEMI, IS, AAR and MSI are best imaged at 7 d post PPCI due to overestimation of necrosis on LGE, and IS at 7 d best predicts final IS, LV remodelling and function and prognosis[5-7,18,20,21]. Human studies suggest that AAR is stable during the first week and function and prognosis[22,138]. Although Fernández-Jiménez et al[143] demonstrated a bimodal AAR peak in pigs, their drop in AAR extent on T2w CMR at 2 d post-reperfusion may be due to a high incidence of IMH in pigs and peak IMH extent at 2 d[74].

Indeed the drop in AAR extent on the gold standard of histological water analysis in their study at 2 d was much less pronounced, and at 7 d AAR extent had returned to stable peak levels. In addition, studies demonstrating close agreement between T2w-derived AAR and the reference non-invasive modality of SPECT[138,139] were undertaken at 7 d post STEMI. MVO and IMH extent peak at 48 h then decrease[140] but are present at 7 d[9,18]. Although undertaking CMR at 7 d may potentially underestimate MVO and IMH extent[9,18,74], this may be minimised by expressing MVO and IMH extent as a proportion of IS rather than LV mass, to correct for the corresponding reduction in IS. Thus, acutely post STEMI for the assessment of IS, MSI, MVO and IMH, imaging at 7 d may provide the best compromise in relation to their
temporal changes\textsuperscript{[5-7,9,18,20,21]} for accurate quantification and prediction of LV function, remodelling and prognosis. This needs to be balanced with contemporary clinical practice where patients are typically discharged at 3–4 d post-PPCI, and the risk of early attrition. Using final IS at follow-up as a primary outcome risks underestimating potential differences in treatment strategies due to greater infarct resorption with the larger infarcts.

Data on the chronology of IS suggests that infarct resorption is essentially complete by 3 mo post-MI\textsuperscript{[9,18,20,24]} However a key objective of follow-up CMR is to assess LV geometry and remodelling and hence must allow the relatively slower adaptations of ventricular volumes (approximately 12 mo), compared with changes in IS and LVEF to complete. LVEF shows no significant change after 1-mo post STEMI. Follow-up CMR at 3 and 6-mo may fail to provide an accurate assessment of LV volumes and remodelling. The evidence base suggests that in order to allow completion of the trio of IS, LVEF and LV volumetric changes, follow-up CMR should be performed at 12-mo post STEMI\textsuperscript{[5,7,18,20,21]} When correlating CMR and clinical outcomes, the longer timepoint of 12-mo also permits more reliable clinical follow-up.

Standardisation of LGE, AAR and IMH sequences and quantification methods is equally important in light of newer T1, T2, and T2*–mapping sequences and inherent image quality issues associated with T2w-TSE.

CONCLUSION

Contrast-enhanced CMR offers robust, validated and reproducible surrogate markers, providing an accurate representation of pathophysiology, assessment of myocardial function and injury, and predictive value for medium to long-term LV function, remodelling and prognosis following PPCI for STEMI. Tables 16 and 17 summarise the key prospective studies investigating the independent predictive value of CMR markers for LV remodelling (studies where \( n > 100 \), follow-up CMR \( \geq 3 \) mo post PPCI) and prognosis (studies where \( n > 100 \), \( \geq 6 \) mo follow-up) respectively.

In the acute phase, CMR can be performed accurately for up to 7 d post PPCI. CMR delivers no radiation to the patient and this makes it ideal for serial studies. The multimodal nature of CMR allows a multiparametric study of cardiac function, structure and volumes within a single study, which can be undertaken within approximately 45 min in the majority of patients. It is likely that CMR will become the mainstay of cardiac imaging, providing an important role in risk stratification and treatment post STEMI. Focus needs to be continued in translating findings on the prognostic importance of surrogate markers to development of therapeutic targets post STEMI.

REFERENCES

1. Group BDW. Biomarkers and surrogate endpoints: preferred definitions and conceptual framework. Clin Pharmacol Ther 2001; 69: 89-95 [PMID: 11240971 DOI: 10.1067/mcp.2001.113989]
2. Desch S, Eitel I, de Waaij S, Fuernau G, Lutz P, Gutterlet M, Schuler G, Thiele H. Cardiac magnetic resonance imaging parameters as surrogate endpoints in clinical trials of acute myocardial infarction. Trials 2011; 12: 204 [PMID: 21917147 DOI: 10.1186/1745-6215-12-204]
3. Pitcher A, Ashby D, Elliot P, Petersen SE. Cardiovascular MRI in clinical trials: expanded applications through novel surrogate endpoints. Heart 2011; 97: 1286-1292 [PMID: 21715443 DOI: 10.1136/hrt.2011.225904]
4. Austin PC. An Introduction to Propensity Score Methods for Reducing the Effects of Confounding in Observational Studies. Multivariate Behav Res 2011; 46: 399-424 [PMID: 21818162 DOI: 10.1080/00273171.2011.568786]
5. Ripa RS, Nilsson JC, Wang Y, Sondergaard L, Jørgensen E, Kastrup J. Short- and long-term changes in myocardial function, morphology, edema, and infarct mass after ST-segment elevation myocardial infarction evaluated by serial magnetic resonance imaging. Am Heart J 2007; 154: 929-936 [PMID: 17967600 DOI: 10.1016/j.ahj.2007.06.038]
6. Hombauch V, Grebe O, Merkle N, Waldenmaier S, Höher M, Kochs M, Wöhre J, Kestler HA. Sequelae of acute myocardial infarction regarding cardiac structure and function and their prognostic significance as assessed by magnetic resonance imaging. Eur Heart J 2005; 26: 549-557 [PMID: 15713695 DOI: 10.1093/eurheartj/ehi147]
7. Engblom H, Hedström E, Heiberg E, Wagner GS, Pahlm O, Århened H. Rapid initial reduction of hyoperenhenled myocardium after reperfusion first myocardial infaraction suggests recovery of the peri-infarction zone: one-year follow-up by MRI. Circ Cardiovasc Imaging 2009; 2: 47-55 [PMID: 19808564 DOI: 10.1161/circimaging.108.802199]
8. Ghugre NR, Ramanan V, Pop M, Yang Y, Barry J, Qiang B, Connelly KA, Dick AJ, Wright GA. Quantitative tracking of edema, hemorrhage, and microvascular obstruction in subacute myocardial infarction in a porcine model by MRI. Magn Reson Med 2011; 66: 1129-1141 [PMID: 21373425 DOI: 10.1002/mrm.22855]
9. Ibrahim T, Hackl T, Nekolla SG, Broxer M, Feldmair M, Schöning A, Schweigier M. Acute myocardial infarction: serial cardiac MR imaging shows a decrease in delayed enhancement of the myocardium during the 1st week after reperfusion. Radiology 2010; 254: 88-97 [PMID: 20032144 DOI: 10.1148/radiol.2009090680]
10. Lund GK, Stork A, Mullerleile K, Barmeyer AA, Bansmann MP, Kniefel M, Schlichting U, Müller M, Verde PE, Adam G, Meinertz T, Saeed M. Prediction of left ventricular remodeling and analysis of infarct resolution in patients with reperfused myocardial infarction by using contrast-enhanced MR imaging. Radiology 2007; 245: 95-102 [PMID: 17885184 DOI: 10.1148/radiol.2451061219]
11. Pfeffer MA, Braunwald E. Ventricular remodeling after myocardial infarction. Experimental observations and clinical implications. Circulation 1990; 81: 1161-1172 [PMID: 21382529 DOI: 10.1161/01.CIR.81.4.1161]
12. Bolognesi L, Neskovic AN, Parodi G, Cerisano G, Buonamici P, Santoro GM, Antonucci D. Left ventricular remodeling after primary coronary angioplasty: patterns of left ventricular dilation and long-term prognostic implications. Circulation 2002; 106: 2351-2357 [PMID: 12403666 DOI: 10.1161/01.CIR.0000036014.90197.FA]
13. Ahn KT, Song YB, Choe YH, Yang JH, Hahn JY, Choi JH, Choi SH, Chang SA, Lee SC, Lee SH, Oh JK, Gwon HC. Impact of transmural necrosis on left ventricular remodeling and clinical outcomes in patients undergoing primary percutaneous coronary intervention for ST-segment elevation myocardial infarction. Int J Cardiovasc Imaging 2013; 29: 835-842 [PMID: 23179749 DOI: 10.1007/s10554-012-0155-9]
14. Masci PG, Ganame J, Francone M, Desmet W, Lorenzoni V, Iacucci I, Barison A, Carboni L, Lombardi M, Agati L, Janssens S, Bogaert J. Relationship between location and size of myocardial infarction and their reciprocal influences on post-infarction left ventricular remodelling. Eur Heart J 2011; 32: 1640-1648 [PMID: 21398642 DOI: 10.1093/eurheartj/eho646]
15. Wagner A, Mahrholdt H, Holly TA, Elliott MD, Regensfus M, Parker...
Bellenger NG, Grothues F, Smith GC, Pennell DJ. Quantification of right and left ventricular function by cardiovascular magnetic resonance. Herz 2000; 25: 392-399 [PMID: 10948775 DOI: 10.1007/s005950050031]

Cerequeira MD, Weissman NJ, Dilisizian V, Jacobs AK, Kaul S, Laskey WK, Pennell DJ, Rumbarger JA, Ryan T, Verani MS. Standardized myocardial segmentation and nomenclature for tomographic imaging of the heart. A statement for healthcare professionals from the Cardiac Imaging Committee of the Council on Clinical Cardiology of the American Heart Association. Circulation 2002; 105: 539-542 [PMID: 11815441 DOI: 10.1161/hc0402.102975]

Mather AN, Fairbairn TA, Artis NJ, Greenwood JP, Plein S. Timing of cardiovascular MR imaging after acute myocardial infarction: effect on estimates of infarct characteristics and prediction of late ventricular remodeling. Radiology 2011; 261: 116-126 [PMID: 21828188 DOI: 10.1148/radiol.11110228]

Beek AM, Kühl HP, Bondarenko O, Tvisk JW, Hofman MB, van Dockum WG, Visser CA, van Rossum AC. Delayed contrast-enhanced magnetic resonance imaging for the prediction of regional functional improvement after acute myocardial infarction. J Am Coll Cardiol 2003; 42: 895-901 [PMID: 12957439 DOI: 10.1016/S0021-3351(03)00835-4]

Ganame J, Messali G, Masi PG, Dymarkowski S, Abbasi K, Van de Werf F, Janssens S, Bogaert J. Time course of infarct healing and left ventricular remodelling in patients with reperfused ST segment elevation myocardial infarction using comprehensive magnetic resonance imaging. Eur Radiol 2011; 21: 693-701 [PMID: 20865262 DOI: 10.1007/s00330-010-1963-8]

Dall’Armellina E, Karia N, Lindsay AC, Karamitsos TD, Ferreira V, Robson MD, Kellman P, Francis JM, Forfar C, Prendergast BD, Banning AP, Channon KM, Kharbanda RK, Neubauer S, Choudhury RP. Dynamic changes of edema and late gadolinium enhancement after acute myocardial infarction and their relationship to functional recovery and salvage index. Circ Cardiovasc Imaging 2011; 4: 228-236 [PMID: 21447711 DOI: 10.1161/circimaging.110.963421]

Orn S, Manhenke C, Anand IS, Squire I, Nagel E, Edvardsen T, Dickstein K. Effect of left ventricular scar size, location, and transmurality on left ventricular remodeling with healed myocardial infarction. Am J Cardiol 2007; 99: 1109-1114 [PMID: 17437737 DOI: 10.1016/j.amjcard.2006.11.059]

Husser O, Bodi V, Sanchis J, Nunez J, Lopez-Lereu MP, Bonnand C, Chastue F, Gomez C, Bosch MJ, Hinarejos R, Chorro FJ, Riegger GA, Llacer A, Bodi V. Cardiovascular magnetic resonance-derived intramyocardial hemorrhage after STEMI: Influence on long-term prognosis, adverse left ventricular remodeling and relationship with microvascular obstruction. Int J Cardiol 2013; 167: 2047-2054 [PMID: 22682700 DOI: 10.1016/j.ijcard.2012.05.055]

Eitel I, Desch S, de Waha S, Fuernau G, Gutberlet M, Schuler G, Thiele H. Long-term prognostic value of myocardial salvage assessed by cardiovascular magnetic resonance in acute reperfused myocardial infarction. Heart 2011; 97: 2036-2045 [PMID: 21990384 DOI: 10.1136/heartjnl-2010-300688]

Amabile N, Jaquier A, Gaudart J, Sarran A, Shiaib A, Panuel M, Moulin G, Bartoli JM, Paganeli F. Value of a new multiparametric score for prediction of microvascular obstruction lesions in ST-segment elevation myocardial infarction revascularized by percutaneous coronary intervention. Arch Cardiovasc Dis 2010; 103: 512-521 [PMID: 21130964 DOI: 10.1016/j.acvd.2010.09.005]

de Waha S, Desch S, Eitel I, Fuernau G, zachrau J, Leuschner A, Gutberlet M, Schuler G, Thiele H. Impact of early vs. late microvascular obstruction assessed by magnetic resonance imaging on long-term outcome after ST-elevation myocardial infarction: a comparison with traditional prognostic markers. Eur Heart J 2010; 31: 2660-2668 [PMID: 20675660 DOI: 10.1093/eurheartj/ehq247]

Cochet AA, Lorigis L, Lalande A, Zeller M, Beer JC, Walker PM, Touzery C, Wolf JE, Brunotte F, Cotton Y. Major prognostic impact of persistent microvascular obstruction as assessed by contrast-enhanced cardiac magnetic resonance imaging in reperfused acute myocardial infarction. Eur Radiol 2009; 19: 2117-2126 [PMID: 19350245 DOI: 10.1007/s00330-009-1395-5]

Bodi V, Sanchis J, Nunez J, Mainar L, Lopez-Lereu MP, Monneneu JV, Runuez I, Chastue F, Trapero I, Husser O, Forzeta MJ, Chorro FJ, Llacer A. Prognostic value of a comprehensive cardiac magnetic resonance assessment soon after a first ST-segment elevation myocardial infarction. JACC Cardiovasc Imaging 2009; 2: 835-842 [PMID: 19608133 DOI: 10.1016/j.jcmg.2009.03.011]
65 Pennell DJ. Cardiovascular magnetic resonance. *Circulation* 2010; 121: 692-705 [PMID: 20142462 DOI: 10.1161/CIRCULATIONAHA.108.811547]

66 Amado LC, Gerber BL, Gupta SN, Rettman DW, Szafr G, Schock R, Nair K, Kuhlman DL, Lima JA. Accurate and objective infarct sizing by contrast-enhanced magnetic resonance imaging in a canine myocardial infarction model. *J Am Coll Cardiol* 2004; 44: 2383-2389 [PMID: 15607402 DOI: 10.1016/j.jacc.2004.09.020]

67 Larose E, Rodés-Cabau J, Pibarot P, Rinfret S, Proulx G, Nguyen CM, Déry JP, Gleeton O, Roy L, Noël B, Barbeau G, Rouleau J, Boudreault Jr, Amyot M, De Larochellière R, Bertrand OF. Predicting late myocardial recovery and outcomes in the early hours of ST-segment elevation myocardial infarction traditional measures compared with microvascular obstruction, salvaged myocardium, and necrosis characteristics by cardiovascular magnetic resonance. *J Am Coll Cardiol* 2010; 55: 2459-2469 [PMID: 20510213 DOI: 10.1016/j.jacc.2010.02.033]

68 Zia MI, Ghugre NR, Roifman I, Strauss BH, Walcararius R, Mohammed M, Sparks JD, Dick AJ, Wright GA, Connelly KA. Comparison of the frequencies of myocardial edema determined by cardiac magnetic resonance in diabetic versus nondiabetic patients having percutaneous coronary intervention for ST elevation myocardial infarction. *Am J Cardiol* 2014; 113: 607-612 [PMID: 24332697 DOI: 10.1016/j.amjcard.2013.10.040]

69 Robbers LF, Eerenberg ES, Teunissen PF, Jansen MF, Hollander MR, Horrevoets AJ, Knappen P, Nijveldt R, Heymans MW, Levi MM, van Rossum AC, Niessen HW, Marcu CB, Beek AM, van Royen N. Magnetic resonance imaging-defined areas of microvascular obstruction after acute myocardial infarction represent microvascular destruction and haemorrhage. *Eur Heart J* 2013; 34: 2346-2353 [PMID: 23594591 DOI: 10.1093/eurheartj/eht100]

70 Malek IA, Spiewak M, Klopotowski M, Miško J, Ružýllo W, Witkowski A. The size does not matter - the presence of microvascular obstruction but not its extent corresponds to larger infarct size in reperfused STEMI. *Eur J Radiol* 2012; 81: 2839-2843 [PMID: 22197092 DOI: 10.1016/j.ejrad.2011.11.053]

71 Kim HW, Farzanch-Far A, Kim RJ. Cardiac magnetic resonance imaging in patients with myocardial infarction: current and emerging applications. *J Am Coll Cardiol* 2009; 55: 1-16 [PMID: 20117357 DOI: 10.1016/j.jacc.2009.06.059]

72 Khan JN, Nazir SA, Horsfield MA, Singh A, Kanagala P, Greenwood JP, Gershlick AH, McCann GP. Comparison of semi-automated methods to quantify infarct size and myocardial salvage by cardiac MRI in a 1.5t and 3.0t field strengths. *Heart* 2014; 100: A76 [PMID: 24313631 DOI: 10.1136/heartjnl-2014-306113.131]

73 O’Regan DP, Affifi B, Baksj AJ, Gordon F, Durugh G, Cook SA. Salveg assessment with cardiac MRI following acute myocardial infarction underestimated potential for recovery of systolic strain. *Eur Radiol* 2013; 23: 1210-1217 [PMID: 23179255 DOI: 10.1007/s00330-012-2751-8]

74 Carrick D, Haig C, Ahmed N, McEntegart M, Petrie MC, Eteiba H, Hood S, Watkins S, Lindsay MM, Davie A, Mahrous A, Mordi I, Raulahamn S, Sattar N, Welsh P, Kadovjenic A, Ford I, Oldroyd KG. Cardiac Magnetic Resonance After Acute Reperfused ST-Segment-Elevation Myocardial Infarction: Relation to Microvascular Obstruction and Prognostic Significance. *Circ Cardiovasc Imaging* 2016; 9: e004418 [PMID: 26763281 DOI: 10.1161/CIRCIMAGING.115.004188]

75 Judd RM, Lugo-Olivier CH, Arari M, Kondo T, Croisille P, Lima JA, Mohan V, Becker LC, Zerouhni EA. Physiological basis of myocardial contrast enhancement in fast magnetic resonance images of 2-day-old reperfused canine infarcts. *Circulation* 1995; 92: 1902-1910 [PMID: 7671355 DOI: 10.1161/01.CIR.92.7.1902]

76 Fieno DS, Hillenbrand HB, Rehwald WG, Harris KR, Decker RS, Parker MA, Klocke FJ, Kim RJ, Judd RM. Infarct resolution, compensatory hypertrophy, and differing patterns of ventricular remodeling following myocardial infarctions of varying size. *J Am Coll Cardiol* 2004; 43: 2124-2131 [PMID: 15172424 DOI: 10.1016/j.jacc.2004.01.043]

77 Altrás AH, Títlak GS, Natanzon A, Hsu LY, Gonzalez FM, Hoyt RF, Arai AE. Retrospective determination of the area at risk for reperfused acute myocardial infarction with T2-weighted cardiac magnetic resonance imaging: histopathological and displacement encoding with stimulated echoes (DENSE) functional validations. *Circulation* 2006; 113: 1865-1870 [PMID: 16606793 DOI: 10.1161/CIRCULATIONAHA.105.576025]

78 Lowe JE, Reimer KA, Jennings RB. Experimental infarct size as a function of the amount of myocardium at risk. *Am J Pathol* 1978; 90: 363-379 [PMID: 6232006]

79 Reimer KA, Jennings RB, Cobb FR, Murdock RH, Greenfield JC, Becker LC, Bulky BH, Hutchins GM, Schwartz RP, Bailey KR. Animal models for protecting ischemic myocardium: results of the NHLBI Cooperative Study. Comparison of unconscious and conscious dog models. *Circ Res* 1985; 56: 651-665 [PMID: 3838923 DOI: 10.1161/01.RES.56.6.651]

80 Christian TF, Schwartz RS, Gibbons RJ. Determinants of infarct size in reperfusion therapy for acute myocardial infarction. *Circulation* 1992; 86: 81-90 [PMID: 16177793 DOI: 10.1161/01.CIR.86.1.81]

81 Hirsch A, Nijveldt R, Haeck JD, Beek AM, Koch KT, Henriquez JP, van der Schaaf RJ, Vis MM, Baan J, de Winter RJ, Tijssen JG, van Rossum AC, Piek JJ. Relation between the assessment of microvascular injury by cardiovascular magnetic resonance and coronary Doppler flow velocity measurements in patients with acute anterior wall myocardial infarction. *J Am Coll Cardiol* 2008; 51: 2230-2238 [PMID: 18534269 DOI: 10.1016/j.jacc.2008.01.064]

82 Francone M, Bucciarelli-Ducci C, Carbone I, Canali E, Scardala R, Calabrese FA, Sardella G, Mancone M, Catalano C, Fedele F, Passariello R, Bogaert J, Agati L. Impact of primary coronary angioplasty delay on myocardial salvage, infarct size, and microvascular damage in patients with ST-segment elevation myocardial infarction. *J Am Coll Cardiol* 2009; 54: 2145-2153 [PMID: 19942086 DOI: 10.1016/j.jacc.2009.08.024]

83 O’Regan DP, Affifi B, Baksj AJ, Gordon F, Durugh G, Cook SA. Salveg assessment with cardiac MRI following acute myocardial infarction underestimated potential for recovery of systolic strain. *Eur Radiol* 2013; 23: 1210-1217 [PMID: 23179255 DOI: 10.1007/s00330-012-2751-8]

84 Carrick D, Haig C, Ahmed N, McEntegart M, Petrie MC, Eteiba H, Hood S, Watkins S, Lindsay MM, Davie A, Mahrous A, Mordi I, Raulahamn S, Sattar N, Welsh P, Kadovjenic A, Ford I, Oldroyd KG. Cardiac Magnetic Resonance After Acute Reperfused ST-Segment-Elevation Myocardial Infarction: Relation to Microvascular Obstruction and Prognostic Significance. *Circ Cardiovasc Imaging* 2016; 9: e004418 [PMID: 26763281 DOI: 10.1161/CIRCIMAGING.115.004188]

85 Judd RM, Lugo-Olivier CH, Arari M, Kondo T, Croisille P, Lima JA, Mohan V, Becker LC, Zerouhni EA. Physiological basis of myocardial contrast enhancement in fast magnetic resonance images of 2-day-old reperfused canine infarcts. *Circulation* 1995; 92: 1902-1910 [PMID: 7671355 DOI: 10.1161/01.CIR.92.7.1902]

86 Fieno DS, Hillenbrand HB, Rehwald WG, Harris KR, Decker RS, Parker MA, Klocke FJ, Kim RJ, Judd RM. Infarct resolution, compensatory hypertrophy, and differing patterns of ventricular remodeling following myocardial infarctions of varying size. *J Am Coll Cardiol* 2004; 43: 2124-2131 [PMID: 15172424 DOI: 10.1016/j.jacc.2004.01.043]
myocardial ischemic cell death. II. Transmural progression of necrosis within the framework of ischemic bed size (myocardium at risk) and collateral flow. *Lab Invest* 1979; **40**: 633-644 [PMID: 449273]

Kloner RA, Ganote CE, Jennings RB. The “no-reflow” phenomenon after temporary coronary occlusion in the dog. *J Clin Invest* 1974; **54**: 1496-1508 [PMID: 4140198 DOI: 10.1172/JCI107898]

Rochitte CE, Lima JA, Bluenke DA, Reeder SB, McVeigh ER, Furuta T, Becker LC, Melin JA. Magnitude and time course of microvascular obstruction and tissue injury after acute myocardial infarction. *Circulation* 1998; **98**: 1006-1014 [PMID: 9737521 DOI: 10.1161/01.CIR.98.10.1006]

Wong DT, Leung MC, Richardson JD, Puri R, Bertaso AG, Williams K, Meredith IT, Teo KS, Worthley MI, Worthley SG. Cardiac magnetic resonance derived late microvascular obstruction assessment post-ST-segment elevation myocardial infarction is the best predictor of left ventricular function: a comparison of angiographic and cardiac magnetic resonance derived measurements. *Int J Cardiovasc Imaging* 2012; **28**: 1971-1981 [PMID: 22310980 DOI: 10.1007/s10554-012-0029-9]

Klug G, Mayr A, Schenk S, Estcherhammer R, Schocke M, Nocker M, Jasek M, Wachinger O, Metzler B. Prognostic value at 5 years of microvascular obstruction after acute myocardial infarction assessed by cardiac magnetic resonance. *J Cardiovasc Magn Reson* 2012; **14**: 46 [PMID: 22788728 DOI: 10.1186/1532-429x-14-46]

Wu KC, Kim RJ, Bluenke DA, Rochitte CE, Zerhoumi EA, Becker LC, Lima JA. Quantification and time course of microvascular obstruction by contrast-enhanced echocardiography and magnetic resonance imaging following acute myocardial infarction and reperfusion. *J Am Coll Cardiol* 1998; **32**: 1756-1764 [PMID: 9822106 DOI: 10.1016/S0735-1097(98)00429-X]

Gerber BL, Rochitte CE, Melin JA, McVeigh ER, Bluenke DA, Wu KC, Becker LC, Lima JA. Microvascular obstruction and left ventricular remodeling early after acute myocardial infarction. *Circulation* 2000; **101**: 2734-2741 [PMID: 10851212 DOI: 10.1161/01.CIR.101.23.2734]

Bekkers SC, Baxres WH, Kim RJ, Snoep G, Gorgels AP, Passos VL, Wu JC, Vanmelle P, Grijsh JH, Sehala S. Detection and characteristics of microvascular obstruction in reperfused acute myocardial infarction using an optimized protocol for contrast-enhanced cardiovascular magnetic resonance imaging. *Eur Radiol* 2009; **19**: 2904-2912 [PMID: 19588152 DOI: 10.1007/s00330-009-1489-0]

Örn S, Manhenke C, Greve OJ, Larsen AI, Bonarjee VV, Edvardsen TD, Dickstein K. Microvascular obstruction is a major determinant of infarct healing and subsequent left ventricular remodeling following primary percutaneous coronary intervention. *Eur Heart J* 2008; **30**: 1978-1985 [PMID: 19502624 DOI: 10.1093/eurheartj/ehp219]

Bogaert J, Kalantzi M, Rademakers FE, Dymarkowski S, Janssens S. Determinants and impact of microvascular obstruction in successfully reperfused ST-segment elevation myocardial infarction. Assessment by magnetic resonance imaging. *Eur Radiol* 2007; **17**: 2572-2580 [PMID: 17361420 DOI: 10.1007/s00330-007-0627-9]

Khan JN, Razvi N, Nazir SA, Singh A, Masca NG, Gershick AH, Squire I, McCann GP. Prevalence and extent of infarct and microvascular obstruction following different reperfusion therapies in ST-elevation myocardial infarction. *J Cardiovasc Magn Reson* 2014; **16**: 38 [PMID: 24884638 DOI: 10.1186/1532-429x-16-38]

Nijveldt R, Beek AM, Hirsch A, Stol MG, Hofman MB, Uman VA, Algra PR, Twisk JW, van Rossum AC. Functional recovery after acute myocardial infarction: comparison between angiography, electrocardiography, and cardiovascular magnetic resonance measures of microvascular injury. *J Am Coll Cardiol* 2008; **52**: 181-189 [PMID: 18617066 DOI: 10.1016/j.jacc.2008.04.006]

Weir RA, Murphy CA, Petrie CJ, Martin TN, Balmain S, Clements S, Steedman T, Wagner GS, Dargie HJ, McMurray J. Microvascular obstruction remains a portrait of adverse remodeling in optimally treated patients with left ventricular systolic dysfunction after acute myocardial infarction. *Circ Cardiovasc Imaging* 2010; **3**: 360-367 [PMID: 20348438 DOI: 10.1161/CIRCIMAGING.109.897439]

Wong DT, Weightman MJ, Baumert M, Tayeb H, Richardson JD, et al. CMR assessment of outcomes in AMI.
February 26, 2017 | Volume 9 | Issue 2 | WJCI www.wjgnet.com

Puri R, Bertaso AG, Roberts-Thomson KC, Sanders P, Worthley MI, Worthley SG. Electro-mechanical characteristics of myocardial infarction border zones and ventricular arrhythmic risk: novel insights from grid-tagged cardiac magnetic resonance imaging. *Eur Radiol* 2012; 22: 1651-1658 [PMID: 22752521 DOI: 10.1007/s00330-012-2417-2]

114 Ye YY, Basse-Lisebrink TC, Arias-Loza PA, Kocsoci V, Kampff T, Gan Q, Bauer E, Spurka S, Helluy X, Hu K, Hiller KH, Boivin-Jahns V, Jakob PM, Jahns R, Bauer WR. Monitoring of monocyte recruitment in reperfused myocardial infarction with intramyocardial hemorrhage and microvascular obstruction by combined fluorine 19 and proton cardiac magnetic resonance imaging. *Circulation* 2013; 128: 1878-1888 [PMID: 24025595 DOI: 10.1161/CIRCULATIONAHA.113.007371]

115 Kidambi A, Mathen AR, Motwani S, Swoboda P, Uddin A, Greenwood JP, Plein S. The effect of microvascular obstruction and intramyocardial hemorrhage on contractile recovery in reperfused myocardial infarction: insights from cardiovascular magnetic resonance. *J Cardiovasc Magn Reson* 2013; 15: 58 [PMID: 23986800 DOI: 10.1186/1532-429x-15-58]

116 Bruder O, Breuckmann F, Jensen C, Joehims M, Naher CK, Barkhausen J, Erbel R, Sabin GV. Prognostic impact of contrast-enhanced CMR early after acute ST segment elevation myocardial infarction (STEMI) in a regional STEMI network: results of the “Herzfunktionsverbund Essen”. *Herz* 2008; 33: 136-142 [PMID: 18344033 DOI: 10.1007/s00059-008-3102-8]

117 Regenfus M, Schlundt C, Krährer R, Schöngen C, Adler W, Ludwig J, Daniel WG, Schmid M. Six-Year Prognostic Value of Microvascular Obstruction After Reperfused ST-Elevation Myocardial Infarction as Assessed by Contrast-Enhanced Cardiovascular Magnetic Resonance. *Am J Cardiol* 2015; 116: 1022-1027 [PMID: 2626097 DOI: 10.1016/j.amjcard.2015.06.034]

118 van Kronenberg M, Magro M, Thiele H, de Waha S, Eitel I, Mather AN, Motwani M, Swoboda P, Uddin A, Kumar A, Cokic I, Tang RL, Tsaftaris S, Friedrich M, setting myocardial hemorrhage in patients with acute myocardial infarction. *Heart* 2010; 96: 1885-1891 [PMID: 20965977 DOI: 10.1136/hrt.2010.200634]

119 Kali A, Kumar A, Cokic I, Tang R, Tsafaris S, Friedrich M, Dharmakumar R. Chronic manifestation of post-reperfusion intramyocardial hemorrhage as regional iron deposition – a cardiovascular mr study with ex vivo validation. *Circulation: Cardiovascular Imaging* 2013; 6: 218-228

120 Kali A, Tang RL, Kumar A, Min JK, Dharmakumar R. Detection of acute reperfusion myocardial hemorrhage with cardiac MR imaging: T2 versus T2. *Radiology* 2013; 269: 387-395 [PMID: 23847253 DOI: 10.1148/radiol.13122397]

121 Zia MI, Ghuerg NR, Connelly KA, Strauss BH, Sparkes JD, Dick AJ, Wright GA. Characterizing myocardial edema and hemorrhage using quantitative T2 and T2* mapping at multiple time intervals post ST-segment elevation myocardial infarction. *Circ Cardiovasc Imaging* 2012; 5: 566-572 [PMID: 22744938 DOI: 10.1161/CIRCIMAGING.112.973222]

122 O’Regan DP, Ahmed R, Karunanithy N, Neuwirth C, Tan Y, Durighel G, Hajnal JV, Nada I, Corbett SJ, Cook SA. Reperfusion hemorrhage following acute myocardial infarction: assessment with T2* mapping and effect on measuring the area at risk. *Radiology* 2009; 250: 916-922 [PMID: 19164125 DOI: 10.1148/radiol.2503081154]

123 Mather AN, Fairbairn TA, Ball SG, Greenwood JP, Plein S. Reperfusion haemorrhage as determined by cardiovascular MRI is a predictor of adverse left ventricular remodelling and markers of late arrhythmical risk. *Heart* 2011; 97: 453-459 [PMID: 21051455 DOI: 10.1136/hrt.2010.202028]

124 Kali A, Kumar A, Cokic I, Tang RL, Tsafaris SA, Friedrich MG, Dharmakumar R. Chronic manifestation of post-reperfusion intramyocardial hemorrhage as regional iron deposition: a cardiac magnetic resonance study with ex vivo validation. *Circ Cardiovasc Imaging* 2013; 6: 218-228 [PMID: 23403335 DOI: 10.1161/CIRCIMAGING.112.100137]

125 Amabile N, Jacques A, Shubah A, Gaudart J, Bartoli JM, Pagenneli F, Moulin G. Incidence, predictors, and prognostic value of intramyocardial hemorrhage lesions in ST elevation myocardial infarction. *Catheter Cardiovasc Interv* 2012; 79: 1101-1108 [PMID: 21805604 DOI: 10.1002/crd.23278]

126 Abdel-Atty H, Simonetti O, Friedman MG. T2-weighted cardiovascular magnetic resonance imaging. *J Magn Reson Imaging* 2007; 26: 452-459 [PMID: 17729358 DOI: 10.1002/jmri.21028]

127 Higgins CR, Herfkens R, Lipton MJ, Sievers R, Sheldon P, Kaufman L, Crooks LE. Nuclear magnetic resonance imaging of acute myocardial infarction in dogs: alterations in magnetic relaxation times. *Am J Cardiol* 1983; 52: 184-188 [PMID: 6859009 DOI: 10.1016/0002-9149(83)90093-0]

128 Arai AE. Magnetic resonance imaging for area at risk, myocardial infarction, and myocardial salvage. *J Cardiovasc Pharmacol Ther* 2012; 16: 313-320 [PMID: 21821534 DOI: 10.1177/1074284911414378]

129 García-Dorado D, Oliveras J, Gil J, Sanz E, Pérez-Villa F, Barbáres J, Carreras MJ, Solares J, Soler-Soler J. Analysis of myocardial oedema by magnetic resonance imaging early after coronary artery occlusion with or without reperfusion. *Cardiovasc Res* 1993; 27: 1462-1469 [PMID: 8297415 DOI: 10.1093/vasj/27.8.1462]

130 Carlsson M, Ubachs JF, Hedström E, Heiberg E, Jovinge S, Arheden H. Myocardium at risk after acute infarction in humans
on cardiac magnetic resonance: quantitative assessment during follow-up and validation with single-photon emission computed tomography. JACC Cardiovasc Imaging 2009; 2: 569-576 [PMID: 19442942 DOI: 10.1016/j.jcmg.2008.11.016]

Hedström R, Engblom H, Fronger F, Aström-Olsson K, Ohlin H, Jovinge S, Arheden H. Infarct evolution in man studied in patients with first-time coronary occlusion in comparison to different species - implications for assessment of myocardial salvage. J Cardiovasc Magn Reson 2009; 11: 38 [PMID: 19775428 DOI: 10.1186/1532-429X-11-38]

Hadamitzky M, Langhans B, Hausleiter J, Sonne C, Kastrati A, Martinoff S, Schömig A, Ibrahim T. The assessment of area at risk and myocardial salvage after coronary revascularization in acute myocardial infarction: comparison between CMR and SPECT. JACC Cardiovasc Imaging 2013; 6: 358-369 [PMID: 23473113 DOI: 10.1016/j.jcmg.2012.10.018]

Viallon M, Mewton N, Thuny F, Guehring J, O'Donnell T, Stemmer A, Bi X, Rapacchi S, Zuehlsdorff S, Revel D, Croisille P. T2-weighted cardiac MRI assessment of the myocardial area-at-risk and salvage area in acute reperfused myocardial infarction: comparison of state-of-the-art dark blood and bright blood T2-weighted sequences. J Magn Reson Imaging 2013; 35: 328-339 [PMID: 21959873 DOI: 10.1002/jmri.22813]

Berry C, Kellman P, Mancini C, Chen MY, Bandettini WP, Lowrey T, Hsu LY, Aletas AH, Araie AE. Magnetic resonance imaging delineates the ischemic area at risk and myocardial salvage in patients with acute myocardial infarction. Circ Cardiovasc Imaging 2010; 3: 527-535 [PMID: 20663104 DOI: 10.1161/ CIRCIMAGING.109.900761]

Goldfarb JW, Arnold S, Han J. Recent myocardial infarction assessment: with enhancement T1-weighted MR imaging. Radiology 2007; 245: 245-250 [PMID: 17885192 DOI: 10.1148/radiol.2451061590]

Croisille P, Kim HW, Kim RJ. Controversies in cardiovascular MR imaging: T2-weighted imaging should not be used to delineate the area at risk in ischemic myocardial injury. Radiology 2012; 265: 12-22 [PMID: 22933217 DOI: 10.1148/radiol.11120633]

Simoniello OP, Kim RJ, Fieno DS, Hillenbrand HB, Wu E, Bundy JM, Finn JP, Judd RM. An improved MR imaging technique for the visualization of myocardial infarction. Radiology 2001; 218: 215-223 [PMID: 11152805 DOI: 10.1148/radiol.2181.01jraa50 215]

Payne AR, Casey M, McClure J, McGeoch R, Murphy A, Woodward R, Saul A, Bi X, Zuehlsdorff S, Oldroyd KG, Tzemis N, Berry C. Bright-blood T2-weighted MRI has higher diagnostic accuracy than dark-blood short tau inversion recovery MRI for detection of acute myocardial infarction and for assessment of the ischemic area at risk and myocardial salvage. Circ Cardiovasc Imaging 2011; 4: 210-219 [PMID: 21427362 DOI: 10.1161/ CIRCIMAGING.111.965095]

Sörensson P, Heiberg E, Saleh N, Bouvier F, Caidahl K, Tornvall P, Rydén L, Pernow J, Arheden H. Assessment of myocardium at risk with contrast enhanced steady-state free precession cine cardiovascular magnetic resonance compared to single-photon emission computed tomography. J Cardiovasc Magn Reson 2010; 12: 25 [PMID: 20433716]

Ubachs JF, Sörensson P, Engblom H, Carlsson M, Jovinge S, Pernow J, Arheden H. Myocardium at risk by magnetic resonance imaging: head-to-head comparison of T2-weighted imaging and contrast-enhanced steady-state free precession. Eur Heart J Cardiovasc Imaging 2012; 13: 1008-1015 [PMID: 22645203 DOI: 10.1093/ehjci/jes091]

Verhaert D, Thavendiranathan P, Siri S, Mihai G, Rajagopalan S, Simonetti OP, Raman SV. Direct T2 quantification of myocardial edema in acute ischemic injury. JACC Cardiovasc Imaging 2011; 4: 269-278 [PMID: 21414575 DOI: 10.1016/j.jcmg.2010.09.023]

Naftzen K, Nensa F, Schlosser T, Bruder O, Umutlu L, Lauenstein T, Madewald S, Ladd ME. Cardiac MRI: T2-Mapping Versus T2-Weighted Dark-Blood TSE Imaging for Myocardial Edema Visualization in Acute Myocardial Infarction. Rofo 2014; 186: 166-172 [PMID: 24081784]

Lönborg J, Engström T, Mathiasen AB, Vejlstrup N. Myocardial area at risk after ST-elevation myocardial infarction measured with the late gadolinium enhancement after scar remodeling and T2-weighted cardiac magnetic resonance imaging. Int J Cardiovasc Imaging 2012; 28: 1455-1464 [PMID: 21971845 DOI: 10.1007/s10554-011-9592-9]

Ubachs JF, Engblom H, Erlinge D, Jovinge S, Hedström E, Carlsson M, Arheden H. Cardiovascular magnetic resonance of the myocardium at risk in acute reperfused myocardial infarction: comparison of T2-weighted imaging versus the circumferential endocardial extent of late gadolinium enhancement with transmural projection. J Cardiovasc Magn Reson 2010; 12: 18 [PMID: 20350309 DOI: 10.1186/1532-429X-12-18]

Kociemba A, Pyda M, Katulka A, Lanocha M, Šiniacki A, Janus M, Grajek S. Comparison of diffusion-weighted with T2-weighted imaging for detection of edema in acute myocardial infarction. J Cardiovasc Magn Reson 2013; 15: 90 [PMID: 24098944 DOI: 10.1186/1532-429X-15-90]

O’Gara PT, Kushner FG, Ascheim DD, Casey DE, Chung MK, de Lemos JA, Ettinger SM, Fang JC, Fesmire FM, Franklin BA, Granger CB, Krumholz HM, Linderbaum JA, Morrow DA, Newby WK, Ornato JP, Ou N, Radford MJ, Tamis-Holland JE, Tomasso CL, Tracy CM, Wu YJ, Zhao DX, Anderson JL, Jacobs AK, Halperin JL, Albert NM, Brindis RG, Creager MA, DeMets D, Gutyon RA, Hochman JS, Kovacs RJ, Kushner FG, Ohman EM, Stevenson WG, Yancy CW. 2013 ACC/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2013; 61: e78-140 [PMID: 23256914 DOI: 10.1016/j.jacc.2012.11.019]

Masci PG, Andreini D, Francione M, Bertella E, De Luca L, Cceceni M, Muhataq S, Mariani M, Carbino I, Pontone G, Agati L, Bogaert JL, Lombardi M. Prodromal angina is associated with myocardial infarction as visualized by cardiovascular magnetic resonance imaging for detection of edema in acute myocardial infarction. J Am Coll Cardiol 2013; 61: 2071-2080 [PMID: 2412117690 DOI: 10.1016/j.jcmg.2012.11.019]
Edema as a very early marker for acute myocardial ischemia: a cardiac magnetic resonance study. J Am Coll Cardiol 2009; 53: 1194-1201 [PMID: 19341860 DOI: 10.1016/j.jacc.2008.10.065]

Fernández-Jiménez R, Sánchez-González J, Agüero J, García-Prieto J, López-Martin G, García-Ruíz JM, Molina-fracetta A, Rosselló X, Fernández-Friera L, Pizarro G, García-Álvarez A, Dall’Armellina E, Macaya C, Choudhry RP, Fuster V, Ibáñez B. Myocardial edema after ischemia/reperfusion is not stable and follows a bimodal pattern: imaging and histological tissue characterization. J Am Coll Cardiol 2015; 65: 313-323 [PMID: 25460833 DOI: 10.1016/j.jacc.2014.11.004]

Abdel-Aty H, Cocker M, Meek C, Tyberg JV, Friedrich MG. Edema as a very early marker for acute myocardial ischemia: a cardiac magnetic resonance study. J Am Coll Cardiol 2009; 53: 1194-1201 [PMID: 19341860 DOI: 10.1016/j.jacc.2008.10.065]

Larose E, Tizon-Marcos H, Rodés-Cabau J, Rinfret S, Déry JP, Nguyen CM, Gleeton O, Boudreault JR, Roy L, Noël B, Proulx G, Rouleau J, Barbeau G, De Larochellière R, Bertrand OF. Improving myocardial salvage in late presentation acute ST-elevation myocardial infarction with proximal embolic protection. Catheter Cardiovasc Interv 2010; 76: 461-470 [PMID: 20506154 DOI: 10.1002/ccd.22588]

Ndrepepa G, Mehilli J, Schwäger M, Schühlen H, Nekolla S, Martinoff S, Schmitt C, Dirschinger J, Schömig A, Kastrati A. Prognostic value of myocardial salvage achieved by reperfusion therapy in patients with acute myocardial infarction. J Nucl Med 2004; 45: 725-729 [PMID: 15316681]

Messroghli DR, Niendorf T, Schulz-Menger J, Dietz R, Friedrich MG. T1 mapping in patients with acute myocardial infarction. J Cardiovasc Magn Reson 2003; 5: 353-359 [PMID: 12765114 DOI: 10.1081/jcmm-120019418]

Mewton N, Liu CY, Croisille P, Bluemke D, Lima JA. Assessment of myocardial fibrosis with cardiovascular magnetic resonance. J Am Coll Cardiol 2011; 57: 891-903 [PMID: 21329834 DOI: 10.1016/j.jacc.2010.11.013]

Salamo N, Kramer CM. Advances in parametric mapping with CMR imaging. JACC Cardiovasc Imaging 2013; 6: 806-822 [PMID: 23845576 DOI: 10.1016/j.jcmg.2013.05.005]

Roujol S, Weingärtner S, Foppa M, Chow K, Kawaiji K, Ngo LH, Kellman P, Manning WJ, Thompson RB, Nezafat R. Accuracy, precision, and reproducibility of four T1 mapping sequences: a head-to-head comparison of MOLLI, ShMOLLI, SASHA, and SAPPHIRE. Radiology 2014; 272: 683-689 [PMID: 24702742 DOI: 10.1148/radiol.141400296]

Messroghli DR, Radjenovic A, Kozerke S, Higgins DM, Sivananthan MU, Ridgway JP. Modified Look-Locker inversion recovery (MOLLI) for high-resolution T1 mapping of the heart. Magn Reson Med 2004; 52: 141-146 [PMID: 15236377 DOI: 10.1002/mrm.20110]

| Author(s) | Title | Journal | Volume | Issue | Pages | PMID | DOI |
|-----------|-------|---------|--------|-------|-------|------|-----|
| Abdel-Aty H, Cocker M, Meek C, Tyberg JV, Friedrich MG. | Edema as a very early marker for acute myocardial ischemia: a cardiac magnetic resonance study. | J Am Coll Cardiol | 2009 | 53 | 1194-1201 | 19341860 | 10.1016/j.jacc.2008.10.065 |
| Ndrepepa G, Mehilli J, Schwäger M, Schühlen H, Nekolla S, Martinoff S, Schmitt C, Dirschinger J, Schömig A, Kastrati A. | Prognostic value of myocardial salvage achieved by reperfusion therapy in patients with acute myocardial infarction. | J Nucl Med | 2004 | 45 | 725-729 | 15316681 | |
| Messroghli DR, Niendorf T, Schulz-Menger J, Dietz R, Friedrich MG. | T1 mapping in patients with acute myocardial infarction. | J Cardiovasc Magn Reson | 2003 | 5 | 353-359 | 12765114 | 10.1081/jcmm-120019418 |
| Mewton N, Liu CY, Croisille P, Bluemke D, Lima JA. | Assessment of myocardial fibrosis with cardiovascular magnetic resonance. | J Am Coll Cardiol | 2011 | 57 | 891-903 | 21329834 | 10.1016/j.jacc.2010.11.013 |
| Salamo N, Kramer CM. | Advances in parametric mapping with CMR imaging. | JACC Cardiovasc Imaging | 2013 | 6 | 806-822 | 23845576 | 10.1016/j.jcmg.2013.05.005 |
| Roujol S, Weingärtner S, Foppa M, Chow K, Kawaiji K, Ngo LH, Kellman P, Manning WJ, Thompson RB, Nezafat R. | Accuracy, precision, and reproducibility of four T1 mapping sequences: a head-to-head comparison of MOLLI, ShMOLLI, SASHA, and SAPPHIRE. | Radiology | 2014 | 272 | 683-689 | 24702742 | 10.1148/radiol.141400296 |

Note: The table above lists some of the references cited in the text. The complete list of references can be found in the original document.
Khan JN et al. CMR assessment of outcomes in AMI

cvr/cvq091

189 Larose E, Ganz P, Reynolds HG, Dorbala S, Di Carli MF, Brown KA, Kwong RY. Right ventricular dysfunction assessed by cardiovascular magnetic resonance imaging predicts poor prognosis late after myocardial infarction. J Am Coll Cardiol 2007; 49: 855-862 [PMID: 17320743 DOI: 10.1016/j.jacc.2006.10.056]

190 Hamon M, Agostini D, Le Page O, Riddell JW, Hamon M. Prognostic impact of right ventricular involvement in patients with acute myocardial infarction: meta-analysis. Crit Care Med 2008; 36: 2023-2033 [PMID: 18552681 DOI: 10.1097/CCM.0b013e31817d213d]

191 Shah PK, Maddahi J, Staniloff HM, Ellrodt AG, Pichler M, Swan HJ, Berman DS. Variable spectrum and prognostic implications of left and right ventricular ejection fractions in patients with and without clinical heart failure after acute myocardial infarction. Am J Cardiol 1986; 58: 387-393 [PMID: 3751905 DOI: 10.1016/0002-9149(86)90001-9]

P- Reviewer: Barison A, Cheng TH, Cosmi E, Kato M, Sato A
S- Editor: Ji FF
L- Editor: A
E- Editor: Lu YJ
