Cardiovascular magnetic resonance imaging in patients with acute myocardial infarction

Aernout M Beek and Albert C van Rossum

Heart 2010 96: 237-243
doi: 10.1136/hrt.2009.172296

NON-INVASIVE IMAGING

Cardiovascular magnetic resonance imaging in patients with acute myocardial infarction

Aernout M Beek, Albert C van Rossum

► Supplementary videos are published online only at http://heart.bmj.com/content/vol96/issue3

Department of Cardiology, VU University Medical Center, Amsterdam, The Netherlands

Correspondence to
Dr A M Beek, Department of Cardiology, VU University Medical Center, De Boelelaan 1117, 1081 HV Amsterdam, The Netherlands; am.beek@vumc.nl

Cardiovascular magnetic resonance imaging (CMR) is increasingly used in the daily practice of the clinical cardiologist. Technical advances in hardware and development of new software have led to major improvements in image quality, spatial and temporal resolution, and imaging speed, allowing the detailed assessment of the whole spectrum of cardiovascular disease. This article reviews the clinical applications of CMR in patients with acute myocardial infarction (AMI).

CMR PULSE SEQUENCES

Cine imaging

Cine imaging forms the backbone of the CMR examination. It is used for the qualitative and quantitative assessment of myocardial anatomy and function, and, with the use of dobutamine stress, to evaluate ischaemia and viability (box 1). In addition, it may be used as an alternative technique to Doppler echocardiography for the evaluation of valvular heart disease. The standard cine pulse sequence is a breath-hold, steady state free precession (SSFP) sequence that provides optimal contrast between blood and myocardium (figure 1; see also supplemental videos 1 and 2). Current cine sequences use retrospective ECG gating, although prospective gating may be required in patients with irregular heart rhythm. When heart rhythm is notably irregular, as with complex ventricular ectopy, real time imaging without ECG gating will still allow the assessment of regional and global function, albeit at the cost of reduced image quality and spatial and temporal resolution (supplemental video 3). The efficiency of data acquisition may be considerably improved by using parallel imaging, which is based on undersampling of the raw data by using information from multiple receiver coils.[1] The improved scan efficiency may be translated into reduced scan time or improved resolution, at the cost of some loss in signal-to-noise. Temporal resolution can also be improved by phase sharing, a technique that uses the raw data of adjacent time frames to calculate additional frames.[2] The improved resolution can be used to reduce acquisition time or to optimise the timing of cardiac events such as the isovolumetric relaxation time.

Global left and right ventricular function and mass can be quantified with high accuracy and reproducibility using dedicated software programs (figure 1). Quantitative analysis may be influenced by various factors such as the ECG gating method (prospective vs retrospective), the sequence type (SSFP vs older gradient echo sequences), or the use of real time imaging or phase sharing. Although the differences in calculated volumes are generally small and clinically non-relevant, identical techniques should therefore be used in comparisons within or between subjects.

Regional analysis of left ventricular function is generally done qualitatively, using the standard 17 segment model. Regional function is ideally quantified with CMR myocardial tagging. With this technique, a saturation grid placed in one of several possible orientations allows the exact characterisation of intramural deformation by the calculation of two dimensional (2D) and three dimensional (3D) strain parameters.[3] Myocardial tagging is a valuable research technique but still requires considerable know-how and time for post-processing and quantitative analysis. Further more, the excellent performance of the standard SSFP cine technique allows the reliable detection of even minimal regional wall motion abnormalities. Therefore, myocardial tagging is only rarely used in clinical CMR examinations.

T2 weighted spin echo imaging

The spin echo sequence is widely used for a large diversity of indications. It provides static images with high soft tissue contrast, and, importantly, may be modified to accentuate or suppress specific tissue components such as fat, blood, or oedema. Acute coronary occlusion leads to intra- and extracellular oedema and causes a prolongation of a tissue specific magnetic property, the T2 relaxation time.[4] On T2 weighted (T2W) spin echo imaging, these regions appear bright, and T2W imaging can therefore be used to visualise acutely ischaemic regions without the use of contrast agents (figure 2). T2W imaging can also be used to visualise oedema in other (acute) myocardial disease states (box 2). As with most cardiac CMR sequences, T2W spin echo imaging is acquired during breath-holding. Additional modifications to suppress the signal of blood and fat are usually included.

Contrast enhanced imaging

Gadolinium chelates (Gd) are extracellular contrast agents that are administered intravenously and

Box 1 Indications for cardiac magnetic resonance (CMR) cine imaging

- Quantitative assessment of left and right ventricular volumes and mass
- Regional left and right ventricular function
- Detection of coronary artery disease using high dose dobutamine stress
- Detection of myocardial viability using low dose dobutamine stress
- Infarct related complications (thrombus, (pseudo-) aneurysm)

distribute rapidly from the intravascular space into the interstitium. Clearance from the myocardium is fast under normal circumstances, but may be considerably delayed in pathological conditions.[5]

Two types of contrast enhanced CMR imaging are used. First pass (FP) myocardial perfusion imaging monitors the changes in myocardial signal intensity resulting from the (first) passage of a bolus (0.05–0.1 mmol/kg) of a Gd based contrast agent. The signal intensity is directly related to the concentration of the contrast agent, which in turn corresponds to regional myocardial perfusion. Accurate monitoring of the changes in signal intensity is ensured by a single shot mode, which allows the acquisition of 3–4 entire images per heartbeat. FP imaging is used to detect stress induced myocardial ischaemia in patients with suspected coronary artery disease. In patients with AMI, it can be used to detect areas of microvascular obstruction (box 3).

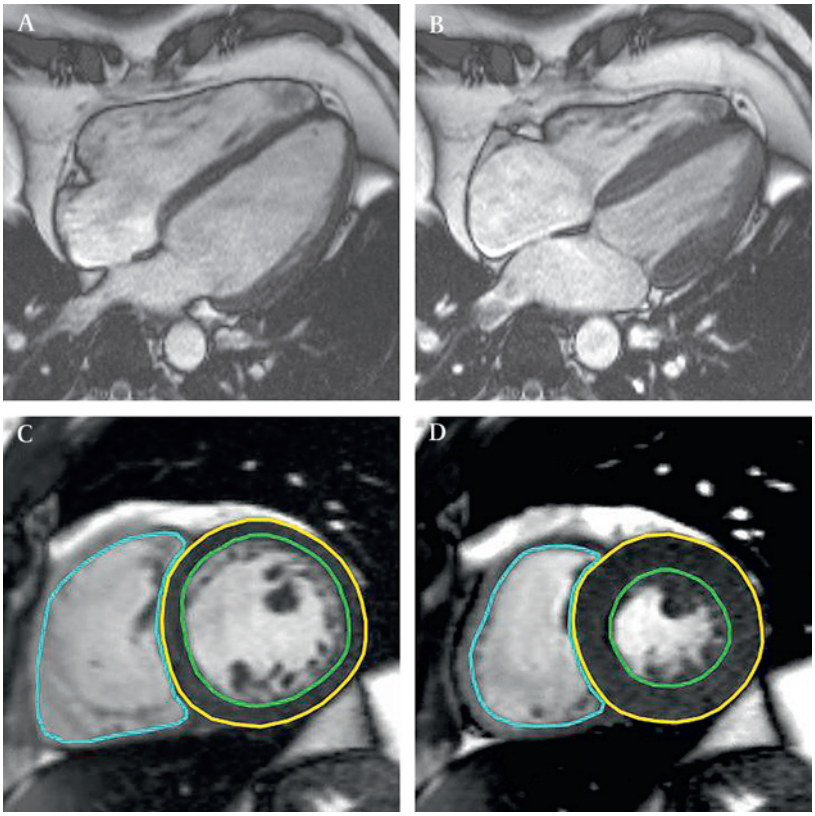

Figure 1 End-diastolic (A, C) and end-systolic (B, D) still frames acquired with steady state free precession (SSFP) cine sequence in four chamber (A, B) and mid ventricular short axis (C, D) position, with left ventricular epicardial (yellow), endocardial (green) and right ventricular endocardial (blue) contours (C, D).

In delayed contrast enhanced imaging, image acquisition is postponed until Gd has reached a steady state, typically 10–15 min after injection of 0.1–0.2 mmol/kg Gd. Delayed enhancement (DE) is characterised by high contrast between the suppressed signal in non-infarcted myocardium and the hyperenhanced infarcted regions (figures 2–5). Experimental studies have shown that Gd only accumulates in areas of infarction and that DE is extremely accurate in detecting irreversible ischaemic damage in any stage of the disease, irrespective of the patency of the infarct related artery.[6] This makes DE the imaging method of choice to depict both acute and chronic myocardial infarction. DE is also the preferred technique to visualise microvascular obstruction which can be seen as hypo-enhanced areas within the hyperenhanced infarcted region (figures 2D, 3D and 5). In addition, DE can be used in non-ischaemic myocardial disease and for the detection of thrombi (box 4, figures 3 and 4).[7]

Recent concern has risen about the safety of gadolinium based contrast agents in patients with advanced renal failure because of a possible association with the development of nephrogenic systemic fibrosis. Despite the rarity of this disorder, preventive measures are therefore now advocated in patients with glomerular filtration rate <30 ml/min/1.73 m^2.[8]

CMR IN PATIENTS WITH AMI

CMR is a safe technique, even in the first days after coronary stent implantation. Artefacts related to stents are minimal and do not interfere with image quality or analysis.

A basic protocol in patients after AMI includes cine imaging and delayed contrast enhanced imaging. It allows the evaluation of function, infarct extent and microvascular obstruction, and can be acquired easily within 30 min. The protocol may be extended by T2 weighted spin echo imaging and first pass imaging for a complete characterisation of the ischaemic region by visualising infarct related oedema and (rest) myocardial perfusion, respectively.

Function

Left ventricular ejection fraction and end-systolic volume are strong predictors of prognosis after AMI.[9] Cine CMR is the gold standard for the quantification of global left and right ventricular volumes, ejection fraction and mass. The high reproducibility of cine CMR ensures the reliable detection of any significant change at follow-up, which makes it the ideal and most cost effective technique for serial evaluation in clinical trials. In successfully reperfused AMI, recovery of stunned myocardium often leads to functional improvement after discharge. Conversely, patients who received late or no reperfusion therapy are at risk of remodelling. Of interest, the cut-off that is generally used to define significant remodelling (an increase in end-diastolic volume ≥20%) is derived from left ventricular invasive contrast angiography, which might not be appropriate when using cine CMR. Current guidelines state that an implantable

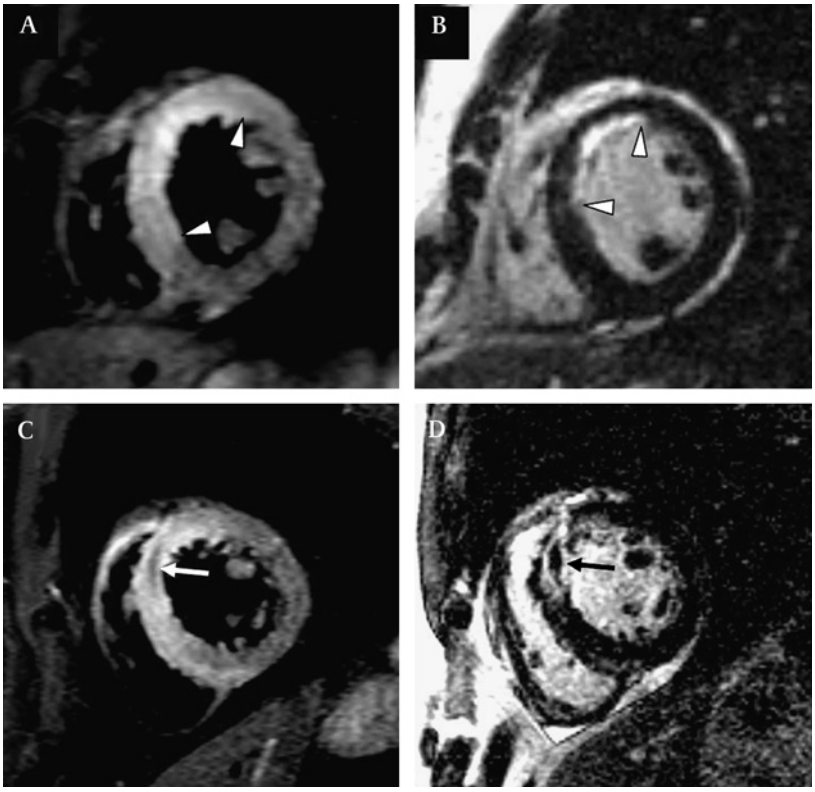

Figure 2 T2 weighted imaging (T2W) versus delayed enhancement (DE). A and B are short axis views from a patient with subendocardial anteroseptal infarction demonstrating infarct-related oedema (white markers, A) extending beyond the borders of the hyperenhanced area (white markers, B). Images C and D are from a patient with transmural anteroseptal infarction showing intramyocardial haemorrhage as a central region of attenuated signal within the region of high signal of infarct related oedema on the T2W image (white arrow, C) and a small central hypo-intense region corresponding to microvascular obstruction on the corresponding DE image (black marker, D).

cardioverter-defibrillator device is indicated when ejection fraction is <30% (<35% in patients in New York Heart Association (NYHA) functional class II–III) 40 days after the acute event.[10] The selection of patients for this expensive therapy requires a technique that provides this information with the highest reproducibility and accuracy possible.

Although the assessment of regional function does not play a major role in risk stratification and prognosis, it may provide the first indication of ischaemic heart disease by showing subtle wall motion abnormalities in the territory of a coronary artery when global volumes and function are still well within normal limits. Right ventricular infarction may complicate inferior infarction and may be detected as regional dysfunction of the diaphragmatic right ventricular wall on the basal short axis cines. However, global function is usually not severely affected, and delayed contrast enhanced imaging may be more sensitive (figure 3C).

Box 2 Indications for T2 weighted spin echo imaging

- Infarct related oedema.
- Myocarditis
- Transplant rejection

Infarct related complications

The large field of view of cine CMR allows the accurate assessment of infarct related complications, such as (pseudo-) aneurysms and pericardial effusion. Mitral regurgitation can be detected with cine CMR, and its mechanism can be further evaluated using contrast enhanced imaging (by showing the infarcted area or papillary muscle involvement). Left ventricular thrombi may develop early after infarction and can be seen as low-intermediate intensity intracavitary structures that may be difficult to differentiate from myocardium that has similar signal intensity on cine images. Thrombi are avascular structures that do not take up contrast and are therefore best detected using delayed contrast enhanced imaging (figure 3D).

Infarct related oedema

The morphological characterisation of acute infarctions by unenhanced T2 weighted (T2W) imaging allows further insight into the pathophysiology of acute coronary syndromes. The reduced cardiomyocyte adenosine triphosphate (ATP) formation that immediately follows acute coronary occlusion inhibits Na^+/K^+-ATPase, and the resulting increased Na^+ and Cl^- concentration leads to intracellular oedema. Inflammation and changes in endothelial permeability further increase myocardial water content. T2W imaging allows the visualisation of infarct related oedema without the use of contrast agents (figure 2).[11]

Oedema is typically related to the acute phase and generally disappears between 3 and 12 weeks after the event. T2W imaging can therefore be used to differentiate between new and old ischaemic disease in patients with suspected acute coronary syndrome and can also be used to evaluate procedure related myocardial injury after percutaneous or surgical revascularisation in patients with old myocardial infarction. Regional increased myocardial water content and high T2W signal intensity is not restricted to acute coronary syndromes but can also be found in other (acute) myocardial disease states, such as myocarditis, transplant rejection or tako tsubo cardiomyopathy.

Since myocardial oedema is one of the earliest manifestations of ischaemia and occurs before the development of definitive and irreversible damage, T2W imaging may be used to visualise the ischaemic area at risk. Both experimental and human studies have shown that the ischaemic region on T2W imaging is consistently larger than the infarcted region at DE imaging (figure 2A).[12] In a canine occlusion–reperfusion model, the area at risk as measured by microspheres showed good correlation with the T2W hyperintense region.[13] The possibility of visualising both the area at risk and the final infarct size in a single (CMR) examination would allow the definition of the amount of salvaged myocardium in patients with reperfused infarction. This would be the ideal end point in

Box 3 Indications for first pass myocardial perfusion CMR

- Detection of coronary artery disease using adenosine stress.
- Microvascular obstruction (no-reflow)

studies evaluating new therapeutic strategies to reduce infarct size. However, further evidence for the relation between area at risk and T2W imaging is needed, and it should be noted that the current T2W imaging technique is not robust and prone to artefacts that may interfere with diagnostic accuracy. In our experience, up to 10–20% of T2W images may be of non-diagnostic quality. Therefore, the exact role of T2W imaging in the assessment of a patient with recent (acute) myocardial infarction remains to be established.

Infarct visualisation

DE imaging is the most sensitive technique for the detection and visualisation of myocardial infarction (figures 2, 3 and 5). Using DE imaging, regional myocardial injury has been demonstrated as early as 1 h after septal ablation in patients with hypertrophic cardiomyopathy, whereas T2W imaging showed regional high signal intensity only after 24 h.[11]

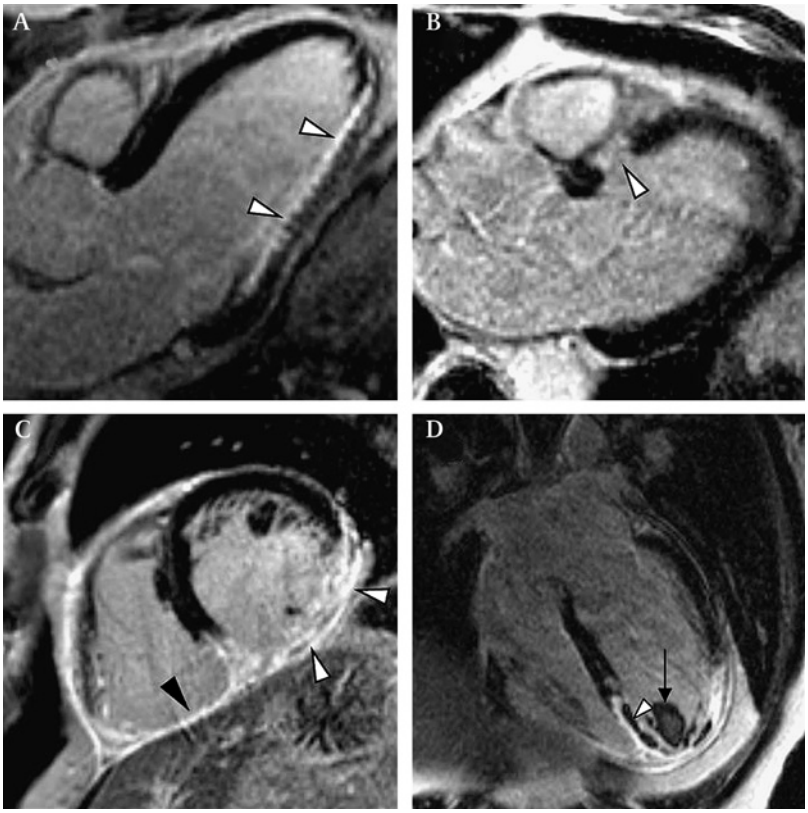

Figure 3 Visualisation of infarction using delayed enhancement imaging. (A) Subendocardial inferolateral infarction. (B) Small but transmural septal infarction with coronary angiography showing occluded first septal branch. (C) Transmural inferolateral infarction (white markers) with right ventricular involvement (black marker). (D) Four chamber view from a patient with 4-day-old reperfused antero-apical infarction, showing transmural hyperenhancement with extensive microvascular obstruction (marker) and a large left ventricular thrombus (arrow).

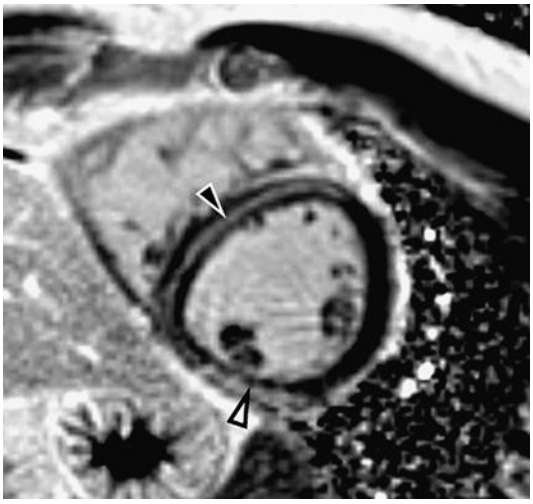

Figure 4 Hyperenhancement in myocarditis. Mid ventricular short axis showing midwall hyperenhancement in the septum (black marker) and subepicardial hyperenhancement in the inferior wall (white marker) from a 40-year-old patient presenting with typical chest pain, positive troponin T, normal ECG and normal coronary arteries.

The high spatial resolution ensures the detection of small, subendocardial infarcts that are missed by single photon emission computed tomography (SPECT).[14] DE detects right ventricular involvement in inferior infarction with higher accuracy than ECG or echocardiography (figure 3C).[15]

In line with the wave front theory, regional extent and transmurality of hyperenhancement may indicate the pathophysiological mechanism of the infarction. Proximal occlusion of a coronary artery followed by timely recanalisation will lead to subendocardial hyperenhancement in a relatively large area corresponding to the coronary artery distribution (figure 3A), whereas permanent (thromboembolic) occlusion of a smaller or distal side branch not accessible to percutaneous revascularisation will cause a smaller, circumscript but more transmural infarction (figure 3B).

The location and transmural extent may also be used to differentiate acute coronary syndromes from myocarditis, which can closely mimic infarction in clinical presentation, enzyme release and ECG. In its typical form, myocarditis shows subepicardial hyperenhancement in the lateral wall or midwall involvement of the septum, in contrast to the subendocardial or transmural enhancement in ischaemic heart disease (figure 4).[16] Tako tsubo or stress related cardiomyopathy mimics acute antero-apical infarction, and may show regional high T2W signal intensity related to oedema, but, as a rule, does not show hyperenhancement despite extensive functional impairment.[17]

Prognosis after AMI is closely related to infarct size. Using DE, both global and segmental infarct size can be quantified and expressed as absolute mass or as a percentage of left ventricular mass. The incremental prognostic value of DE infarct size was recently demonstrated in a study that evaluated 122 patients with ST elevation myocardial

Heart 2010;**96**:237–243. doi:10.1136/hrt.2009.172296

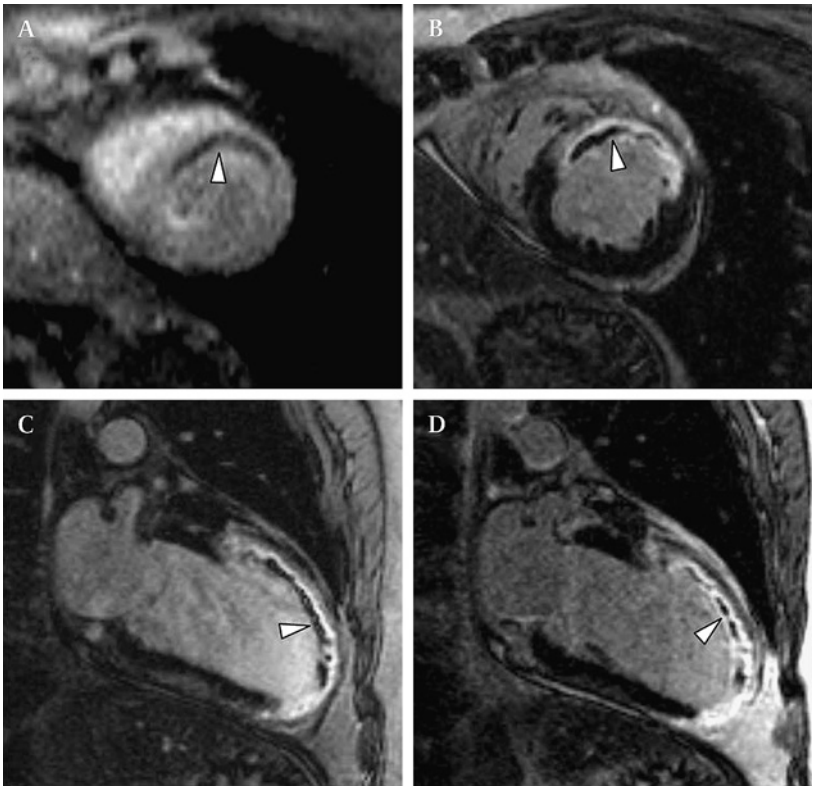

Figure 5 Microvascular obstruction (marker) in a patient with 3-day-old reperfused anterior infarction, as seen on mid ventricular short axis first pass image (A) and DE images in corresponding view (B) and in two chamber orientation (C, D). Delayed enhancement images were acquired 10 (B, C) and 30 min (D) after contrast injection.

infarction.[18] Although left ventricular volumes, ejection fraction and total infarct size were all associated with outcome, total infarct size was the only predictor at multivariate analysis.

Box 4 Indications for delayed contrast enhanced CMR

Ischaemic heart disease:

- Visualisation of acute and chronic myocardial infarction
- Quantification of regional and global infarct extent
- Microvascular obstruction (no-reflow)
- Myocardial viability
- Detection of underlying coronary artery disease in patients with congestive heart failure
- Differentiation between ischaemic and non-ischaemic cardiac disease
- Intracavitary thrombus

Non-ischaemic heart disease:

- Myocarditis
- Hypertrophic cardiomyopathy
- Dilated cardiomyopathy
- Arrhythmogenic right ventricular cardiomyopathy
- Cardiac sarcoidosis
- Cardiac amyloidosis
- Other secondary cardiomyopathies (eg, Gaucher, Fabry, hypereosinophilic syndrome)
- Intracardiac tumour
- Pulmonary hypertension

Viability

Myocardial stunning refers to the prolonged post-ischaemic contractile impairment that can be seen in acute ischaemic syndromes after restoration of flow. The likelihood of functional recovery of stunned myocardium depends on the degree of irreversible damage and is therefore predicted by the transmural extent of hyperenhancement, that can be quantified and is typically expressed as a percentage of segmental area.[19 20] We evaluated 30 patients after acute, reperfused, myocardial infarction and found a strong inverse relation between the likelihood of improvement and segmental infarct extent: dysfunctional segments without hyperenhancement were 3, 14 and 20 times more likely to improve than segments with 1–25%, 26–50%, 51–75% and 76–100% transmural extent of hyperenhancement, respectively.[20] Using the transmural infarct extent to predict functional outcome acknowledges the fact that viability is a gradual rather than a binary phenomenon. Although the use of a single cut-off to separate viable from non-viable facilitates the traditional description of diagnostic accuracy (sensitivity, specificity), it underestimates the full potential of DE imaging.

Low dose dobutamine stress cine CMR is feasible and produces results comparable to echocardiography.[21] However, DE imaging is simpler and more robust and is therefore the preferred technique.

Microvascular obstruction

No-reflow refers to the lack of adequate restoration of flow despite successful revascularisation of the occluded infarct related epicardial coronary artery.[22] It is characterised by regions of ultrastructural damage to the myocardial microvascular bed ('reperfusion injury') with severely impaired tissue perfusion. No-reflow, or its tissue equivalent microvascular obstruction (MVO), is a major prognostic factor after reperfused AMI.

Experimental studies using contrast enhanced CMR have demonstrated that regions that are hypo-enhanced in the first 2 min after contrast injection correspond to no-reflow regions as defined by thioflavin S staining, and are characterised by severely impaired microsphere myocardial blood flow.[5] Serial contrast studies have been used to evaluate the dynamic nature of MVO and its close relation to reperfusion. Very early after reperfusion, blood flow is high, even in thioflavine S-negative (no-reflow) areas, but this is followed by a progressive decrease in flow and an increase in the size of MVO up to threefold during the first 48 h after reperfusion.[23] MVO extent subsequently remains stable between 2 and 9 days after reperfusion, which is therefore considered the optimal window to detect and quantify MVO.[24]

Current contrast enhanced CMR sequences are very sensitive in the detection of MVO. Both first pass imaging and DE imaging can be used to visualise MVO. First pass images reflect myocardial perfusion, which is profoundly impaired in MVO and therefore results in hypo-enhanced regions of

CMR in patients with AMI: key points

In a patient with acute myocardial infarction:

- CMR is a safe examination and can be performed without risks even in the first days after coronary stent implantation.
- Use of gadolinium contrast agents is preferably avoided when glomerular filtration rate is < 30 ml/min/1.73 m^2.
- CMR is optimally performed between 2 and 9 days after reperfusion.

CMR should be considered:

- When there is uncertainty about the diagnosis, and differentiation from other acute, non-ischaemic heart disease (eg, myocarditis) is required.
- When quantification of left or right ventricular volumes, mass or function, or valvular insufficiency is required.
- To assess presence and extent of suspected infarct related complications, such as (pseudo) aneurysm formation or left ventricular thrombus.
- When echocardiography shows moderate or severe impairment of left ventricular function, to provide baseline ejection fraction, estimate the likelihood of functional recovery, and to indicate ICD implantation by providing ejection fraction at follow-up.
- In a patient with (suspected) no-reflow, to help to predict functional outcome and prognosis.

CMR may be used to:

- Evaluate new treatment strategies to reduce infarct size by estimating the amount of salvaged myocardium by using T2W imaging and delayed enhancement imaging.
- Evaluate new treatment strategies to reduce reperfusion injury by the assessment of presence and extent of microvascular damage by contrast enhanced techniques.

varying transmurality (figure 5A). After contrast injection, gadolinium quickly accumulates in the infarcted region, but contrast diffusion into areas with severe microvascular damage is considerably slowed or even absent. With subsequent delayed contrast enhanced imaging, acquired 10–15 min after contrast injection, MVO can be detected as persistent areas of hypo-enhancement, often with a patchy, heterogeneous character and located central and mostly subendocardial, but always spatially confined within the hyperenhanced, infarcted zone (figure 5B–D). Although infarct size remains unchanged on DE images between 5 and 30 min after contrast injection, ongoing slow Gd diffusion into areas with microvascular damage may reduce MVO size (figure 5C,D). MVO is typically related to the acute phase, and myocardial perfusion generally improves at follow-up although impaired perfusion may persist in some regions with the most severe microvascular damage.

First pass imaging is the most sensitive technique, and current sequences detect MVO in 65–87% of patients with reperfused AMI. There is high concordance between the presence of MVO on first pass and DE images, although it follows from the gadolinium kinetics that prevalence at DE imaging is lower with a reported 28–58%.[25 26] Persistent MVO reflects the more severely injured areas and several studies have shown that its presence is a strong marker of outcome, being related to clinical as well as functional adverse events.[20 25–27] Nijveldt *et al* recently compared the prognostic value of first pass and DE to TIMI (Thrombolysis In Myocardial Infarction) flow grade, myocardial blush grade and ST segment resolution in a group of 60 patients with successfully reperfused AMI.[26] Of all parameters, persistent MVO was the most powerful predictor of global left ventricular functional outcome. Furthermore, it had diagnostic value beyond infarct transmurality for the prediction of regional functional outcome.

DE imaging may be the ideal technique to evaluate new strategies to reduce reperfusion injury. MVO can be quantified and expressed as absolute quantity or as a percentage of total infarct mass. For the quantification and comparison of MVO extent, a strict methodology is essential with respect to the time between contrast injection and data acquisition, because the MVO area may shrink with time due to ongoing contrast wash-in.

Severe microvascular injury in large reperfused infarcts may lead to endothelial disruption and extravasation of erythrocytes.[22] The resulting intramyocardial haemorrhage may be demonstrated by non-enhanced T2W imaging, because haemoglobin breakdown products alter regional magnetic tissue properties (figure 2C).[28] CMR may thus provide additional insight into the pathophysiological changes after myocardial infarction and reperfusion. However, the significance of these findings is not yet clear and further study is needed to explore the relation of reperfusion related haemorrhage to infarction, microvascular obstruction and clinical outcome.

CONCLUSIONS

CMR provides a comprehensive evaluation of the patient with recent AMI. The detailed morphological and functional characterisation allows the detection and localisation of infarction and its

You can get CPD/CME credits for Education in Heart

Education in Heart articles are accredited by both the UK Royal College of Physicians (London) and the European Board for Accreditation in Cardiology—you need to answer the accompanying multiple choice questions (MCQs). To access the questions, click on **BMJ Learning: Take this module on BMJ Learning** from the content box at the top right and bottom left of the online article. For more information please go to: http://heart.bmj.com/misc/education.dtl

- **RCP credits:** Log your activity in your CPD diary online (http://www.rcplondon.ac.uk/members/CPDdiary/index.asp)—pass mark is 80%.
- **EBAC credits:** Print out and retain the BMJ Learning certificate once you have completed the MCQs—pass mark is 60%. EBAC/ EACCME Credits can now be converted to AMA PRA Category 1 CME Credits and are recognised by all National Accreditation Authorities in Europe (http://www.ebac-cme.org/newsite/?hit=men02).

Please note: The MCQs are hosted on BMJ Learning—the best available learning website for medical professionals from the BMJ Group. If prompted, subscribers must sign into *Heart* with their journal's username and password. All users must also complete a one-time registration on BMJ Learning and subsequently log in (with a BMJ Learning username and password) on every visit.

Heart 2010;**96**:237–243. doi:10.1136/hrt.2009.172296

complications, and the differentiation from other, non-ischaemic acute heart diseases. CMR can be used to predict functional recovery of stunned myocardium, and it identifies microvascular obstruction which is a major prognostic factor after AMI. In addition, it may be used to evaluate new treatments to reduce infarct size and reperfusion injury, by assessing the area at risk and the extent of microvascular obstruction, respectively.

Contributors AM Beek conceptualised and wrote the article. AC van Rossum was involved in revision and final approval of the article.

Competing interests In compliance with EBAC/EACCME guidelines, all authors participating in Education in *Heart* have disclosed potential conflicts of interest that might cause a bias in the article. The authors have no competing interests.

Provenance and peer review Commissioned; not externally peer reviewed.

REFERENCES

1. **Kozerke S,** Plein S. Accelerated CMR using zonal, parallel and prior knowledge driven imaging methods. *J Cardiovasc Magn Reson* 2008;**10**:29.
2. **Kunz RP,** Oellig F, Krummenauer F, *et al*. Assessment of left ventricular unctions by breath-hold cine MR imaging: comparison of different steady-state free precession sequences. *J Magn Reson Imaging* 2005;**21**:140—8.
3. **Gotte MJW,** Germans T, Russel IK, *et al*. Myocardial strain and torsion quantified by cardiovascular magnetic resonance tissue tagging: studies in normal and impaired left ventricular function. *J Am Coll Cardiol* 2006;**48**:2002—11.
4. **Higgins CB,** Herfkens R, Lipton MJ, *et al*. Nuclear magnetic resonance imaging of acute myocardial infarction in dogs: alterations in magnetic relaxation times. *Am J Cardiol* 1983;**52**:184—8.
5. **Judd RM,** Lugo-Olivieri CH, Arai M, *et al*. Physiological basis of myocardial contrast enhancement in fast magnetic resonance images of 2-day-old reperfused canine infarcts. *Circulation* 1995;**92**:1902—10.

► **Key experimental study, that relates the CMR contrast patterns of hypo- and hyperenhancement to their respective pathophysiological mechanisms of no-reflow and non-viable scar.**

6. **Kim RJ,** Fieno DS, Parrish TB, *et al*. Relationship of MRI delayed contrast enhancement to irreversible injury, infarct age, and contractile function. *Circulation* 1999;**100**:1992—2002.

► **Landmark paper that set the stage for delayed contrast enhanced CMR.**

7. **Marcu CB,** Nijveldt R, Beek AM, *et al*. Delayed contrast enhancement magnetic resonance imaging for the assessment of cardiac disease. *Heart Lung Circ* 2007;**16**:70—8.
8. **Kuo PH,** Kanal E, Abu-Alfa AK, *et al*. Gadolinium-based MR contrast agents and nephrogenic systemic fibrosis. *Radiology* 2007;**242**:647—9.
9. **White HD,** Norris RM, Brown MA, *et al*. Left ventricular end-systolic volume as the major determinant of survival after recovery from myocardial infarction. *Circulation* 1987;**76**:44—51.
10. **Epstein AE,** DiMarco JP, Ellenbogen KA, *et al*. ACC/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the ACC/AHA/NASPE 2002 Guideline Update for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices) developed in collaboration with the American Association for Thoracic Surgery and Society of Thoracic Surgeons. *J Am Coll Cardiol* 2008;**51**:e1—62.
11. **Schulz-Menger J,** Gross M, Messroghli D, *et al*. Cardiovascular magnetic resonance of acute myocardial infarction at a very early stage. *J Am Coll Cardiol* 2003;**42**:513—8.

► **This study demonstrated the early changes in signal intensity in T2W and DE images in patients with hypertrophic cardiomyopathy undergoing septal ablation.**

12. **Friedrich MG,** Abdel-Aty H, Taylor A, *et al*. The salvaged area at risk in reperfused acute myocardial infarction as visualized by cardiovascular magnetic resonance. *J Am Coll Cardiol* 2008;**51**:1581—7.
13. **Aletras AH,** Tilak GS, Natanzon A, *et al*. 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—70.

► **Experimental study showing the potential value of T2W imaging in the depiction of the area at risk.**

14. **Ibrahim T,** Bulow HP, Hackl T, *et al*. Diagnostic value of contrast-enhanced magnetic resonance imaging and single-photon emission computed tomography for detection of myocardial necrosis early after acute myocardial infarction. *J Am Coll Cardiol* 2007;**49**:208—16.
15. **Kumar A,** Abdel-Aty H, Kriedemann I, *et al*. Contrast-enhanced cardiovascular magnetic resonance imaging of right ventricular infarction. *J Am Coll Cardiol* 2006;**48**:1969—76.
16. **Mahrholdt H,** Wagner A, Deluigi CC, *et al*. Presentation, patterns of myocardial damage, and clinical course of viral myocarditis. *Circulation* 2006;**114**:1581—90.
17. **Haghi D,** Fluechter S, Suselbeck T, *et al*. Cardiovascular magnetic resonance findings in typical versus atypical forms of the acute apical ballooning syndrome (Takotsubo cardiomyopathy). *Int J Cardiol* 2007;**120**:205—11.
18. **Wu E,** Ortiz JT, Tejedor P, *et al*. Infarct size by contrast enhanced cardiac magnetic resonance is a stronger predictor of outcomes than left ventricular ejection fraction or end-systolic volume index: prospective cohort study. *Heart* 2008;**94**:730—6.
19. **Choi KM,** Kim RJ, Gubernikoff G, *et al*. Transmural extent of acute myocardial infarction predicts long-term improvement in contractile function. *Circulation* 2001;**104**:1101—7.
20. **Beek AM,** Kuhl HP, Bondarenko O, *et al*. 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.
21. **Kramer CM,** Malkowski MJ, Mankad S, *et al*. Magnetic resonance tagging and echocardiographic response to dobutamine and functional improvement after reperfused myocardial infarction. *Am Heart J* 2002;**143**:1046—51.
22. **Reffelmann T,** Kloner RA. The "no-reflow" phenomenon: basic science and clinical correlates. *Heart* 2002;**87**:162—8.
23. **Rochitte CE,** Lima JA, Bluemke DA, *et al*. Magnitude and time course of microvascular obstruction and tissue injury after acute myocardial infarction. *Circulation* 1998;**98**:1006—14.

► **Key paper that (with ref 24) elucidated the dynamics of MRI contrast patterns in the first week after infarction.**

24. **Wu KC,** Kim RJ, Bluemke DA, *et al*. 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—64.
25. **Hombach V,** Grebe O, Merkle N, *et al*. 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—57.

► **Established the importance of MVO as a prognostic factor after myocardial infarction.**

26. **Nijveldt R,** Beek AM, Hirsch A, *et al*. 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—9.
27. **Wu KC,** Zerhouni EA, Judd RM, *et al*. Prognostic significance of microvascular obstruction by magnetic resonance imaging in patients with acute myocardial infarction. *Circulation* 1998;**97**:765—72.

► **First study to demonstrate the independent prognostic significance of MVO as visualised by contrast enhanced CMR.**

28. **Lotan CS,** Bouchard A, Cranney GB, *et al*. Assessment of postreperfusion myocardial hemorrhage using proton NMR imaging at 1.5 T. *Circulation* 1992;**86**:1018—25.

► **First study that showed the feasibility of T2W imaging to characterise intramyocardial haemorrhage in reperfused infarction.**