

Cardiovascular MRI in acute myocardial infarction

At present, cardiovascular MRI is the only noninvasive diagnostic tool that can combine the assessment of regional and global function, morphology and tissue-specific information in a single investigation. With good spatial and temporal resolution and high contrast-to-noise ratio, cardiovascular MRI is an accurate and feasible tool for the evaluation of ischemic heart disease. It is not only considered to be the gold standard for assessment of myocardial function, but also for the detection of myocardial necrosis and fibrosis. In addition, cardiovascular MRI provides clinically relevant information on stunning, microvascular obstruction, transmural extent of the infarction, hemorrhage and postmyocardial infarction complications such as thrombus, Dressler syndrome and aneuryms.

KEYWORDS: acute myocardial infarction cardiovascular MRI cine delayed enhancement first-pass perfusion hemorrhage microvascular obstruction T2-weighted imaging

Survival of acute myocardial infarction (AMI) has increased in the past decades owing to revascularization by thrombolytic agents, percutaneous coronary intervention (PCI) and improved medical treatment (e.g., β-blockers and ACEinhibitors). Despite this improvement, ischemic heart disease is still the leading cause of death within the Western world mostly due to heart failure, late cardiac death, increased lifespan and increased contributing risk factors (e.g., diabetes mellitus, obesity and smoking) [1]. Patients with nonfatal myocardial infarction (MI) have a risk of illness and premature death up to 15-times higher than the general population owing to recurrent MI, sudden death, angina pectoris, heart failure and stroke [1]. Therefore, the diagnosis of MI is clinically relevant.

At present, the diagnosis of AMI is based on the rise or fall of cardiac biomarkers (e.g., troponines and creatine kinase-MB) in combination with one of the following criteria: ECG changes indicative of ischemia (e.g., ST-elevation, new left bundle branch block and Q-waves), imaging evidence of new loss of viable myocardium or new regional wall motion abnormalities [2]. Although cardiac biomarker elevation is very sensitive for myocardial necrosis, the time window is very small. Furthermore, no information on the infarct location is provided [3]. A limitation of the ECG is the possibility of non-Q-wave infarction and the resolution of the Q-waves over time [3]. Enzymes can be negative and ECG changes can be subtle to none, especially in patients with absent or atypical chest pain,

Echocardiography is an important imaging tool for the detection of (regional) wall motion abnormalities, especially in the acute phase; however, it is not able to give tissue-specific information such as edema or fibrosis owing to ischemic events. Although SPECT and PET are able to give tissue-specific and functional information, the spatial resolution is low. Furthermore, both techniques neglect the transmural extent of the infarction (TEI) and subendocardial infarctions can be missed [4].

All these tools have diagnostic value, but their accuracy is limited. For therapeutic decisionmaking, the extent of the infarction as well as residual left ventricular function are becoming increasingly important. Cardiovascular MRI (CMR) is a good noninvasive diagnostic tool in ischemic heart disease, providing accurate, reproducible and well-validated measurements [5-8]. CMR combines assessment of cardiac morphology, global and regional cardiac function, infarct size, TEI, microvascular obstruction (MVO) and area at risk (AAR) in just one investigation [5-14].

This article provides an overview of the different techniques of CMR and their relevance within patients with AMI.

MRI of the heart

In MRI, a high-strength magnetic field is used in combination with radiofrequency pulses, which causes excitation of the nucleus, giving a signal that can be detected by coils. Therefore, MRI is a safe and noninvasive imaging tool that does not

Tirza Springeling¹, Alexia Rossi¹, Adriaan Moelker¹ & Robert-Jan M van Geuns^{†1}

¹Departments of Cardiology & Radiology, Erasmus University Medical Center, Rotterdam, The Netherlands ¹Author for correspondence: PO box 2040, 3000 CA Rotterdam, The Netherlands Tel.: +31 611 351 486 Fax: +31 107 034 320

-uture

involve exposure to radiation. However, the disadvantage of MRI is that it is a time-consuming technique. To create an image with sufficient spatial resolution, multiple acquisitions need to be acquired. Owing to cardiac and respiratory movement, as well as flow artefacts, imaging of the heart by MRI is challenging. With the introduction of ECG-gating it became possible to synchronize the MRI data acquisition to the heart cycle. Gating can be performed in a prospective or retrospective way depending on the MRI sequence that is used. Prospective gating is used in static imaging using the R-wave as a gating pulse (T1 and T2 imaging) and retrospective gating is used in dynamic imaging (cine and flow imaging). Although gating has overcome most of the cardiac movement difficulties, irregular heart rhythm is still a problem. Realtime imaging is an option, although image quality is reduced. Respiratory movement of the heart can be prevented using breath-holds. Owing to technical advantages and the development of new software, scan time is reduced, which allows imaging within one breath-hold.

At present, the field strength of 1.5 Tesla is preferred for CMR, but 3 Tesla imaging is promising. The higher magnetic field strength increases the signal-to-noise ratio (SNR), which can result in higher spatial resolution [9]. There are still some technical problems to overcome, such as field inhomogeneities and high-energy depositions. Cardiac imaging made by 3 Tesla is especially difficult owing to cardiac movement as well as the increased influence of the magnetic field on the ECG, which induces more gating problems. Breathing artefacts are also prone to influence the image quality. The influence of a higher magnetic field is not equal in the different image modalities. For example, dynamic functional cine imaging is highly susceptible to field inhomogeneity, causing more artefacts and less contrast-to-noise ratio (CNR) [10]. This is in contrast with static imaging, such as morphology and contrast imaging, in which the higher spatial and temporal resolution improves the image quality and may allow reduction of the contrast dose [9]. In addition, perfusion defects are more reliably detected using 3 Tesla, owing to the higher SNR [11].

Assessment of myocardial function

Functional imaging by CMR, also termed cine imaging, is the gold standard for the assessment of left and right ventricular function. At present, the steady-state-free precession (SSFP) technique is preferred for the assessment of ventricular function. Owing to good spatial (1-2 mm) and temporal resolution (20-50 ms) and the high CNR, SSFP allows excellent visualization of the myocardium and its endocardial and epicardial borders. SSFP imaging enables complete coverage of the left ventricle (LV) in several breathholds. The LV is segmentated into several short axis (SA) slices [7,12], allowing the assessment of global function, as well as regional wall motion, visually or quantitatively [5,8]. The SA provides the most reliable imaging planes for measuring LV volumes and myocardial mass. To quantify the global function of the LV, contours are drawn of the endocardial and epicardial border of the ventricular wall. Using the Simpson rule, the end-diastolic volume (EDV), endsystolic volume (ESV), cardiac output, stroke volume and LV ejection fraction (LVEF) can be calculated [13].

Although the interstudy reproducibility is high, care should be taken not to include the most basal slice, which could be a part of the left atrium, and thereby overestimate the left ventricular volume [14]. The partial volume effect of the distal apex can also cause over- or underestimation. This problem can be partly solved by adding the long axis information (four- and two-chamber view) to the SA slices, thereby also reducing the the interstudy variability [7].

Compared with CMR, 2D echocardiography is less accurate and reproducible [14]. 3D echocardiography is more accurate and reproducible compared with 2D echocardiography, with a better correlation with CMR. However, 3D echocardiography tends to underestimate the EDV and ESV and has a wider variability compared with CMR [15,16]. This underestimation can be caused by poor image quality of the apex and inclusion of ventricular trabeculation in the left ventricular mass [15].

Owing to the high CNR, CMR shows accurate regional wall motion abnormalities, as shown in FIGURE 1. In patients with AMI, wall motion abnormalities are the result of ischemia. First, the wall motion becomes hypokinetic; if the ischemia proceeds, it can become akinetic, which can then lead to the wall motion becoming dyskinetic [17,18]. These wall motion abnormalities are reversible if ischemia is resolved before necrosis develops [19–22]. The recovery may take several days and in this period the myocardium is referred to as 'stunned'. The decreased regional wall thickening is directly related to the global function of the LV, resulting in decreased LVEF. After 4–6 months of primary PCI, the LVEF will

be increased in most cases, with 2–7% owing to recovery of stunned myocardium [23–25]. In most patients, there is an increase in EDV and either no decrease or a small decrease in ESV, thereby preserving the cardiac output and stroke volume [23,24,26]. The infarct mass decreases but the remote myocardium mass increases owing to eccentric hypertrophy [27]. The extent of remodeling is influenced by many parameters such as time to reperfusion, no-reflow, collateral filling and TEI.

In addition to cine MRI, regional wall motion can be quantified using a technique known as myocardial tagging. Myocardial tagging applies a saturation grid within the myocardial wall, which allows the characterization of the intramural myocardial wall deformation in three different orientations: longitudinal, radial and in the circumferential direction. Furthermore, this technique allows quantification of torsion, untwisting and diastolic and systolic strain. This technique, although promising, is mostly used for research and is not often used in clinical settings [28].

The functional result of CMR has great prognostic value on its own and is one of the evaluation tools for new therapeutic treatments as an independent prognostic factor. Not only is CMR the gold standard for LVEF and LV volumes, it can also detect post-MI complications such as aneurysms, thrombus and Dressler syndrome (FIGURE 2). Functional CMR can have a direct impact on the management of the patient (e.g., the use of medication and medical devices); and is more frequently used as a primary end point in clinical trials. At present, at least 23 clinical trials use CMR as a primary clinical end point [101].

Cardiovascular MRI & myocardial infarction

Reperfusion by primary PCI is the most optimal treatment for AMI. Infarct size reduction, preserved left ventricular function and improved survival are achieved. The perfusion bed of the occluded coronary artery is defined as the AAR and includes an area of necrosis surrounded by reversible injury [19,29]. The AAR can be divided into three zones: the infarct zone, the no-reflow zone and the salvaged zone. These zones can be visualized using different techniques (Figure 3).

 The infarct area is defined as a necrotic zone of irreversibly damaged myocardial cells. This can be visualized by contrast-enhanced imaging 10 min after the injection of gadolinium.



Figure 1. Regional wall motion abnormalities in the acute and chronic phase. A patient with a reperfused anterior infarction. A two-chamber cine image in the end-diastolic (left) and end-systolic (right) phase in the acute (above) and chronic (below) phase. In the acute phase, there is almost no wall motion in the systolic phase owing to stunning in the anterior wall (arrow). In the chronic phase, the wall motion is partly recovered.

- The no-reflow zone refers to a state of limited or no reperfusion within the infarct core after restoration of flow in the coronary artery and is caused by MVO [21,30,31]. This can be visualized by first-pass perfusion contrast imaging (FPP) and contrast-enhanced imaging 2–10 min after injection of the contrast.
- The salvaged zone can be defined as the area of injury surrounding the necrotic tissue [19,29] that proves reversible after revascularization. This viable edematous tissue shows prolonged postischemic contractile dysfunction (i.e., stunning). It requires hours to days before function is fully restored [32,33]. The salvaged zone is the difference between the actual and potential infarct size. This zone cannot be visualized by one sequence but can be calculated by the difference between the AAR (visualized by T2-weighted imaging) and infarct size (visualized by delayed contrast enhancement).

Assessment of myocardial infarction

Although functional CMR can give an impression of the infarcted area, this assessment is still



Figure 2. Complications of acute myocardial infarction. (A & D) A fourchamber view of a patient with an aneurysm in the lateral wall (arrow) as can be seen in the end-diastolic phase of the cine image **(A)** and the contrast-enhanced image **(D). (B & E)** A four-chamber view of a patient with a thrombus in the apex (arrow) as can be seen in the end-diastolic phase of the cine image **(B)** and the contrast-enhanced image **(E). (C & F)** A four-chamber view of a patient with a large reperfused anterior infarction and Dressler syndrome (arrow), as can be seen in the end-diastolic phase of the cine image **(C)** and the contrast-enhanced image **(F)**.

limited owing to stunning. After administration of gadolinium-based contrast agents, CMR can distinguish between nonviable and viable myocardium regardless of wall motion abnormalities in both acute and chronic infarction [34].

In the normal myocardium there is an influx of gadolinium in the interstitial space but not in the myocytes. In AMI, the cellular membrane of the necrotic myocytes are ruptured. Owing to the rupture, gadolinium can diffuse into the cells. This causes a diminished washout of the gadolinium in the infarcted myocardium compared with the normal myocardium. After at least 10 min the washout of the contrast in the normal myocardium is almost complete, while there is still a high concentration of gadolinium in the infarcted myocardium. This high concentration of contrast gives high signal intensity (SI) (hyperenhancement) on T1-weighted imaging.

Chronic infarction is characterized by collagenous scars with increased interstitial space between the collagenous fibers. The washout of gadolinium is reduced owing to the lack of blood flow, resulting in an increased contrast concentration causing hyperenhancement of the chronic infarct area [35]. There is a good correlation between infarct size and mass imaged by hyperenhancement and histology (TTC staining) in the acute and chronic stadium of the infarction [34-37]. Although the extent and intensity of the hyperenhancement are more pronounced in the chronic infarction, the sensitivity is lower (94%) compared with the acute stadium (99%) in enzyme-proven infarction [27]. Delayed contrast-enhanced imaging is able to visualize subendocardial infarctions owing to the high spatial resolution. Although very small infarctions, CK-MB less than threetimes the normal value are sometimes difficult to detect [27].

The technique used for infarct imaging is a T1-weighted inversion recovery gradient echo technique, also termed delayed enhancement (DE), contrast-enhanced or late-gadoliniumenhancement. The paramagnetic property of gadolinium causes a shortening of the T1 relaxation time, which results in enhancement of



Figure 3. Cardiovascular MRI findings on T2-weighted and delayed enhancement images. (**A**) Schematic model of the short axis, (**B**) T2-weighted image and (**C**) contrast-enhanced image of a patient with a reperfused anterior infarction. (**A**) Schematic model representing the different zones within the perfusion territory of the occluded artery. 1: Normal myocardium, 2: area at risk, 3: infarct zone, 4: microvascular obstruction, 5: salvaged area. (**B**) The T2-weighted image shows the area at risk as a high signal intensity (2). Within the area at risk, hemorrhage is visible as an area with low signal intensity (asterisk). (**C**) The contrast-enhancement image shows the hyperenhancement of the infarcted area (3) and within the core of the infarction a hypoenhanced area is visible, representing microvascular obstruction.

the infarcted area. The inversion pulse is used to depress (null) the signal of the normal myocardium to achieve enormous contrast with the infarcted area (bright). The timing of this inversion pulse is manually selected and depends on the contrast agent, pharmacokinetics and cardiac function. Images are acquired at least 10 min after the intravenous injection of the contrast agent. Infarct imaging can be performed until at least 30 min after the injection of the contrast [27].

Hyperenhancement can be detected in the AAR at least 1 h after acute ischemic injury [38,39]. The necrosis starts in the subendocardial border and then progresses in a wavefront towards the epicardium with increasing occlusion time of the culprit lesion [4]. After re-establishment of blood flow, the infarct size increases in the first 24-48 h owing to the reperfusion injury and apoptosis, but also owing to edema and cellular elements, and can almost double in this time period [40]. After the first 2 days, the area of enhancement remains approximately the same size for up to 14 days. In the following weeks to months, the infarct size decreases by approximately 19-31% [24,38,41]. The decrease in infarct size and mass is caused by the combination of resolvement of edema, hemorrhage and inflammation, as well as replacement of necrotic myocytes by collagenous scar tissue [34,40,42]. Infarct size (in combination with functional CMR) is becoming more popular for the use as primary end point in new trials [101].

Besides DE, both SPECT and PET are able to detect MIs, but DE imaging is more sensitive for subendocardial infarctions and the TEI [13,35]. TEI is an important prognostic factor for regional function of dysfunctional segments. Segments with smaller TEI are more likely to improve in contractile function owing to the significant amount of preserved unenhanced stunned myocardium. The improvement of dysfunctional segments can be seen in patients with an AMI and primary PCI, but also in patients with a chronic (total) occlusion who are revascularized [24,43,44]. In AMI, dysfunctional segments with a TEI up to 75% have a good chance of improvement, probably owing to the presence of stunned myocardium [24,27]. In FIGURE 4 the myocardial function and TEI of two patients with a reperfused left anterior descending artery occlusion are shown; patient A with a transmural infarction and patient B with a nontransmural infarction.

Although the initial infarct size is a good predictor for global functional follow-up [25,45], the TEI takes into account the amount of viable tissue that can be functional at follow-up. Therefore, TEI is a better predictor for improvement of the global and regional contractile function compared with infarct size [4].

Delayed enhancement is able to detect scarring in patients with or without symptoms or ECG changes. Patients without a history of MI but with hyperenhancement have a higher chance for adverse cardiac events and a higher mortality rate compared with patients without hyperenhancement [46]. Meijs *et al.* demonstrated that in a high-risk population without a history of MI or angina pectoris the prevalence of myocardial scarring is 9.4% [47]. In patients with angina pectoris, but no history of MI, the prevalence is even higher at 20–28% [46,48–50].

Patients with MI have a higher chance of sudden cardiac death owing to ventricular tachycardia or ventricular fibrillation. Although at present a low LVEF is considered an indication for an implantable-cardioverter defibrillator (ICD), Bello *et al.* demonstrated that infarct size



Figure 4. Cardiovascular MRI findings on function and delayed enhancement in the acute and chronic phase. Patient A had a reperfused left anterior descending artery occlusion. The two-chamber delayed enhancement image shows a transmural infarction of the anterior wall and apex (bright). In the acute phase, there is no wall motion in the anterior wall, although the end-diastolic wall thickness is normal. In the chronic phase, there is decreased end-diastolic wall thickness and aneurysmatic wall motion. Patient B had a reperfused left anterior descending artery occlusion. The two-chamber delayed enhancement image shows a nontransmural infarction of the anterior wall and apex (bright). In the acute phase, there is no wall motion in the anterior wall, although the end-diastolic wall thickness is still normal. In the chronic phase, the end-diastolic wall thickness is still normal. In the chronic phase, the wall motion is partly recovered. measured by DE is a better predictor for monomorphic ventricular tachycardia [51]. DE is able to visualize the infarct size and the tissue heterogeneity within the infarct zone. In the periphery of the infarct and the border zone the enhancement of the infarct is not homogenous, probably owing to areas with necrosis and bundles of viable myocytes [52]. The extent of tissue heterogeneity in the infarct periphery correlates well with an increased susceptibility to ventricular arrhythmias and with higher all-cause mortality [53,54]. The tissue heterogeneity can be quantified into the core and peri-infarct regions based on SI thresholds. A region of interest is chosen in the remote, noninfarcted myocardium, and the upper limit of normal SI was defined as peak remote SI. The total infarcted area has more than one SI, the core of the infarction has more than three SI and the peri-infarct region has teo to three SI above remote normal myocardium, as can be seen in FIGURE 5 [53,54]. Although promising, the impact of tissue heterogeneity in daily clinical practice is not yet clear and more research should be carried out.

Another major advantage of DE is the pattern of hyperenhancement. Rather than simply the presence or extent of enhancement, the pattern may offer important information on the origin of myocardial damage. The pattern of hyperenhancement can differentiate between differential diagnoses of acute chest pain with elevated cardiac enzymes; for example, between AMI and myocarditis [55,56].

Assessment of perfusion defects

Reperfusion of the myocardium is not always complete after successful revascularization of the culprit lesion by primary PCI. This can be seen



Figure 5. Gray zone measurement. (A) Delayed enhancement short axis image of a patient with an infarction of the septal and anterior wall. **(B)** Analyzed image; epicardial contour (gray line), endocardial contour (dashed), infarct area (area within dotted line), infarct core (dark gray area between the arrows in the infarct area).

by persistent ST-elevation on ECG or diminished myocardial blush grade despite thrombolysis in myocardial infarction (TIMI) 3 flow [57]. This is caused by focal regions of inadequate flow owing to MVO, the so-called no-reflow zone or no-flow phenomenon [32,33,58]. The mechanism of reperfusion damage has not yet been completely delineated but is thought to be caused by multiple processes including disturbed endothelial function, production of oxygen free radicals, altered vascular reactivity, cell swelling, microemboli and cell damage owing to attraction and activation of neutrophils. In 30–87% of the revascularized patients, MVO is present [23,24,41,59], which is related to adverse clinical outcome [13,57].

Microvascular obstruction causes diminished or no wash in of the contrast and can be visualized by CMR with two different techniques (FIGURE 6). First, FPP – also termed early hypoenhancement - visualizes the contrast uptake (wash in) of the myocardium directly after injection of the contrast agent. FPP is a dynamic technique acquiring images during at least 40 consecutive heart beats while administrating contrast, thereby acquiring multiple SA slices every R-R interval, or in case of a very high heart rate, every two R-R intervals. MVO is shown by a persistent region of hypoenhancement in the subendocardial layer of the AAR. The limitations of FPP are the relatively low spatial resolution, low CNR and not full coverage of the LV. Second, T1-weighted inversion recovery gradient echo, which is the same sequence that is used for DE. As the infarction is visualized by the bright hyperenhanced area, MVO is visualized by the persistent region of hypoenhancement in the subendocardial core of the infarcted myocardium. For MVO, this technique can be used after 2 min and after 10 min, known as intermediate and late MVO, respectively. In the waiting period after the administration of contrast, the contrast can diffuse into the MVO. Therefore, DE can miss a less obstructed myocardium, which will fill in with contrast within the waiting period and can then be seen on FPP. Late hypoenhancement seems to indicate more severe MVO. Nijveldt et al. compared the different techniques to visualize MVO and showed that late MVO was the best predictor for global and regional function recovery [20]. To our knowledge, no other comparison has been made to date.

The presence of MVO predicts a worse clinical outcome [45], with a higher chance of cardiovascular events such as death, reinfarction, congestive heart failure, stroke and unstable angina than predicted for patients without MVO [31].



Figure 6. Different cardiovascular MRI techniques for microvascular obstruction. First-pass perfusion; **(A)** before contrast injection, **(B)** contrast in the right ventricle, **(C)** contrast in the left and right ventricle, **(D)** inflow in the myocardium of the left ventricle with no inflow of contrast (owing to microvascular obstruction) in the septal and anterior wall (between the arrows). **(E)** Delayed enhancement image of the same patient. Within the infarct area (bright area between asterisks) there is still no inflow of contrast owing to severe microvascular obstruction (black area between arrows).

Several studies investigated the relationship between MVO, infarct size and the recovery of LV function. There appears to be a positive relationship between the presence and the extent of the MVO and an increased reperfusion time [26]. Furthermore, the infarct size is larger and LVEF is decreased and will not improve at follow-up [20,23,45,60,61]. The end-diastolic wall thickness is more decreased and wall thickening is more impaired in patients at follow-up compared with patients without MVO. In addition, there is an inverse relationship between the transmural extent of the MVO and the wall thickening at follow-up [23,24,45].

Both MVO and infarct size are independent predictors for remodeling at follow-up. At present, it is not clear which is best for predicting change in LVEF and LV volumes. Baks *et al.* showed that infarct size was the best predictor for adverse remodeling [45]; in the study by Nijveldt *et al.*, late MVO was the best predictor [20], Shapiro *et al.* demonstrated that TEI was the most robust predictor [12] and Hombach *et al.* proposed a combination of infarct size, TEI and MVO [60]. Further research is needed to determine the predictive value of MVO with or without infarct size.

First-pass perfusion contrast imaging can also be used for the detection of ischemia by comparing stress and rest FPP. This technique has been established in patients with stable and unstable angina and has the potential to detect ischemia in AMI patients with multivessel disease after treatment of the culprit lesion by primary PCI [62–66]. The prognostic value of CMR in patients with AMI and the combination of viability and ischemia detection in one diagnostic investigation can be beneficial, but is still under research at present.

Assessment of the area at risk & salvaged area

The current goal for medical and interventional therapies is to minimize infarct size. The best way to demonstrate the effect of therapies is to relate the infarct size to the initial AAR. The AAR is dependent on multiple factors including time to reperfusion, collateral flow and preconditioning [67]. The salvaged area is the portion of the AAR that survives the ischemic period. To determine the salvaged area we have to make a distinction between stunned-viable and necrotic myocardium within the AAR. During ischemia the myocytes swell owing to failure of energy-regulated membrane channels and subsequent sodium and water influx causing edema. If the ischemia persists, cell membranes disintegrate, causing the onset of actual necrosis [68]. The stunned myocardium can be distinguished from necrotic myocardium by wall

motion improvement during low-dose dobutamine therapy. However, this approach can be problematic if a residual stenosis is present in the infarct-related artery and it is also difficult to determine the lateral borders [4]. SPECT is currently considered the reference technique for quantifying the AAR in humans. Disadvantages of this technique are the necessity of 24-h availability of the isotope, injection of the tracer during coronary occlusion, imaging shortly after reperfusion therapy and radiation [18,67]. Recently, unenhanced T2-weighted spin echo (T2) imaging has been re-evaluated as a measure for the AAR visualizing the infarct related edema. Myocardial edema gives a high SI owing to the long T2-relaxation time of protons bound in free water [68,69]. T2 has been considered technically challenging owing to the long echo times, the reduced spatial resolution and low SNR. Current pulse sequences with dedicated cardiac coils have overcome some of these problems [67].

Several human and animal studies support the finding that T2 can retrospectively visualize the AAR. In animal research, a strong correlation is shown between the high T2 SI and fluorescent microspheres for the AAR [19,70]. There was also no significant difference in the determination of the AAR between SPECT and T2 imaging [18].

Recently, Abdel-Aty et al. demonstrated that in dogs T2 is able to image edema in acute ischemic myocyte injury before onset of irreversible injury [68]. Approximately 28 min (maximum 34 min) after the onset of coronary occlusion, there was a visual change in SI and the CNR increased. After reperfusion, the CNR increased even further [68]. In humans, edema could not be seen in patients 1 h after acute induced MI by alcohol in patients with hypertrophic obstructive cardiomyopathy, but could be seen after 1 day. In patients with acute coronary syndrome, who were enzyme-negative before MRI, edema was seen on T2 in 69% of the patients who developed positive biomarkers within 14 h after onset of symptoms [71]. The edema can be visualized for at least 1 month after acute ischemic injury and is not detectable after 3 months [38]. Therefore, T2-imaging is suggested to reliably differentiate between acute and chronic MI [67,72] and can quantify the AAR and the salvage area [67,73]. This makes T2-imaging an useful diagnostic tool in clinical settings such as unstable ischemia and evolving infarction, although it is not standardized procedure and is still under study [68].

Assessment of the hemorrhage in the infarction core

T2-weighted imaging can also differentiate between hemorrhagic and nonhemorrhagic infarctions. Reperfusion can cause intramyocardial hemorrhage by extravazation of red blood cells through severely damaged endothelial cell walls into the extravascular space. This hemorrhaged zone expands gradually after reperfusion as has been demonstrated in experimental research [74,75]. Owing to the paramagnetic effects of deoxygenated hemoglobin and methemoglobin, there is a shortening of the T2 relaxation time, causing a hypointense core within the infarction (FIGURE 3). The prevalence of hemorrhage in patients with AMI is approximately 24-49% [76,77]. Hemorrhage is only observed in patients with MVO and is associated with longer time to reperfusion, diminished TIMI flow before revascularization and more necrosis [78,79]. In addition, the infarct size and the extent and size of MVO is larger in patients with hemorrhage compared with patients without hemorrhage [77]. In patients

Table 1. Appropriateness criteria for cardiac computed tomography and cardiovascular MRI.	
Indication	Appropriateness
Evaluation of LV function following AMI in patients with low image quality from echocardiogram	А
Evaluation of LV function following AMI	U
Quantification of LV function in patients with discordant information	А
Evaluation of differential diagnosis (myocarditis) in CAG-negative but positive cardiac enzymes	А
Determination of the location and extent of myocardial necrosis including no reflow after AMI	А
Determination viability prior to revascularization	А
Detection of CAD by stress imaging in patients with chest pain syndrome, intermediate pretest probability and the echocardiogram being uninterpretable or unable to exercise	А
Detection of CAD by stress imaging in patients with acute chest pain and ST-elevations and/or enzyme elevation	
Evaluation of cardiac mass (suspected thrombus)	А
Evaluation of pericardial conditions	А
A: Appropriate; AMI: Acute myocardial infarction; CAD: Coronary artery disease; I: Inappropriate; LV: Left ventricular; U: Uncertain.	

Data adapted from [80

with hemorrhage, LV volumes are increased and LVEF is decreased in the acute and chronic stadium compared with patients without hemorrhage. There is more adverse remodeling and no improvement of LVEF at follow-up by contrast to patients without hemorrhage [77]. Like infarct size and MVO, it is unclear whether hemorrhage is a better predictor for the change in LVEF and LV volumes. Beek *et al.* showed that the presence of hemorrhage is no predictor for the change in LVEF [76], but Ganame *et al.* showed that hemorrhage is the best predictor regardless of the initial infarct size [77].

More research should be carried out to conclude the influence of MVO, hemorrhage and infarct size on remodeling.

Cardiovascular MRI indications & protocols

Although CMR is able to evaluate and quantify ventricular function, volumes and mass, as well as the AAR, viability and no-reflow in one investigation, CMR is not yet a standard tool in the evaluation of patients with AMI. This is mainly because it is a relatively expensive specialized technology with cheaper and more practical options for follow-up available, such as echocardiography.

The advantage of CMR is that it is able to differentiate between MI and differential diagnoses such as myocarditis, pericarditis, Tako–Tsubo syndrome and coronary spasm owing to drug abuse (e.g., cocaine).

Therefore, CMR should always be considered in patients, presenting with acute chest pain and (ischemic) ECG abnormalities or enzyme elevation but with normal coronaries in angiography. Another indication for CMR is for the evaluation of ventricular function and volumes in patients with poor echocardiogram image quality [80]. In addition, CMR is a sensitive tool in the detection of postinfarction complications such as pericardial effusion (Dressler syndrome), (pseudo)aneurysms, ventricular septum defect and thrombus, especially in the apical part of the heart or the inferolateral wall and the right ventricle. Quantification of ventricular function and volumes in order to identify patients who are at high risk for heart failure or have an indication for an ICD is another possible indication for CMR [80]. In patients with multivessel disease, CMR could be an interesting tool for the detection of ischemia in the nonculprit lesion with stress FPP as well as viability testing of the nonacute infarcted segments. However, this is still being researched and is not yet clinically

implemented. CMR is a relative new technology and as such the indications for CMR in daily practice are not yet standardized. In 2006, the American College of Cardiology Foundation (ACCF), together with key specialty, and subspecialty societies evaluated the appropriate use



Figure 7. Different cardiovascular MRI techniques and their current clinical indication and performing time in patients with acute myocardial infarction. of CMR in patients to improve patient care and health outcomes in a cost-effective manner. TABLE 1 shows a selection of the criteria concerning patients with AMI and their appropriateness [80]. These criteria should be seen as an initial guide for the responsible use of CMR.

In addition, the current protocols for specific cardiac disease are not standardized worldwide. In 2008, the task force of the Society for CMR recommended protocols for different cardiac disease. The following protocol was recommended in AMI patients: LV structure and function (using SSFP); T2-weighted imaging at least in the areas with wall motion abnormalities (although this is optional); FPP (early no-reflow) and consideration to repeat FPP or early gadolinium enhancement within the first 1-3 min after contrast infusion (intermediate no-reflow); and late gadolinium enhancement for late noreflow and necrosis imaging [81]. FIGURE 7 shows an overview of our CMR protocol for patients with AMI with the different techniques, the indications and the performing time.

Cardiovascular MRI contraindications

There are some patient-related contraindications for MRI and CMR in certain circumstances such as hemodynamic instability, nonsinus rhythm, dyspnea, inability to hold breath for at least 10–15 s, obesity and claustrophobia.

Owing to the high magnetic field and the rapid changes of magnetic field necessary to generate an image, there are some contraindications for MRI such as the presence of a pacemaker, ICD, Schwan–Ganz catheters, intra-aortic balloon pump, metal clips for (brain) aneurysms and metal in the orbita. Coronary stents are no contraindication and patients with stents can be scanned immediately after placement.

Furthermore, there are contraindications for the use of gadolinium-based contrast agents such as known or suspected allergy to gadolinium, pregnancy, breastfeeding and known or suspected renal failure. The use of gadolinium in patients with a glomerular filtration rate of less than 30 ml/min is a risk for developing nephrogenic systemic fibrosis.

Conclusion

Owing to the good spatial and temporal resolution, accuracy and reproducibility, CMR is an adequate and reliable noninvasive diagnostic tool for cardiac disease and in patients with AMI. At present, CMR is the gold standard for quantitative measurements of left ventricular functional parameters as well as infarct determination. In patients with a diagnosis of AMI, CMR is able to accurately visualize the global and regional function (cine imaging), distinguish between viable and nonviable myocardium (using DE), as well as between differential diagnoses such as myocarditis, and CMR can visualize the no-reflow zone (FPP and DE), the AAR (T2) and hemorrhage in the infarct core (T2). Besides the diagnostic value of CMR, CMR results can have direct impact on the management of AMI patients.

Executive summary

Assessment of myocardial function

Owing to good spatial and temporal resolution and high contrast-to-noise ratio, cardiovascular MRI (CMR) is the gold standard for the assessment of global and regional function and is therefore an excellent tool for the assessment of remodeling.

Assessment of myocardial infarction

- Delayed enhanced imaging allows visualization of acute myocardial necrosis and collagenous fibrosis.
- Infarct size and the transmural extent of infarction are good predictors for improvement of function.

Assessment of microvascular obstruction

- Microvascular obstruction can be visualized by first-pass perfusion and by delayed enhancement.
- Patients with microvascular obstruction have increased remodeling of the left ventricle and have a worse clinical outcome.

Assessment of the area at risk

Edema can be visualized by T2-weighted imaging and therefore allows for the noninvasive identification of the area at risk in patients with acute myocardial infarction.

Assessment of hemorrhage

- CMR T2-weighted imaging is the only noninvasive tool for the imaging of myocardial hemorrhage.
- Patients with hemorrhage have increased remodeling of the left ventricle.

Conclusion

- CMR allows assessment of regional and global function, morphology and tissue-specific information in one investigation with a good spatial and temporal resolution and a high contrast-to-noise ratio.
- CMR is the gold standard for assessment of myocardial function and viability in acute and chronic myocardial infarction.
- CMR allows visualization of the remodeling process after acute myocardial infarction.
- More research should be carried out in order to determine the relationship between time to reperfusion, infarct size, microvascular obstruction and hemorrhage and the changes in left ventricular volumes and ejection fraction.

Future perspective

Cardiovascular MRI is becoming more generally available, and new and improved techniques are being developed, making CMR an excellent noninvasive diagnostic tool. Clinical research has already proven that CMR has influence on the management and prognosis in patients with AMI. Therefore, CMR is a promising tool in daily clinical practice as well as end points in (clinical) research.

Bibliography

Papers of special note have been highlighted as: • of interest

of considerable interest

- Rosamond W, Flegal K, Furie K *et al.*: Heart disease and stroke statistics – 2008 update: a report from the American heart association statistics committee and stroke statistics subcommittee. *Circulation* 117(4), E25–E146 (2008).
- 2 Thygesen K, Alpert JS, White HD *et al.*: Universal definition of myocardial infarction. *Circulation* 116(22), 2634–2653 (2007).
- Alpert JS, Thygesen K, Antman E, Bassand JP: Myocardial infarction redefined

 a consensus document of the joint
 European Society of Cardiology/American
 College of Cardiology committee for the
 redefinition of myocardial infarction.
 J. Am. Coll. Cardiol. 36(3), 959–969 (2000).
- 4 Choi KM, Kim RJ, Gubernikoff G, Vargas JD, Parker M, Judd RM: Transmural extent of acute myocardial infarction predicts long-term improvement in contractile function. *Circulation* 104(10), 1101–1107 (2001).
- 5 Sechtem U, Sommerhoff BA, Markiewicz W, White RD, Cheitlin MD, Higgins CB: Regional left ventricular wall thickening by magnetic resonance imaging: evaluation in normal persons and patients with global and regional dysfunction. *Am. J. Cardiol.* 59(1), 145–151 (1987).
- 6 Pennell DJ, Sechtem UP, Higgins CB et al.: Clinical indications for cardiovascular magnetic resonance (CMR): consensus panel report. Eur. Heart J. 25(21), 1940–1965 (2004).
- 7 Kirschbaum SW, Baks T, Gronenschild EH et al.: Addition of the long-axis information to short-axis contours reduces interstudy variability of left-ventricular analysis in cardiac magnetic resonance studies. *Invest. Radiol.* 43(1), 1–6 (2008).
- 8 Peshock RM, Rokey R, Malloy GM et al.: Assessment of myocardial systolic wall thickening using nuclear magnetic resonance imaging. J. Am. Coll. Cardiol. 14(3), 653–659 (1989).

Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

- Klumpp B, Fenchel M, Hoevelborn T *et al.*: Assessment of myocardial viability using delayed enhancement magnetic resonance imaging at 3.0 Tesla. *Invest. Radiol.* 41(9), 661–667 (2006).
- 10 Michaely HJ, Nael K, Schoenberg SO et al.: Analysis of cardiac function – comparison between 1.5 Tesla and 3.0 Tesla cardiac cine magnetic resonance imaging: preliminary experience. *Invest. Radiol.* 41(2), 133–140 (2006).
- Araoz PA, Glockner JF, Mcgee KP *et al.*: 3 Tesla MR imaging provides improved contrast in firST-pass myocardial perfusion imaging over a range of gadolinium doses. *J. Cardiovasc. Magn. Reson.* 7(3), 559–564 (2005).
- 12 Shapiro MD, Nieman K, Nasir K et al.: Utility of cardiovascular magnetic resonance to predict left ventricular recovery after primary percutaneous coronary intervention for patients presenting with acute ST-segment elevation myocardial infarction. Am. J. Cardiol. 100(2), 211–216 (2007).
- 13 Shapiro MD, Guarraia DL, Moloo J, Cury RC: Evaluation of acute coronary syndromes by cardiac magnetic resonance imaging. *Top. Magn. Reson. Imaging* 19(1), 25–32 (2008).
- 14 Grothues F, Moon JC, Bellenger NG, Smith GS, Klein HU, Pennell DJ: Interstudy reproducibility of right ventricular volumes, function, and mass with cardiovascular magnetic resonance. *Am. Heart J.* 147(2), 218–223 (2004).
- 15 Soliman OI, Kirschbaum SW, van Dalen BM et al.: Accuracy and reproducibility of quantitation of left ventricular function by real-time three-dimensional echocardiography versus cardiac magnetic resonance. Am. J. Cardiol. 102(6), 778–783 (2008).
- 16 Kim WY, Sogaard P, Kristensen BO, Egeblad H: Measurement of left ventricular volumes by 3-dimensional echocardiography with tissue harmonic imaging: a comparison with magnetic resonance imaging. *J. Am. Soc. Echocardiogr.* 14(3), 169–179 (2001).

- 17 Cerqueira MD, Weissman NJ, Dilsizian V et al.: 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 105(4), 539–542 (2002).
- 18 Hedstrom E, Engblom H, Frogner F et al.: 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. 11(1), 38 (2009).
- 19 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* 113(15), 1865–1870 (2006).
- 20 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.* 52(3), 181–189 (2008).
- One of the first studies that compared different parameters concerning microvascular obstruction.
- 21 Rochitte CE, Lima JA, Bluemke DA et al.: Magnitude and time course of microvascular obstruction and tissue injury after acute myocardial infarction. *Circulation* 98(10), 1006–1014 (1998).
- 22 Schulz-Menger J, Strohm O, Waigand J, Uhlich F, Dietz R, Friedrich MG: The value of magnetic resonance imaging of the left ventricular outflow tract in patients with hypertrophic obstructive cardiomyopathy after septal artery embolization. *Circulation* 101(15), 1764–1766 (2000).

- 23 Choi CJ, Haji-Momenian S, Dimaria JM et al.: Infarct involution and improved function during healing of acute myocardial infarction: the role of microvascular obstruction. J. Cardiovasc. Magn. Reson. 6(4), 917–925 (2004).
- 24 Baks T, van Geuns RJ, Biagini E *et al.*: Recovery of left ventricular function after primary angioplasty for acute myocardial infarction. *Eur. Heart J.* 26(11), 1070–1077 (2005).
- 25 Nijveldt R, Beek AM, Hofman MB *et al.*: Late gadolinium-enhanced cardiovascular magnetic resonance evaluation of infarct size and microvascular obstruction in optimally treated patients after acute myocardial infarction. *J. Cardiovasc. Magn. Reson.* 9(5), 765–770 (2007).
- 26 Francone M, Bucciarelli-Ducci C, Carbone I et al.: Impact of primary coronary angioplasty delay on myocardial salvage, infarct size, and microvascular damage in patients with ST-segment elevation myocardial infarction: insight from cardiovascular magnetic resonance. J. Am. Coll. Cardiol. 54(23), 2145–2153 (2009).
- 27 Kim RJ, Albert TS, Wible JH *et al.*: Performance of delayed-enhancement magnetic resonance imaging with gadoversetamide contrast for the detection and assessment of myocardial infarction: an international, multicenter, double-blinded, randomized trial. *Circulation* 117(5), 629–637 (2008).
- First international, multicenter study that assessed myocardial infarction by delayed enhancement.
- 28 Rademakers F, van de Werf F, Mortelmans L, Marchal G, Bogaert J: Evolution of regional performance after an acute anterior myocardial infarction in humans using magnetic resonance tagging. J. Physiol. 546(Pt 3), 777–787 (2003).
- 29 Tilak GS, Hsu LY, Hoyt RF Jr, Arai AE, Aletras AH: *In vivo* T2-weighted magnetic resonance imaging can accurately determine the ischemic area at risk for 2-day-old nonreperfused myocardial infarction. *Invest. Radiol.* 43(1), 7–15 (2008).
- 30 Jaffe R, Charron T, Puley G, Dick A, Strauss BH: Microvascular obstruction and the no-reflow phenomenon after percutaneous coronary intervention. *Circulation* 117(24), 3152–3156 (2008).
- 31 Wu KC, Zerhouni EA, Judd RM *et al.*: Prognostic significance of microvascular obstruction by magnetic resonance imaging in patients with acute myocardial infarction. *Circulation* 97(8), 765–772 (1998).
- 32 Kloner RA, Jennings RB: Consequences of brief ischemia: stunning, preconditioning, and their clinical implications: part 2. *Circulation* 104(25), 3158–3167 (2001).

- 33 Kloner RA, Jennings RB: Consequences of brief ischemia: stunning, preconditioning, and their clinical implications: part 1. *Circulation* 104(24), 2981–2989 (2001).
- 34 Kim RJ, Fieno DS, Parrish TB et al.: Relationship of MRI delayed contrast enhancement to irreversible injury, infarct age, and contractile function. *Circulation* 100(19), 1992–2002 (1999).
- 35 Mahrholdt H, Klem I, Sechtem U: Cardiovascular MRI for detection of myocardial viability and ischaemia. *Heart* 93(1), 122–129 (2007).
- 36 Moelker AD, Baks T, van den Bos EJ et al.: Reduction in infarct size, but no functional improvement after bone marrow cell administration in a porcine model of reperfused myocardial infarction. Eur. Heart J. 27(24), 3057–3064 (2006).
- 37 Moelker AD, Baks T, Wever KM et al.: Intracoronary delivery of umbilical cord blood derived unrestricted somatic stem cells is not suitable to improve LV function after myocardial infarction in swine. J. Mol. Cell. Cardiol. 42(4), 735–745 (2007).
- 38 Schulz-Menger J, Gross M, Messroghli D, Uhlich F, Dietz R, Friedrich MG: Cardiovascular magnetic resonance of acute myocardial infarction at a very early stage. J. Am. Coll. Cardiol. 42(3), 513–518 (2003).
- One of the first papers to visualize the area at risk of necrosis over time by T2-weighted imaging and delayed enhancement.
- 39 Hillenbrand HB, Kim RJ, Parker MA, Fieno DS, Judd RM: Early assessment of myocardial salvage by contrast-enhanced magnetic resonance imaging. *Circulation* 102(14), 1678–1683 (2000).
- 40 Reimer KA, Jennings RB: The changing anatomic reference base of evolving myocardial infarction. Underestimation of myocardial collateral blood flow and overestimation of experimental anatomic infarct size due to tissue edema, hemorrhage and acute inflammation. *Circulation* 60(4), 866–876 (1979).
- 41 Nijveldt R, Hofman MB, Hirsch A *et al.*: Assessment of microvascular obstruction and prediction of short-term remodeling after acute myocardial infarction: cardiac MR imaging study. *Radiology* 250(2), 363–370 (2009).
- 42 Matsuzaki M, Gallagher KP, Kemper WS, White F, Ross J Jr: Sustained regional dysfunction produced by prolonged coronary stenosis: gradual recovery after reperfusion. *Circulation* 68(1), 170–182 (1983).
- 43 Baks T, van Geuns RJ, Duncker DJ *et al.*: Prediction of left ventricular function after drug-eluting stent implantation for chronic total coronary occlusions. *J. Am. Coll. Cardiol.* 47(4), 721–725 (2006).

- 44 Kirschbaum SW, Baks T, van den Ent M et al.: Evaluation of left ventricular function three years after percutaneous recanalization of chronic total coronary occlusions. Am. J. Cardiol. 101(2), 179–185 (2008).
- 45 Baks T, van Geuns RJ, Biagini E *et al.*: Effects of primary angioplasty for acute myocardial infarction on early and late infarct size and left ventricular wall characteristics. *J. Am. Coll. Cardiol.* 47(1), 40–44 (2006).
- 46 Kwong RY, Chan AK, Brown KA *et al.*: Impact of unrecognized myocardial scar detected by cardiac magnetic resonance imaging on event-free survival in patients presenting with signs or symptoms of coronary artery disease. *Circulation* 113(23), 2733–2743 (2006).
- 47 Meijs MF, Bots ML, Cramer MJ et al.: Unrecognised myocardial infarction in subjects at high vascular risk: prevalence and determinants. *Heart* 95(9), 728–732 (2009).
- 48 Kim HW, Klem I, Shah DJ et al.: Unrecognized non-Q-wave myocardial infarction: prevalence and prognostic significance in patients with suspected coronary disease. *PLoS Med.* 6(4), E1000057 (2009).
- 49 Kwong RY, Sattar H, Wu H et al.: Incidence and prognostic implication of unrecognized myocardial scar characterized by cardiac magnetic resonance in diabetic patients without clinical evidence of myocardial infarction. *Circulation* 118(10), 1011–1020 (2008).
- 50 Barbier CE, Bjerner T, Johansson L, Lind L, Ahlstrom H: Myocardial scars more frequent than expected: magnetic resonance imaging detects potential risk group. *J. Am. Coll. Cardiol.* 48(4), 765–771 (2006).
- 51 Bello D, Fieno DS, Kim RJ *et al.*: Infarct morphology identifies patients with substrate for sustained ventricular tachycardia. *J. Am. Coll. Cardiol.* 45(7), 1104–1108 (2005).
- 52 Saeed M, Lund G, Wendland MF, Bremerich J, Weinmann H, Higgins CB: Magnetic resonance characterization of the periinfarction zone of reperfused myocardial infarction with necrosis-specific and extracellular nonspecific contrast media. *Circulation* 103(6), 871–876 (2001).
- 53 Yan AT, Shayne AJ, Brown KA *et al.*: Characterization of the peri-infarct zone by contrast-enhanced cardiac magnetic resonance imaging is a powerful predictor of post-myocardial infarction mortality. *Circulation* 114(1), 32–39 (2006).
- 54 Schmidt A, Azevedo CF, Cheng A et al.: Infarct tissue heterogeneity by magnetic resonance imaging identifies enhanced cardiac arrhythmia susceptibility in patients with left ventricular dysfunction. *Circulation* 115(15), 2006–2014 (2007).

- 55 Mahrholdt H, Wagner A, Judd RM, Sechtem U, Kim RJ: Delayed enhancement cardiovascular magnetic resonance assessment of non-ischaemic cardiomyopathies. *Eur. Heart J.* 26(15), 1461–1474 (2005).
- Important paper discussing the delayed enhancement patterns and their differential diagnosis.
- 56 Mccrohon JA, Moon JC, Prasad SK *et al.*: Differentiation of heart failure related to dilated cardiomyopathy and coronary artery disease using gadolinium-enhanced cardiovascular magnetic resonance. *Circulation* 108(1), 54–59 (2003).
- 57 Schroder R, Dissmann R, Bruggemann T et al.: Extent of early ST segment elevation resolution: a simple but strong predictor of outcome in patients with acute myocardial infarction. J. Am. Coll. Cardiol. 24(2), 384–391 (1994).
- 58 Kloner RA, Ganote CE, Jennings RB: The 'no-reflow' phenomenon after temporary coronary occlusion in the dog. *J. Clin. Invest.* 54(6), 1496–1508 (1974).
- 59 Nijveldt R, Beek AM, Hirsch A *et al.*: 'No-reflow' after acute myocardial infarction: direct visualisation of microvascular obstruction by gadolinium-enhanced CMR. *Neth. Heart J.* 16(5), 179–181 (2008).
- 60 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.* 26(6), 549–557 (2005).
- 61 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.* 17(10), 2572–2580 (2007).
- 62 Bernhardt P, Engels T, Levenson B, Haase K, Albrecht A, Strohm O: Prediction of necessity for coronary artery revascularization by adenosine contrast-enhanced magnetic resonance imaging. *Int. J. Cardiol.* 112(2), 184–190 (2006).
- 63 Bernhardt P, Spiess J, Levenson B et al.: Combined assessment of myocardial perfusion and late gadolinium enhancement in patients after percutaneous coronary intervention or bypass grafts: a multicenter study of an integrated cardiovascular magnetic resonance protocol. JACC Cardiovasc. Imaging 2(11), 1292–1300 (2009).
- 64 Bettencourt N, Chiribiri A, Schuster A, Nagel E: Assessment of myocardial ischemia and viability using cardiac magnetic resonance. *Curr. Heart Fail. Rep.* 6(3), 142–153 (2009).

- 65 Klein C, Gebker R, Kokocinski T *et al.*: Combined magnetic resonance coronary artery imaging, myocardial perfusion and late gadolinium enhancement in patients with suspected coronary artery disease. *J. Cardiovasc. Magn. Reson.* 10(1), 45 (2008).
- 66 Lerakis S, Mclean DS, Anadiotis AV et al.: Prognostic value of adenosine stress cardiovascular magnetic resonance in patients with low-risk chest pain. J. Cardiovasc. Magn. Reson. 11(1), 37 (2009).
- 67 Wright J, Adriaenssens T, Dymarkowski S, Desmet W, Bogaert J: Quantification of myocardial area at risk with T2-weighted CMR: Comparison with contrast-enhanced CMR and coronary angiography. *JACC* 2(7), 825–831 (2009).
- 68 Abdel-Aty H, Cocker M, Meek C, Tyberg JV, Friedrich MG: Edema as a very early marker for acute myocardial ischemia: a cardiovascular magnetic resonance study. *J. Am. Coll. Cardiol.* 53(14), 1194–1201 (2009).
- First experimental study that demonstrated that T2-weighted imaging is able to detect early edema.
- 69 Garcia-Dorado D, Oliveras J, Gili J et al.: Analysis of myocardial oedema by magnetic resonance imaging early after coronary artery occlusion with or without reperfusion. *Cardiovasc. Res.* 27(8), 1462–1469 (1993).
- 70 Dymarkowski S, Ni Y, Miao Y et al.: Value of T2-weighted magnetic resonance imaging early after myocardial infarction in dogs: comparison with bis-gadoliniummesoporphyrin enhanced T1-weighted magnetic resonance imaging and functional data from cine magnetic resonance imaging. *Invest. Radiol.* 37(2), 77–85 (2002).
- 71 Cury RC, Shash K, Nagurney JT et al.: Cardiac magnetic resonance with T2weighted imaging improves detection of patients with acute coronary syndrome in the emergency department. *Circulation* 118(8), 837–844 (2008).
- 72 Abdel-Aty H, Zagrosek A, Schulz-Menger J et al.: Delayed enhancement and T2-weighted cardiovascular magnetic resonance imaging differentiate acute from chronic myocardial infarction. *Circulation* 109(20), 2411–2416 (2004).
- 73 Friedrich MG, Abdel-Aty H, Taylor A, Schulz-Menger J, Messroghli D, Dietz R: The salvaged area at risk in reperfused acute myocardial infarction as visualized by cardiovascular magnetic resonance. *J. Am. Coll. Cardiol.* 51(16), 1581–1587 (2008).
- 74 Ito H: No-reflow phenomenon and prognosis in patients with acute myocardial infarction. *Nat. Clin. Pract.* 3(9), 499–506 (2006).

- 75 van den Bos EJ, Baks T, Moelker AD *et al.*: Magnetic resonance imaging of haemorrhage within reperfused myocardial infarcts: possible interference with iron oxide-labelled cell tracking? *Eur. Heart J.* 27(13), 1620–1626 (2006).
- First study demonstrating hemorrhage by noninvasive imaging.
- 76 Beek AM, Nijveldt R, van Rossum AC: Intramyocardial hemorrhage and microvascular obstruction after primary percutaneous coronary intervention. *Int. J. Cardiovasc. Imaging* 26(1), 49–55 (2010).
- 77 Ganame J, Messalli G, Dymarkowski S *et al.*: Impact of myocardial haemorrhage on left ventricular function and remodelling in patients with reperfused acute myocardial infarction. *Eur. Heart J.* 30(12), 1440–1449 (2009).
- 78 Garcia-Dorado D, Theroux P, Solares J et al.: Determinants of hemorrhagic infarcts. Histologic observations from experiments involving coronary occlusion, coronary reperfusion, and reocclusion. Am. J. Pathol. 137(2), 301–311 (1990).
- 79 Pislaru SV, Barrios L, Stassen T, Jun L, Pislaru C, van de Werf F: Infarct size, myocardial hemorrhage, and recovery of function after mechanical versus pharmacological reperfusion: effects of lytic state and occlusion time. *Circulation* 96(2), 659–666 (1997).
- Hendel RC, Patel MR, Kramer CM et al.: 80 ACCF/ACR/SCCT/SCMR/ASNC/NASCI/ SCAI/SIR 2006 appropriateness criteria for cardiac computed tomography and cardiac magnetic resonance imaging: a report of the American College of Cardiology Foundation Quality Strategic Directions Committee Appropriateness Criteria Working Group, American College of Radiology, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, American Society of Nuclear Cardiology, North American Society for Cardiac Imaging, Society for Cardiovascular Angiography and Interventions, and Society of Interventional Radiology. J. Am. Coll. Cardiol. 48(7), 1475-1497 (2006).
- 81 Kramer CM, Barkhausen J, Flamm SD, Kim RJ, Nagel E: Standardized cardiovascular magnetic resonance imaging (CMR) protocols, society for cardiovascular magnetic resonance: board of trustees task force on standardized protocols. *J. Cardiovasc. Magn. Reson.* 10(1), 35 (2008).

Website

101 Health USNIo: clinicaltrials.gov (2009) http://clinicaltrials.gov/ct2/results?term=mag netic+resonance+infarct+size&pg=1