EuroIntervention

Magnetic resonance imaging for myocardial viability

Hans-Marc J. Siebelink[1]*, MD, PhD; Hildo J. Lamb[2], MD, PhD

1. Department of Cardiology, Leiden University Medical Center, Leiden, The Netherlands; 2. Department of Radiology, Leiden University Medical Center, Leiden, The Netherlands*

The authors have no conflicts of interest to declare.

KEYWORDS
Magnetic resonance imaging, viability, revascularisation, cardiomyopathy

Abstract

Detection of myocardial viability is an important issue that needs to be addressed when patients with dysfunctional myocardium are considered to be revascularised. The pathophysiological substrate may include myocardial hibernation, myocardial stunning, or both. The greatest benefit is in terms of myocardial function recovery and prognosis is obtained if the revascularised vascular territory contains viable myocardium. Viable myocardium can be detected with nuclear techniques (SPECT, PET), low dose dobutamine stress echocardiography and MRI. With MRI robust detection of viable myocardium can be performed with delayed enhancement (with gadolinium contrast agent), low dose dobutamine stress, and stress/rest perfusion imaging.

For recovery of myocardial function there are relatively small differences between all available techniques, whereas for improvement of prognosis all techniques perform equally. Myocardial delayed enhancement imaging can also visualise micro-embolisation as a result of percutaneous coronary intervention. Furthermore, MRI delayed enhancement enables differentiation between ischaemic and non-ischaemic heart disease and can identify specific cardiomyopathies.

** Corresponding author: Department of Cardiology C-5-P, Leiden University Medical Center, PO Box 9600, 2300 RC Leiden, The Netherlands*
E-mail: h.j.siebelink@lumc.nl

Introduction

Myocardial viability assessment plays an important role in clinical management to select patients who will benefit or not from coronary revascularisation. Historically, myocardial viability was assessed with nuclear techniques en stress echocardiography. Magnetic resonance imaging (MRI) is rapidly emerging as an alternative technique to assess myocardial viability. Moreover, MRI allows comprehensive assessment of cardiac anatomy and function in a non-invasive fashion, which can contribute to patient management.

Viability assessment: why?

Medical treatment in patients with chronic coronary artery disease results in impaired survival compared to revascularisation and the impact on survival is related to the severity of left ventricular (LV) dysfunction[1,2].

The pathophysiology related to this observation is that a mismatch of demand and supply leads to myocardial hibernation, myocardial stunning, and/or repetitive stunning and results in impaired LV function. Although, hibernation, stunning, and/or repetitive stunning seem separate entities, there is considerable overlap. Therefore, the term viable dysfunctional myocardium is better for clinical practice. Non-invasive imaging techniques can help to identify viable dysfunctional myocardium. Revascularisation of viable dysfunctional myocardium has been demonstrated to result in improved LV function as demonstrated by Tillisch[3] and various other groups. From a clinical point of view also prognosis is important. Patients with evidence of viable dysfunctional myocardium benefit from revascularisation for prognosis, but similar patients who were treated medically were at high risk for cardiac events[4]. It was also demonstrated that patients without viable dysfunctional myocardium are at increased risk for perioperative complications and should be treated medically[5]. This concept of benefit in prognosis from revascularisation of viable dysfunctional myocardium only, and medical management of patients without viable dysfunctional myocardium was confirmed in a meta-analysis of 3,088 patients (Figure 1)[6].

Thus, detection of viable dysfunctional myocardium is relevant for clinical management and data show that patients with moderately and also with severely impaired LV function benefit from revascularisation if dysfunctional myocardium is viable. To date MR imaging, echocardiography and nuclear techniques are available for this purpose and all can differentiate between viable dysfunctional myocardium and irreversibly damaged (infarcted) dysfunctional myocardium.

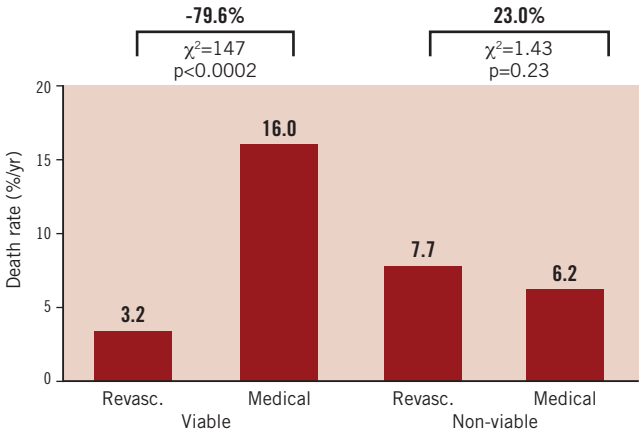

Figure 1. Data from a meta-analysis of 3,088 patients[6]. Death rates for patients with and without myocardial viability treated by revascularisation or medical therapy. There is 79.6% reduction in mortality for patients with viability treated by revascularisation (p<0.0001). In patients without myocardial viability, there was no significant difference in mortality with revascularisation versus medical therapy. Reprinted with permission from the publisher Elsevier.

Assessment of viable dysfunctional myocardium

MRI functional imaging

MR imaging provides reproducible and high resolution (1.5-2.0 mm; depending on used sequences and equipment) images of cardiac anatomy and cardiac function. Imaging of myocardial function may reveal no wall motion abnormalities in regions with an infarct to up to 50% transmurality. The reason that these areas are not detected as dysfunctional is that the remaining non-infarcted myocardium may compensate for the loss on contractile function. Another reason is that areas of normal myocardium adjacent to the infarcted myocardium may draw the infarcted myocardium in systole, thus showing (passive) myocardial motion called tethering. Functional MR imaging can also detect areas with dysfunctional myocardium that may contain viable but dysfunctional myocardium, or show non-viable dysfunctional myocardium.

As mentioned before, it is important to detect the viable dysfunctional myocardial regions that may recover function after revascularisation and that may lead to an improved prognosis for the patient. For assessment of viable dysfunctional myocardium different MRI techniques can be used. Most important techniques are delayed enhancement imaging, and dobutamine stress imaging. Also myocardial perfusion MR imaging provides information on myocardial viability.

MRI delayed enhancement imaging

Gadolinium chelates are used in MR imaging as contrast agents. Gadolinium is a metabolically inert molecule that is distributed in the extracellular compartment. In normal myocardium the gadolinium shows rapid diffusion from intravascular compartment to extracellular compartment and then is rapidly washed out. In case of acute myocardial infarction, cellular membrane integrity has been lost, thereby increasing the extracellular compartment. In chronic infarcted myocardium, myocardial cells are replaced with fibrosis, and this also causes increased extracellular compartment. With gadolinium administration the increased extracellular compartment will contain a greater amount of gadolinium and shows a slower washout rate compared to normal myocardium. This physiological property is the key to the visualisation of non-viable dysfunctional myocardium. When imaging is performed the heart is

given a magnetic pre-pulse to change the magnetisation of the myocardium. This magnetisation is gradually lost and magnetisation will return to zero. Normal myocardium and infarcted myocardium have different rates of losing magnetisation and will reach the zero level at a different time. Imaging of the area of interest is then chosen at the moment when the normal myocardium reaches the zero level and will appear black. The infarcted myocardium has not reached the zero level and will therefore appear white (delayed enhancement). An example is shown in Figure 2. This technique was first applied by McNamara and coworkers in 1986 in dogs[8]. Since then the technique has been refined by other groups and to date delayed enhancement is the cornerstone of MR viability imaging[8]. Histological data confirmed that areas with delayed enhancement show cellular necrosis and fibrosis[9]. However, in the acute setting of myocardial infarction the infarcted area is also oedematous as result of the myocardial damage. This leads to increased extracellular space and increases the area of delayed enhancement on MR imaging in the acute setting. However, this phenomena is only temporary because, when the oedema resolves after 1-4 weeks, the delayed enhancement volume will be reduced 30% and then remains at a stable level[8,10].

The high spatial resolution of MR imaging – in contrast to nuclear and echocardiographic techniques – enables differentiation between sub-endocardial and transmural infarcts. This is particularly important in management of patients, because before performing a revascularisation procedure the benefit of this procedure in terms of left ventricular function recovery and prognosis must be weighted to the periprocedural risks. Kim and coworkers demonstrated that the likelihood of recovery of function is inversely correlated to the amount of the transmural extent of delayed enhancement[11]. In 50 patients MR delayed enhancement imaging was performed before revascularisation and almost no segments with >75% transmural extent showed recovery of contractile function, whereas segments without delayed enhancement showed very high likelihood of functional recovery (Figure 3). In clinical practice usually 50% of transmural extent is considered a discriminatory value between reversible and irreversible myocardial injury (Figure 2).

A specific entity of non-viable infarcted myocardium that can be detected with delayed enhancement imaging is microvascular obstruction (MVO). Infarcted myocardium may show persistent limited perfusion in the infracted area as a result of microvascular obstruction by necrotic debris, micro-emboli, platelets and other cells. As a result on delayed enhancement imaging this area appears black – as gadolinium cannot penetrate this area – within the area of delayed enhanced myocardium (white). Microvascular obstruction was observed to be a prognostic factor that predicts post infarct complications (i.e., death, heart failure) and left ventricular remodelling[12]. An example of this phenomena is shown in Figure 4.

The evidence that delayed enhancement predicts recovery of myocardial function is confirmed by several groups; however reports on the relation between delayed enhancement and prognosis are scarce. Small studies reported that larger degree of infarctions are associated with a higher risk of post infarct complications, heart failure and the inducibility of ventricular tachycardia[12,13]. A larger study of 857 patients showed that the presence of delayed enhancement was an independent predictor of adverse outcome for patients with and without coronary artery disease[14]. This observation remained also valid when only patients

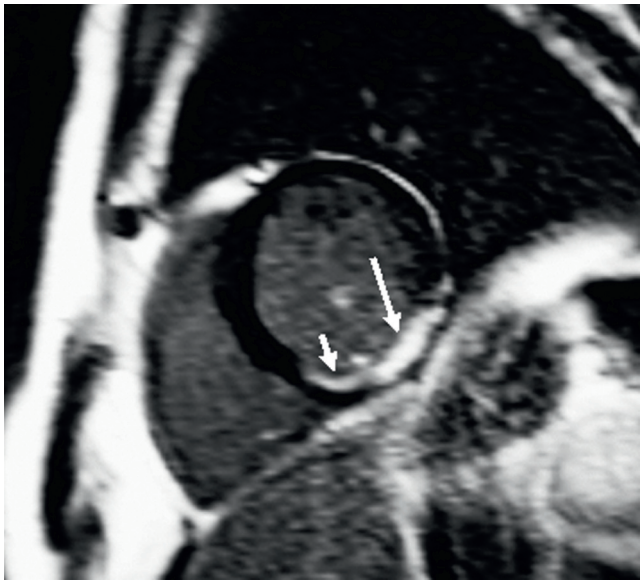

Figure 2. Short axis delayed enhancement image of left ventricle. Normal myocardium is depicted in black. Non-viable infarcted myocardium is white (arrows). Long arrow points out transmural delayed enhancement and short arrow non-transmural delayed enhancement.

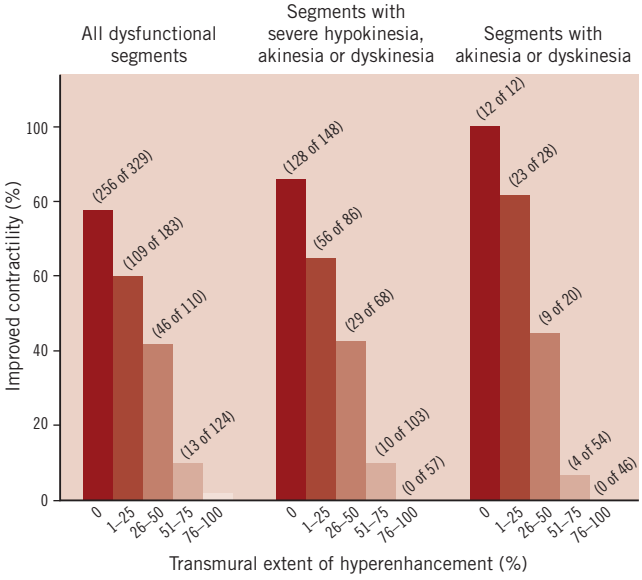

Figure 3. Relation between the transmural extent of hyperenhancement before revascularisation and the likelihood of increased contractility after revascularisation. Data are shown for all 804 dysfunctional segments and separately for the 462 segments with at least severe hypokinesia and the 160 segments with akinesia or dyskinesia before revascularisation. For all three analyses, there was an inverse relation between the transmural extent of hyperenhancement and the likelihood of improvement in contractility[11]. Reprinted with permission from the publisher NEJM.

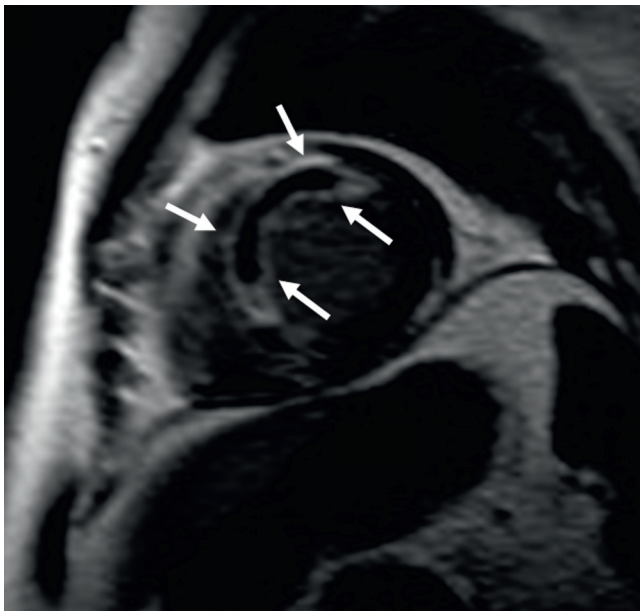

Figure 4. Short axis delayed enhancement image of left ventricle. Microvascular obstruction is shown as a black core surrounded by white delayed enhancement (arrows).

with coronary artery disease were studied (n=642) and delayed enhancement predicted adverse events in patients with preserved and non-preserved left ventricular ejection fraction. Another study illustrates the strength of delayed enhancement imaging by demonstrating that in 76% of patients without known coronary artery disease an unrecognised myocardial infarction was present at MRI which was not detected with electrocardiography and that even the presence of very small areas (2%) of delayed enhancement resulted in higher risk for adverse events[15]. This observation is in agreement with the fact that patients who experienced non-Q wave infarctions are at increased risk for adverse events. Thus, the data show that the presence and extent of delayed enhancement is associated to an impaired prognosis. However, to date there are no MR imaging data that show improved prognosis after revascularisation of viable dysfunctional myocardium. The evidence of benefit from revascularisation of viable dysfunctional myocardium is largely derived from nuclear and echocardiographic data6, but there is no reason that this concept is not applicable to viable dysfunctional myocardium detected with MR imaging.

MRI dobutamine stress

For prediction of recovery of myocardial function, delayed enhancement imaging delineates the non-viable myocardium. The other dysfunctional surrounding regions which appear viable, are considered to bear the potential to recover function when revascularised. However, delayed enhancement does not assess the functional state of the surrounding (viable) myocardium. The surrounding myocardium may be normal, remodelled, hibernating, stunned, and or ischaemic and there may exist different degrees of dysfunction. Therefore not all revascularised myocardium recovers function as predicted with delayed enhancement. To address this issue a "positive" selection of the viable dysfunctional can be made with dobutamine stress MR imaging. Low-dose dobutamine infusion may improve contractile function and cellular energetics in hypoperfused myocardium. A typical observed pattern is the biphasic response: first improvement in contractile function at low dose due to stimulation of the inotropic reserve of the viable myocardium and then at higher dose a worsening of contractile function due to prolonged imbalance between demand and supply. In contrast infarcted non-viable myocardium does not show any change in contractility in response to dobutamine infusion (Figure 5). This concept has been extensively validated in echocardiography[16]. For MR imaging dobutamine stress provides good prediction of myocardial recovery. Compared to delayed enhancement imaging prediction may be even better with dobutamine stress due to the "positive" selection principle[17], but whether dobutamine stress selection leads to a better prognosis is not investigated.

MRI perfusion imaging

MRI perfusion imaging is predominantly a technique to assess impairment of myocardial perfusion reserve to detect haemodynamically significant stenosis. Gadolinium contrast is infused in the blood pool, spreads to the myocardium and then is washed out. Infusion of contrast can be done during vasodilator stress and in resting conditions. The changes in perfusion can be depicted with series of multiple images at different locations of the heart (typically: apical, mid, and basal region) and can be assessed visually and quantitatively. Irrespective of the stress result, myocardium that is viable shows a normal perfusion at rest. When both stress and rest perfusion show abnormal perfusion in a dyskinetic region the myocardium depicts non-viable myocardium (Figure 5). In clinical practice both perfusion imaging and delayed enhancement are combined so that after perfusion sequences, delayed enhancement imaging is performed[18].

Quantification in MRI

Data on function, delayed enhancement and perfusion obtained with MR imaging are preferably analysed and displayed according to the American Heart Association Working Group proposed 17 segment model and vascular territories (Figure 6)[19]. The left ventricle is divided into four short axis slices (basal, six segments; mid, six segments; apical, four segments; apex, one segment) to allow regional analysis. Assessment of regional function is done by interpreting all 17 myocardial segments preferably in short- and long axis slices. Wall thickening is usually scored using: 0=normal, 1=mild hypokinesia, 2=severe hypokinesia, 3=akinesia, 4=dyskinesia. Wall motion can also be assessed quantitatively with programs that involve delineation of endo- and epicardial contours in systole and diastole. Delayed enhancement is scored by determination of the transmural extent of enhancement: 0=no enhancement; 1=1-25% enhancement; 2=26-50% enhancement; 3=51-75% enhancement; 4=76-100% enhancement. Delayed enhancement can also be assessed quantitatively and then enhancement will be stated as a percentage of the total myocardium. For perfusion imaging using visual scoring perfusion defects are defined as focal areas of diminished myocardial enhancement and appear darker compared to normal segments. Myocardial perfusion can also be assessed quantitatively using

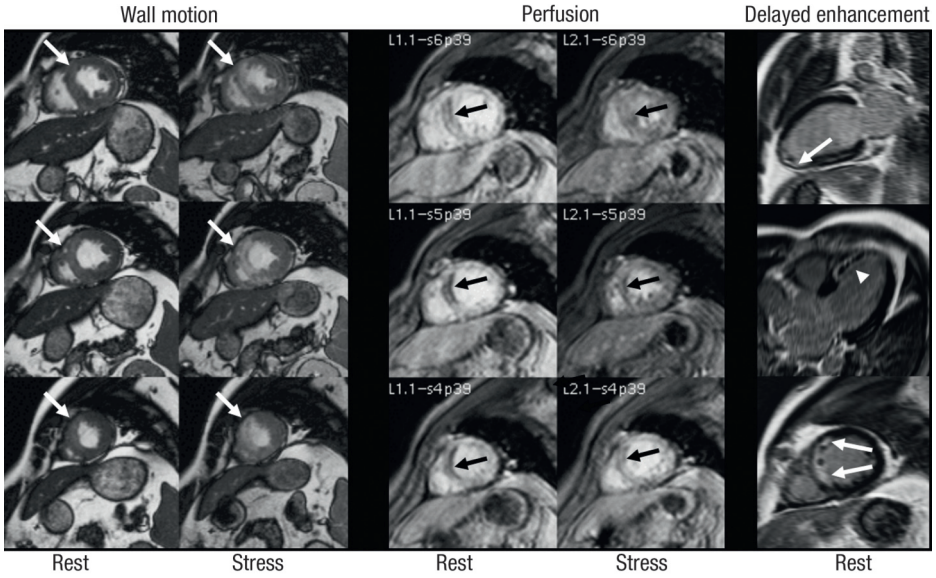

Figure 5. Short-axis views at mid ventricular to apical levels of end-systolic regional wall motion and myocardial perfusion at rest and during dobutamine stress. After administration of 10 gamma low dose dobutamine no improvement in wall motion is seen (white arrows). The perfusion images show a fixed perfusion defect during rest and stress (black arrows). Delayed enhancement images show delayed enhancement (white arrows) and microvascular obstruction (arrowhead) in the interventricular septum on 2-chamber, 4-chamber, and short-axis views. The absent regional wall motion, the fixed perfusion defect and almost transmural delayed enhancement with microvascular obstruction are compatible with non-viable myocardium.

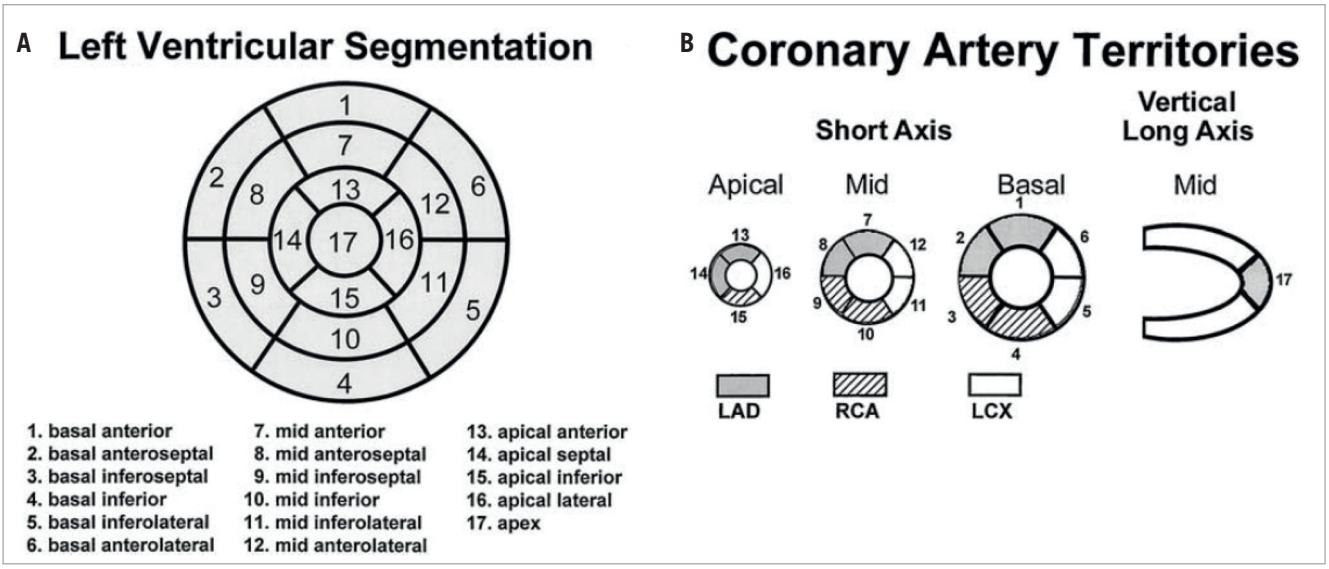

Figure 6 A) Display, on a circumferential polar plot, of the 17 myocardial segments and the recommended nomenclature for tomographic imaging of the heart[19]. Reprinted with permission from the publisher Elsevier. B) Assignment of the 17 myocardial segments to the territories of the left anterior descending (LAD), right coronary artery (RCA), and the left circumflex coronary artery (LCX)[19]. Reprinted with permission from the publisher Elsevier.

technically rather difficult modelling. However, for clinical management visual interpretation is more practical and shows high sensitivity (93%), but only moderate specificity (60%) compared to angiography.

Comparison to other techniques

Detection of myocardial viability is, apart from MR imaging, also feasible with nuclear techniques such as positron emission tomography (PET), single photon emission computerised tomography (SPECT) and low dose dobutamine echocardiography. All techniques are robust and can be used for clinical management of viability issues. However, when comparing effectiveness of techniques, the quality of the data is dependent on the amount of experience with the technique in a specific centre. Frequently centres concentrate on 2-3 techniques, rather than performing all. The use of MR imaging is restricted to patients who do not have cardiac devices, do not have metal objects and are not claustrophobic. Since viability issues frequently play a role in patients with heart failure it is recommended that heart failure patients undergo viability evaluation before internal cardiac defibrillator (ICD) implantation. For patients who already have an ICD, nuclear techniques or

echocardiography would be the techniques of choice until MR-compatible devices are available.

The advantage of MR imaging is that because of the high spatial resolution, it can detect small infarcts that were missed by SPECT imaging[20]. The 'postitive' detection of viable dysfunctional myocardium with nuclear techniques and dobutamine stress MRI or echocardiography are the advantages over MRI delayed enhancement imaging. For recovery of LV function all techniques show good sensitivity and specificity (Figure 7)[21] and MRI shows comparable results (sensitivity 96%, specificity 84%)[22]. Data on prognosis of outcome after revascularisation or refraining from revascularisation show that PET, SPECT or dobutamine echocardiography show similar results[6]. For MR imaging no such data are available yet.

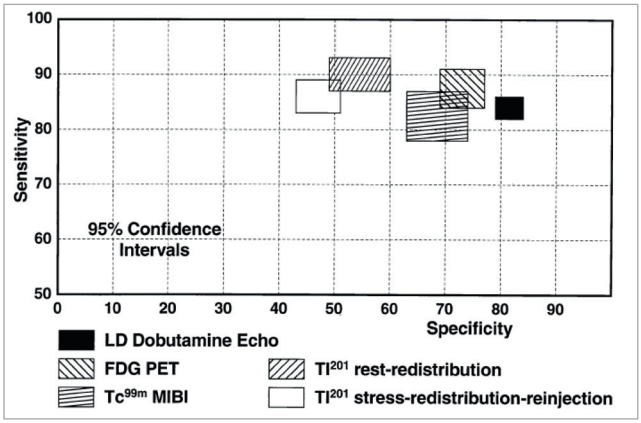

Figure 7. Receiver operating characteristic display, indicating 95% confidence intervals for each technique. The most effective modalities are located closer to the upper right corner of the graph. In this display, the smaller the square, the better the technique. A square (as opposed to a rectangle) indicates a good balance between sensitivity and specificity. A small symbol reflects narrow confidence intervals. LD: low dose[21]. Reprinted with permission from the publisher Elsevier.

Viability testing after percutaneous coronary intervention

Percutaneous coronary interventions (PCI) often are accompanied by the rise of blood troponin levels. When delayed enhancement imaging is performed after a complex PCI, regularly new areas of delayed enhancement can be observed. This is presumably caused by distal embolisation of remnants of thrombus and/or atherosclerotic plaque that are mobilised during PCI (Figure 8). MR imaging and computed tomography techniques are able to detect these heterogeneous micro-infarcts in the in the territory of intervention. The amount of myocardial delayed enhancement correlates to the observed troponin levels shortly after the procedure[23]. This finding is not known to have significant impact on prognosis of patients, but suggests that the use of a distal protection device can prevent this irreversible myocardial damage.

Differential diagnosis of delayed enhancement patterns

In coronary artery disease delayed enhancement imaging typically shows enhancement with a subendocardial to epicardial gradient resembling the wavefront progression towards the epicardium with

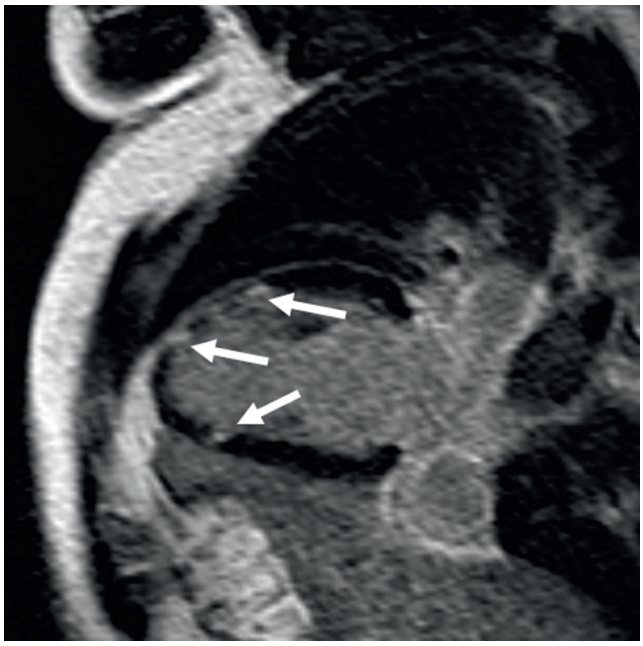

Figure 8. Two chamber delayed enhancement image of left ventricle showing multiple spots of delayed enhancement (arrows) depicting small embolisation after percutaneous coronary intervention.

increased ischaemic time. Moreover, in ischaemic heart disease the distribution of the delayed enhancement is according to the epicardial vascular territories (LAD, LCX, RCA). In non-ischaemic heart disease myocardial fibrosis can also be detected with delayed enhancement imaging. These areas of myocardial fibrosis also exhibit a greater extracellular volume that takes up gadolinium and depicts white at delayed enhancement imaging. Furthermore, myocardial fibrosis in non-ischaemic heart disease is not typically distributed according to epicardial vascular territories and the pattern is usually patchy and involves the midwall and epicardium[24]. Delayed enhancement in the midwall can be found in approximately 30% of patients with idiopathic dilated cardiomyopathies (Figure 9A). Also in hypertrophic cardiomyopathy fibrosis can be found at the junctions of the septum and the right ventricle and in the hypertrophic septum in case of hypertrophic obstructive cardiomyopathy (Figure 9B). Myocardial fibrosis in these patients may be a substrate to arrhythmias and may be predictive of impaired prognosis. Patients with cardiac amyloidosis demonstrate a characteristic pattern with a rim of subendocardial delayed enhancement represented by increased deposition of amyloid compared to the midwall and epicardial region (Figure 9C). Acute myocarditis can be detected by delayed enhancement in epicardial regions. In the acute stage this enhancement does not depicts fibrosis but oedema, which also leads to increased extracellular space (Figure 9D). In the chronic phase of myocarditis typical epicardial fibrosis can be detected.

Conclusion

MR imaging is a comprehensive technique to assess viable dysfunctional myocardium with delayed enhancement imaging, dobutamine stress imaging and perfusion imaging. MRI also

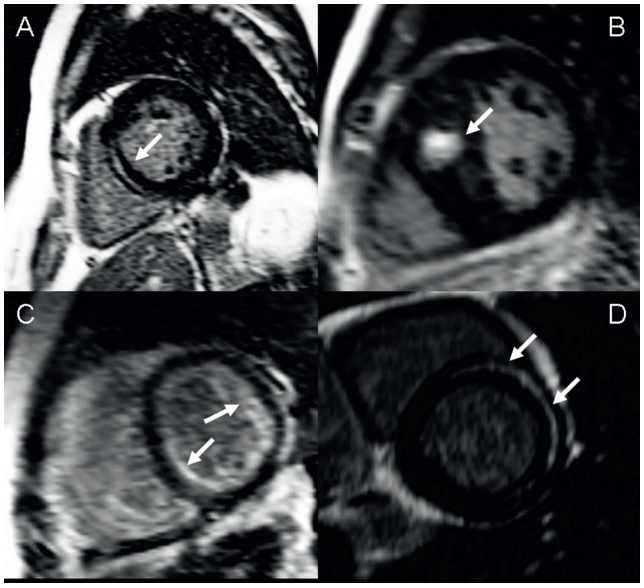

Figure 9. Short axis delayed enhancement image of left ventricle. Delayed enhancement depicting fibrosis (arrow) in the mid wall in idiopathic dilated cardiomyopathy (A), focal in the septum in hypertrophic obstructive cardiomyopathy (B), endocardial rim of delayed enhancement in amyloidosis (C), and epicardial-mid wall enhancement in chronic state after acute myocarditis (D).

provides additional information on anatomy and function with high spatial resolution and enables differentiation between ischaemic and non-ischaemic heart diseases. The use of MR imaging to detect viable myocardium is limited to patients who have no contraindications for MRI. It is expected that in the future development of MR compatible devices will overcome this limitation.

References

1. European Coronary Surgery Study Group. Long-term results of prospective randomised study of coronary artery bypass surgery in stable angina pectoris. *Lancet.* 1982;2:1173-80.

2. Emond M, Mock MB, Davis KB, Fisher LD, Holmes DR Jr, Chaitman BR, Kaiser GC, Alderman E, Killip T 3rd. Long-term survival of medically treated patients in the Coronary Artery Surgery Study (CASS) Registry. *Circulation.* 1994;90:2645-57.

3. Tillisch J, Brunken R, Marshall R, Schwaiger M, Mandelkern M, Phelps M, Schelbert H. Reversibility of cardiac wall-motion abnormalities predicted by positron tomography. *N Engl J Med.* 1986;314:884-8.

4. Eitzman D, al-Aouar Z, Kanter HL, vom Dahl J, Kirsh M, Deeb GM, Schwaiger M. Clinical outcome of patients with advanced coronary artery disease after viability studies with positron emission tomography. *J Am Coll Cardiol.* 1992;20:559-65.

5. Di Carli MF, Davidson M, Little R, Khanna S, Mody FV, Brunken RC, Czernin J, Rokhsar S, Stevenson LW, Laks H, Hawkins R, Schelbert HR, Phelps ME, Maddahi J. Value of metabolic imaging with positron emission tomography for evaluating prognosis in patients with coronary artery disease and left ventricular dysfunction. *Am J Cardiol.* 1994;73:527-33.

6. Allman KC, Shaw LJ, Hachamovitch R, Udelson JE. Myocardial viability testing and impact of revascularization on prognosis in patients with coronary artery disease and left ventricular dysfunction: a meta-analysis. *J Am Coll Cardiol.* 2002;39:1151-8.

7. McNamara MT, Tscholakoff D, Revel D, Soulen R, Schechtmann N, Botvinick E, Higgins CB. Differentiation of reversible and irreversible myocardial injury by MR imaging with and without gadolinium-DTPA. *Radiology.* 1986;158:765-9.

8. Kim HW, Farzaneh-Far A, Kim RJ. Cardiovascular magnetic resonance in patients with myocardial infarction: current and emerging applications. *J Am Coll Cardiol.* 2009;55:1-16.

9. Kim RJ, Fieno DS, Parrish TB, Harris K, Chen EL, Simonetti O, Bundy J, Finn JP, Klocke FJ, Judd RM. Relationship of MRI delayed contrast enhancement to irreversible injury, infarct age, and contractile function. *Circulation.* 1999;100:1992-2002.

10. Ibrahim T, Hackl T, Nekolla SG, Breuer M, Feldmair M, Schömig A, Schwaiger M. Acute myocardial infarction: serial cardiac MR imaging shows a decrease in delayed enhancement of the myocardium during the 1st week after reperfusion. *Radiology.* 2010;254:88-97.

11. Kim RJ, Wu E, Rafael A, Chen EL, Parker MA, Simonetti O, Klocke FJ, Bonow RO, Judd RM. The use of contrast-enhanced magnetic resonance imaging to identify reversible myocardial dysfunction. *N Engl J Med.* 2000;343:1445-53.

12. Wu KC, Zerhouni EA, Judd RM, Lugo-Olivieri CH, Barouch LA, Schulman SP, Blumenthal RS, Lima JA. Prognostic significance of microvascular obstruction by magnetic resonance imaging in patients with acute myocardial infarction. *Circulation.* 1998;97:765–772.

13. Roes SD, Borleffs JW, van der Geest RJ, Westenberg JJM, Ajmone Marsan N, Kaandorp TAM, Reiber JHC, Zeppenfeld K, Lamb HJ, de Roos A, Schalij MJ, Bax JJ. Contrast-Enhanced MRI Predicts Spontaneous Ventricular Arrhythmia in Patients With Ischemic Cardiomyopathy and Implantable Cardioverter-Defibrillator. *Circ Cardiovasc Imaging.* 2009;2:183-190.

14. Cheong BYC, Muthupillai R, Wilson JM, Sung A, Huber S, Amin S, Elayda MA, Lee VV, Flamm SD. Prognostic Significance of Delayed-Enhancement Magnetic Resonance Imaging Survival of 857 Patients With and Without Left Ventricular Dysfunction. *Circulation.* 2009;120:2069-2076.

15. Kwong RY, Chan AK, Brown KA, Chan CW, Reynolds G, Tsang S, Davis RB. 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.* 2006;113:2733-2743.

16. Vanoverschelde JL, D'Hondt AM, Marwick T, Gerber BL, De Kock M, Dion R, Wijns W, Melin JA. Head-to-head comparison of exercise-redistribution-reinjection thallium single-photon emission computed tomography and low dose dobutamine echocardiography for prediction of reversibility of chronic left ventricular ischemic dysfunction. *J Am Coll Cardiol.* 1996;28:432-42.

17. Wellnhofer E, Olariu A, Klein C, Gräfe M, Wahl A, Fleck E, Nagel E. Quantification for the Prediction of Functional Recovery Magnetic Resonance Low-Dose Dobutamine Test Is Superior to Scar. *Circulation.* 2004;109;2172-2174.

18. Bucciarelli-Ducci C, Lyne JC, Gatehouse PD, Pennell DJ. Cardiovascular magnetic resonance myocardial perfusion: methods and applications in patients with coronary artery disease. *Heart.* 2007 supplement autumn 4-11.

19. Cerqueira MD, Weissman NJ, Dilsizian V, Jacobs AK, Kaul S, Laskey WK, Pennell DJ, Rumberger JA, Ryan T, Verani MS; Standardized myocardial segmentation and nomenclature for tomographic imaging of the heart: a statement for healthcare professionals from the Cardiac Imaging Committee of the Council on Clinical Cardiology of the American Heart Association.

American Heart Association Writing Group on Myocardial Segmentation and Registration for Cardiac Imaging. *J Nucl Cardiol.* 2002;9:240-5.

20. Ibrahim T, Bülow HP, Hackl T, Hörnke M, Nekolla SG, Breuer M, Schömig A, Schwaiger M. 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.

21. Bax JJ, Wijns W, Cornel JH, Visser FC, Boersma E, Fioretti PM. Accuracy of currently available techniques for prediction of functional recovery after revascularization in patients with left ventricular dysfunction due to chronic coronary artery disease: comparison of pooled data. *J Am Coll Cardiol.* 1997;30:1451-60.

22. Kuhl HP, Beek AM, van der Weerdt AP, Hofman MBM, Visser CA, Lammertsma AA, Heussen N, Visser FC, van Rossum AC. Myocardial Viability in Chronic Ischemic Heart Disease.Comparison of Contrast-Enhanced Magnetic Resonance Imaging With 18F-Fluorodeoxyglucose Positron Emission Tomography. *J Am Coll Cardiol.* 2003;41:1341-8.

23. Selvanayagam JB, Porto I, Channon K, Petersen SE, Francis JM, Neubauer S, Banning AP. Troponin Elevation After Percutaneous Coronary Intervention Directly Represents the Extent of Irreversible Myocardial Injury. Insights From Cardiovascular Magnetic Resonance Imaging. *Circulation.* 2005;111:1027-1032.

24. Mahrholdt H, Wagner A, Judd RM, Sechtem U, Kim RJ. Delayed enhancement cardiovascular magnetic resonance assessment of non-ischaemic cardiomyopathies. *Eur Heart J.* 2005;26:1461-74.