SUMMARY

This thesis addresses the clinical applications of Cardiovascular Magnetic Resonance imaging (CMR) in patients with myocardial infarction. The introduction of steady state free-precession (SSFP) cine imaging and delayed contrast-enhanced (DCE) imaging around the turn of the century has triggered a major step forward in the position of CMR in the field of cardiac imaging. CMR is now the definitive reference technique for the non-invasive evaluation of left and right ventricular function, mass and regional scar. Other CMR techniques are T2-weighted spin-echo (T2W) imaging and first pass myocardial perfusion imaging. T2W imaging is sensitive to regional high water content and can therefore be used to visualise infarct-related myocardial oedema. First pass perfusion imaging is used to assess myocardial perfusion and microvascular obstruction. The latest developments of these techniques in both the acute and the chronic phase of myocardial infarction are reviewed in chapter 1.

Chapters 2-4 focus on the use of CMR in patients with acute myocardial infarction. Regions that are severely dysfunctional early after infarction may show (partial) recovery of function when the occluded coronary artery is timely reperfused. The likelihood of recovery depends on the local extent of irreversibly damaged tissue, which can be visualised as areas of high signal intensity (hyperenhancement) on DCE images. In Chapter 2, we showed that DCE can be used to predict functional recovery of stunned myocardium after acute infarction. We evaluated 30 patients after a first reperfused acute myocardial infarction using cine imaging and DCE at one week and follow-up cine at 3 months. The likelihood of improvement of dysfunctional segments was strongly and inversely related to the segmental extent of hyperenhancement.

Microvascular obstruction (MVO), or no-reflow, refers to the fact that, in acute myocardial infarction, successful revascularisation of the epicardial coronary artery is not always followed by the restoration of myocardial perfusion. MVO is a well-known predictor of poor functional recovery and less favourable outcome. On DCE images, it can be seen as regions of low signal intensity within the hyperenhanced infarction. Coronary angiography, electrocardiography and echocardiography can also be used to assess MVO. In chapter 3, we directly compared angiographic, electrocardiographic and CMR measures of microvascular obstruction in 60 patients after primary stenting for a first acute myocardial infarction. We found that DCE imaging was a very sensitive marker of MVO and that it was the strongest predictor of changes in left ventricular volumes and ejection fraction at follow-up.

Microvascular obstruction may lead to intramyocardial haemorrhage by extravasation of erythrocytes through severely damaged endothelial walls. It is not known whether haemorrhage has additional unfavourable impact or whether it is a mere side effect. In
In Chapter 4, we used non-enhanced T2W imaging to assess the clinical significance of infarct-related intramyocardial haemorrhage in relation to infarct size, microvascular obstruction, baseline function and functional outcome. Regional infarct-related oedema normally causes high-intensity areas on T2W images, but the high signal is attenuated by the presence of haemorrhage, which alters regional magnetic properties. Haemorrhage was detected in 22 of 45 patients, and its presence was related to a larger infarct size, the presence of MVO and lower ejection fraction. The best predictor of functional changes, however, was MVO, and, in this study, the presence of haemorrhage was of no additional value.

Chapters 5 and 6 focus on the use of CMR in patients with chronic ischemic heart disease. In these patients, left ventricular systolic dysfunction may result from infarction and irreversibly scarred myocardium or from chronic hypoperfusion in which the function may recover after restoration of flow. As in acute myocardial infarction, the likelihood of functional recovery depends on the regional scar extent, which can be visualised by DCE imaging. In Chapter 5, we showed that DCE imaging correlated well to the current reference imaging standard of viability, 18F-fluorodeoxyglucose positron emission tomography (PET). In 26 patients with chronic coronary artery disease and left ventricular dysfunction, segmental extent of hyperenhancement was inversely related to segmental glucose uptake by PET. At 37% segmental extent of hyperenhancement, DCE imaging optimally differentiated viable from non-viable segments defined by PET (sensitivity 96%, specificity 84%). After successful revascularisation, chronically ischemic, dysfunctional myocardium does not always improve despite proven viability. This may be explained by a delayed time course of recovery and premature follow-up imaging. This issue was addressed in Chapter 6. We assessed functional outcome and temporal changes in relation to baseline extent of hyperenhancement in 35 patients with chronic ischemic LV dysfunction 1 month before, and 3, 6 and 24±12 months after revascularisation. The study showed that improvement of dysfunctional but viable myocardium can be considerably delayed and that both likelihood and time course of long-term functional improvement were related to the baseline amount of scar.

Both cine images and DCE images are generally assessed in a qualitative way ("eyeballing"). However, quantitative assessment is preferable for comparison within patients, between patients and between different centers. Chapters 7 and 8 address the quantitative analysis of cine images and DCE images. Regional left ventricular function can be quantified as systolic wall thickening which is the difference between regional end-diastolic wall thickness and end-systolic wall thickness and is expressed in absolute millimetres or as a percentage of end-diastolic wall thickness. Although systolic wall thickening is widely used in the literature, there is a surprising scarcity of systematic reports.
on its normal range, and even prominent CMR publications use normal values from old echocardiographic reports. In Chapter 7, we therefore used cine imaging and the centerline method to provide the normal range for regional wall thickness and wall thickening in 36 healthy volunteers. Regional end-diastolic and end-systolic wall thickness and percent systolic wall thickening showed significant heterogeneity that was in line with previous reports. The results in this study further suggested that the traditionally used definition of myocardial hypertrophy may not be valid when using current high resolution cine CMR sequences. DCE images can easily be quantified, but the resulting regional and global infarct extent strongly depend on image window setting, which generally reflects the personal preference of the observer and may differ considerably especially between the various centers. A range of quantification methods of varying complexity has been proposed, but their value remains unsure because of the lack of an in-vivo, human standard of regional scar. In Chapter 8, we therefore used functional outcome after revascularisation, which is considered the clinical standard of viability, to evaluate two DCE quantification methods in 38 patients with chronic ischemic myocardial dysfunction. Hyperenhancement was quantified by thresholding window setting at: 2-8 standard deviations above mean signal intensity of a remote normal region, and according to the full-width-at-half-maximum method. We found that, although the quantification method had a strong impact on the quantified global and segmental extent of hyperenhancement, it had relatively little influence on the accuracy to predict segmental functional improvement after revascularization.

CONSIDERATIONS

When considering the studies presented in this thesis, along with many others published so far, it can be safely concluded that CMR is a valuable technique in patients with myocardial infarction. The advantages of CMR compared to other techniques as echocardiography and radionuclide perfusion imaging of CMR are clear: wide field-of-view, high resolution, high quality, one-stop (function-perfusion-viability) examination, and simple quantification without geometrical assumptions. In addition, as a unique feature, it allows the in-vivo demonstration of oedema, haemorrhage, microvascular obstruction and acute or chronic infarct extent. It is this tissue characterisation that has created new possibilities in the management of patients with myocardial infarction that will be addressed in the coming years: e.g. oedema as a marker of area at risk; microvascular obstruction and haemorrhage as markers of infarct and prognostic markers, and as endpoints in reperfusion studies; infarct heterogeneity as a marker of ventricular arrhythmia. So, the cardiac imager is happy, and so is the researcher, but what about the clinician, the referring cardiologist, and the patient with myocardial infarction? Are the advantages of CMR translated into improved
diagnosis and management? In the early phase after myocardial infarction, echocardiography is adequate to answer most clinical questions, especially in patients with an uncomplicated course. CMR has additional value when diagnosis is unsure, when complications are suspected but cannot be adequately depicted, when prediction of functional recovery is relevant and, importantly, in the quantification of LV function in ICD candidates. In the chronic phase of infarction, management critically depends on quantification of ventricular function and the assessment of viability, and CMR should be strongly considered in any patient with (suspected) chronic infarction or (ischemic) cardiomyopathy. However, the ultimate impact of CMR on management and outcome of patients with myocardial infarction is hard to define because current availability is still limited compared to other techniques. Put in other words: the list of publications favouring its use is growing considerably quicker than the number of CMR imaging centres. This may be explained by a variety of potential hurdles, such as the need for collaboration between cardiologists and radiologists, the lack of a clear reimbursement that acknowledges the contribution of all those involved and the need for training and credentialing of technical and medical staff. CMR is about to make its final growth spurt, but only after these issues are solved.