Cardiac magnetic resonance assessment of regional ventricular function in ischemic heart disease

Rezonans magnetyczny w chorobie niedokrwiennej serca

Victor A. Ferrari¹, Ewa Księżycka², Kevin Duffy¹, Craig H. Scott¹, Martin G. St. John Sutton¹

¹University of Pennsylvania, Philadelphia, USA ²Institute of Cardiology, Warsaw, Poland

Postępy w Kardiologii Interwencyjnej 2007; 3, 1 (7): 7-14

Streszczenie

Obrazowanie w kardiologii przy użyciu rezonansu magnetycznego (ang. cardiac magnetic resonance – CMR) jest cennym narzędziem oceny choroby wieńcowej zarówno w stanach ostrych, jak i przewlekłych. Rezonans magnetyczny w czasie jednej rejestracji umożliwia uzyskanie różnorodnych informacji zawierających dane dotyczące zarówno kurczliwości komory, ukrwienia mięśnia sercowego, jak i jego żywotności. W pewnych sytuacjach te informacje mogą być użyte dla określenia rokowania, w szczególności rozwinięcia się niewydolności serca, wystąpienia kolejnych epizodów sercowych czy śmiertelności. Dodatkowo do informacji mogących pochodzić z innych metod diagnostycznych, unikatowa technika CMR znakowania (ang. tagging) pozwala na ilościową analizę odcinkowej kurczliwości komory.

Prezentowana praca opisuje obecne i możliwe w przyszłości zastosowanie CMR do badania odcinkowej kurczliwości komory w chorobie niedokrwiennej serca.

Key words: magnetic resonance imaging, ischemic heart disease, myocardium, post-infarction remodeling, ventricular mechanics, viability

Słowa kluczowe: rezonans magnetyczny – obrazowanie, choroba niedokrwienna serca, remodeling pozawałowy, kurczliwość lewej komory

Introduction

Prior to the availability of percutaneous coronary intervention (PCI) and thrombolysis (TL), few tools were available to interrupt an acute myocardial infarction (MI) and thereby limit infarct size. Currently, we are faced with making decisions regarding prognosis and the potential risks and benefits of revascularization strategies in patients with recent PCI or TL and an admixture of stunned, infarcted, and normal myocardium. Our understanding of the post-infarction remodeling process has changed significantly in the last decade. Data from the SAVE trial [1] have proven the benefits of angiotensin converting enzyme inhibitor (ACEI) therapy in attenuating the maladaptive remodeling which occurs following moderate or large infarctions. Long term data from this group of patients also demonstrated the importance of left ventricular (LV) size and shape on outcome [2].

In the mid-1990's, additional support for the benefits of an open infarct-related artery was elucidated [3, 4]. Some of the salutary effects are likely related to delivery of cytokines and signaling factors to the healing ultrastructure of the injured myocardium and border zone of the infarct. In fact, the presence of microvascular obstruction at the infarct core is a predictor of poor myocardial functional recovery and is followed by cardiovascular complications [5-7]. Patients in the early post-infarction period often require multiple imaging modalities to assess cardiac structure and function, infarct size, the status of the coronary arteries, and the location and degree of residual inducible ischemia.

Cardiac magnetic resonance (CMR) has emerged as a technique which provides excellent definition of cardiac anatomy and function. CMR can assess both global and regional function accurately and reproducibly. Methods have been developed to perform stress testing in the

Adres do korespondencij/Corresponding author: Victor A. Ferrari, MD, Associate Director, Noninvasive Imaging Laboratory, Hospital of the University of Pennsylvania, 9023 E. Gates Pavilion, 3400 Spruce Street, Phila., PA 19104, tel. +01 215 662 29 12, fax +01 215 615 36 52, e-mail: ferrariv@mail.med.upenn.edu

CMR scanner, and studies of viability and inducible ischemia have been validated in animal models and in patients with coronary artery disease. Recent advances in magnetic resonance perfusion imaging serve to make CMR an ideal noninvasive technique to study patients with ischemic heart disease [8]. Furthermore, new approaches to evaluate the integrity of the microcirculation, particularly microvascular obstruction and perhaps in the future ²³Na imaging, can provide novel prognostic information and accurate assessment of infarct size noninvasively. Finally, the potential for evaluating not only the degree of coronary artery obstructive disease, but also to potentially characterize the vulnerability of atherosclerotic plaques makes CMR a unique tool among noninvasive modalities.

An integrated examination may one day permit, in a single study, the evaluation of cardiac structure and function, response to stress (dobutamine or persantine), coronary anatomy, and provide data on the risk/benefit of revascularization and prognosis. Much of this future potential rests on accurate quantitation of ventricular function in association with other CMR-derived measurements.

CMR methods are particularly attractive since they are noninvasive and have an excellent safety profile. Many hospitals have, or soon will have, MRI scanners, which play an important role in the evaluation of other parts of the cardiovascular system as well, such an evaluation of the aorta or cerebral vessels. While the majority of patients are eligible for examination, some patients with permanent pacemakers or internal defibrillator devices, those with unstable rhythm abnormalities, or whose weight is greater then 280 pounds are generally excluded for safety or technical reasons. However, it is not uncommon for patients with unstable angina on intravenous nitroglycerin and/or heparin/GPIIb/IIIa inhibitors to undergo scanning if they have been clinically stable for 8-12 hours. Newer scanner designs now permit very obese patients to undergo CMR examination. Even patients with newly placed intracoronary stents may be safely scanned at 1,5 T, as recent work suggests [9].

The purpose of this paper will be to review the evaluation of regional LV function assessment in patients with ischemic heart disease, especially the role of myocardial tissue tagging and its relationship to newer CMR techniques.

Detection of myocardial ischemia

CMR provides a highly accurate and reproducible depiction of segmental wall motion and quantitative contractile function. Excellent blood-endocardial contrast improves assessment of wall thickness, cavity volumes, and LV ejection fraction. Many noninvasive imaging techniques, including echocardiography, assume some degree of geometric uniformity when calculating cavity volumes. When the LV shape is deformed, such as in a dilated or an infarcted heart, significant errors may be introduced due to these assumptions. However, MRI makes no assumptions regarding LV geometry since image acquisition is via a stacked set of image locations. The improved spatial resolution of CMR permits accurate assessment of regional function as well.

One of CMR's most novel features is its ability to measure intramural myocardial function, which had historically been performed with surgically implanted ultrasound crystals or radiopaque beads. This technique uses an alternating grid of stripes along parallel or perpendicular axes to produce intramyocardial lines of unexcited protons (water molecules). These 'tags' are tracked via analysis programs to create triangular finite elements that measure regional contractile function (Fig. 1). An analysis method using a homogeneous strain analysis converts one-dimensional stretches to two or three-dimensional strain values. This multidimensional analysis permits measurements to be made at any region in the heart from base to apex or within the myocardial walls. Studies have demonstrated the detailed relationship between transmural myocardial function in normal and abnormal states [10, 11].

Assessment of regional left ventricular function

Weiss et al. [12] reported on a technique to assess regional LV wall thickening as an index of regional ischemia by utilizing 3D geometry to calculate the perpendicular wall thickness of a 3D myocardial volume element. This approach provided improved identification of ischemic zones in a canine model of acute ischemia. Regional LV function assessment has been greatly improved using myocardial tissue tagging, in which a grid of stripes - representing an organized array of unexcited protons (water molecules) - act as intramyocardial markers, permitting tracking of areas of interest during translation and rotation of the heart throughout the cardiac cycle. Lima et al. [13] determined that CMR with tissue tagging and the 3D volume element approach permits augntitative measurement of systolic wall thickening, which correlates well with invasive sonomicrometer assessment. Others have also explored the use of a multiplanar tagged CMR approach for determination of regional LV function. Using radially-oriented tags, another group of investigators demonstrated that endocardial dysfunction was the best parameter for identifying ischemia [14, 15]. Scott et al. [16] studied a group of normal subjects using tagged CMR and measured myocardial displacement and strain (radial thickening and circumferential shortening) at baseline and during a graded dobutamine infusion. Dobutamine increased all parameters from baseline to 10 µg/kg/min infusion, but without a significant increase at greater doses (Fig. 2). Thus, the dose-response curve for





Ryc. 1. Obraz przy użyciu znakowania fazy końcowoskurczowej i towarzysząca mapa maksymalnego naprężenia (naprężenie promieniowe odpowiadające grubości ściany) u pacjenta z zawałem przegrody w ostrej fazie zawału – w 7. dniu po zawale (**A** i **B**) i po roku obserwacji (**C** i **D**). Zauważmy, że zarówno w ostrej, jak i w przewlekłej fazie kurczliwość jest bardzo upośledzona (małe odkształcenia znakowania w obrębie przegrody). Po roku obserwacji obszar ten wykazuje znaczne ścieczenie i pozostają istotne zaburzenia kurczliwości

dobutamine in the normal heart demonstrates a plateau in function following the 10 μ g/kg/min dose. This may be explained in part by reaching a state of maximum inotropy, but also may relate to a reduction in preload.

Assessment of stress induced ischemia

Dobutamine stress echocardiography (DSE) uses inducible wall motion or functional abnormalities to identify patients with myocardial ischemia. CMR has also been combined with pharmacological stress for evaluation of patients with potential CAD. One advantage of CMR is its ability to acquire images even in patients with poor quality echo images, large body habitus, or the coexistence of pulmonary diseases. Hundley et al. [17] examined 153 patients using a standard dobutamine stress magnetic resonance (DSMR) protocol who had poor acoustic windows and were referred for assessment of stress-induced ischemia. Dobutamine infusion (up to 40 μ g/kg/min) and atropine (when indicated) were used to produce a peak heart rate ≥85% of the maximal predicted heart rate. During testing, a fast cine imaging sequence



Fig. 2. Graphs showing developed left ventricular strain versus dobutamine infusion rate. Top, radial strain (E₁) increases from baseline to 10 µg/kg/min infusion but reaches a plateau, whereas rate-pressure product (RPP) continues to rise. Bottom, circumferential strain (E₂) increases (becomes more negative) from baseline to 10 µg/kg/min and also reaches a plateau. Modified from Scott CH et al. [16] **Ryc. 2.** Krzywe obrazujące narastanie naprężenia lewej komory podczas wlewu dobutaminy. Górna krzywa – naprężenie promieniowe (E₁) wzrasta podczas wlewu do 10 µg/kg/min i osiąga plateau, podczas gdy współczynnik częstości serca-ciśnienia (RPP) nadal przyrasta. Dolna krzywa – naprężenie okrężne przyrasta (E₂) (staje się bardziej ujemne) od początku wlewu do dawki 10 µg/kg/min i również osiąga plateau. Źródło: Scott CH i wsp. [16], za zgodą

was used to monitor regional LV wall motion and function as dosing levels were increased. The study established that the sensitivity for detecting stenoses >50% ranged from 75% for 1-vessel disease up to 92% in the presence of three vessel and/or left main disease, with a specificity of 83%. Of 103 patients who had a negative DSMR study, occurrence-free survival rate was 97%, underscoring DSMR's excellent negative predictive capability.

A second important DSMR study was performed by Nagel et al. [18] in 208 consecutive patients with suspected coronary artery disease but limited acoustic windows. The authors used high dose dobutamine (up to 40 μ g/kg/min) and compared their results in the same patients to DSE. DSMR images were improved vs. DSE (good or very good in 82% vs. 51%, respectively). DSMR had improved vs. DSE for sensitivity (increased from 74.3% to 86.2%) and specificity (increased from 69.8% to 85.7%). There was good correspondence between DSMR and DSE in patients with good or very good acoustic windows. DSMR was found to have a smaller number of errors due to observer bias, better image quality (more successful studies in the challenging imaging group), and improved endocardial and epicardial definition. The latter advantage permits more accurate quantitation of global and regional function.

One important limitation to the utility of tagged CMR is the time necessary for data analysis (>1 hour/study), which makes its real-time implementation impractical (for quantitative, but not qualitative, use). More rapid quantitative analysis of tagged image data is available with a noevel method [19] that uses a modification of the tagging technique, called harmonic phase imaging (HARP) to follow motion patterns of the tags and derive functional information from these patterns. Analysis of a full data set by the HARP method was 10 times faster than the conventional analysis method, and could potentially make this approach more clinically useful. Newer quantitative 2-dimensional methods (such as the DENSE technique) are becoming more common to track rapid and complex LV motion [20], which may permit earlier detection of ischemia.

Infarction

Regional assessment of myocardial infarction

CMR is a very useful technique for the diagnosis and quantification of MI. Assessment of the location and extent of infarction is vital for both diagnostic and prognostic purposes. The exact characterization of an infarct can be complex due to multiple factors. The size of an infarction can vary due to the size and anatomic location of the occluded artery, the extent of the risk region, and the degree of collateralization. In addition, the extent to which the myocardial wall is affected can vary from minimal endocardial involvement to complete transmural cell death. CMR is an excellent method for fully characterizing the subtleties of infarct definition due to its excellent spatial resolution and the ability to differentiate viable from nonviable tissue, with greater accuracy than SPECT imaging [21]. We will focus on two methods of MI characterization: functional assessment via regional wall motion analysis and myocardial reserve using perfusion imaging.

CMR with tissue tagging depicts differences in segmental myocardial function using quantitative assessment of ventricular mechanics, or strain. Strain analysis identifies infarcted regions as well as the effects of infarction on the non-infarcted (remote) zones. In patients with reperfused anteroapical infarctions, CMR techniques [22] have demonstrated that circumferential and longitudinal strains are decreased both in the infarcted and remote zones. In addition, both the infarcted and remote regions have increased radii of curvature in the affected segments. Since the increased wall stress due to a large infarction affects both infarcted as well as noninfarcted tissue, the end result is frequently an overall decrease in global function and often a generalized post-MI chronic cardiomyopathy. In another study of anteroapical infarctions [23], tagged CMR with two-dimensional finite element analysis demonstrated decreased wall strain and a reorientation of the short axis vector of myocardial contraction away from the LV centroid (expected direction) and more toward the circumferential (abnormal) direction. Increased remote zone function was seen early after infarction, indicating a possible compensatory increase in function in regions distant from the infarcted territory. Within infarcted regions, average short and long axis strain values decreased to approximately 25% of normal. On the basis of the strain analysis in these patients with large infarctions, the authors suggest that CMR could be a useful technique to predict which of these infarctions will result in unfavorable ventricular remodeling. A third study examined infarcts from all LV territories [24] and demonstrated similar findings of decreased strain values and associated non-radial direction of maximal contraction.

Regional assessment of myocardial perfusion post-infarction

CMR also provides information on regional perfusion abnormalities in infarcted myocardium. Perfusion or enhancement CMR is performed by injecting a bolus of a gadolinium-containing contrast agent and following the myocardial signal enhancement of the bolus as it travels from the LV blood pool through the myocardium, and beyond. In a combined tagged CMR/perfusion study by Rogers et al., first-pass perfusion images were obtained immediately after contrast injection (steady state, 45 to 50 cardiac cycles) and delayed images were acquired after approximately 5 to 9 minutes [9]. Myocardium with a hypoenhanced signal intensity on first-pass imaging - regardless of the delayed contrast pattern - showed limited recovery of function (using 1-dimensional % circumferential shortening) by 7 weeks post-MI and likely represents mostly infarcted myocardium. However, myocardial segments exhibiting delayed hyperenhancement without initial hypoenhancement had significant late functional recovery and probably contained a preponderance of viable myocardium. In addition, the transmural extent of hyperenhancement can also predict recovery of LV function. Recently, Baks et al. studied patients who underwent stenting of totally occluded arteries and found that those patients who had a transmural extent of hyperenhancement of <25% had a greater likelihood of recovering function [25]. The size of the peri-infarct zone can also provide prognostic information. Yan et al. found that mortality was higher in patients with larger peri-infarct zones [26].

Microvascular obstruction (MO) is a major predictor of unfavorable remodeling following MI. The mechanism of this disorder appears to be, in part, a necrosis of the capillary beds due to formation of microvascular thrombus or sludge in the infarct zone - which impairs proper healing of the injured tissues early after infarction or reperfusion. This 'no-reflow' territory may sometimes be seen after angioplasty of acute infarctions, when poor runoff exists even when the epicardial vessel is unobstructed. CMR can evaluate both regional perfusion and assess the extent of MO. Importantly, CMR can follow the effect of MO on regional and global function in a serial manner. Infarcted myocardium demonstrates hyperenhancement late after contrast is injected (10 to 15 minutes), while MO regions demonstrate hypoenhancement (a 'dark' zone) within the first several minutes following contrast injection. MO is present at 1 week post-infarction, but is not seen late (6 months) after infarction, likely due to infarct remodeling and fibrosis [5].

The relationship between MO and remodeling has been studied using a canine infarct model [27]. More unfavorable remodeling, as assessed by CMR functional imaging, occurred within 10 days of infarction in those animals with a greater extent of MO. Regional radial strain (similar to wall thickening) differs with the extent of MO involvement; Figure 3 shows the differences in radial strain for large areas of MO (>35% of infarct volume) compared to small areas (<35% infarct volume). While in general, myocardial strain decreased in infarcted regions, the strain was even more significantly reduced in areas of infarction with more extensive MO. In addition to reduced strain in infarcted areas, the strain was also decreased in normally perfused adjacent regions. Therefore, both functional and perfusion parameters are necessary to fully characterize infarcted and viable areas. Imaging techniques such as CMR that provide combined information on function and perfusion are likely to improve our diagnostic and prognostic abilities. Wu et al. found that large areas of MO within an infarction can predict cardiovascular complications in a human population [28]. MO by CMR was a more powerful predictor of post-MI cardiovascular complications of death, reinfarction, CHF, embolic stroke, and unstable angina than patency of the infarct-related artery. This predictive power existed even when controlling for infarct size. Complication rates were much higher in those patients who had evidence of MO compared to those that did not



Fig. 3. Bar graphs of radial strain in dogs with high (>35%, solid bar) and low (<35%, gray bar) amounts of MO within infarcted myocardium. Strain measurements can distinguish between these two states in the adjacent zone. Modified from Gerber BL et al. [27], with permission of *Circulation*

Ryc. 3. Słupki obrazujące naprężenie promieniowe u psów z dużymi (>35%, czarny słupek) i małymi (<35%, szary słupek) zaburzeniami w mikrokrążeniu w strefie zawału. Pomiary naprężenia pozwalają na różnicowanie pomiędzy tymi dwoma stanami w przylegających do zawału strefach bliskiej i odległej. Źródło: Gerber BL i wsp. [27], za zgodą Circulation

(45% vs. 9%, p < 0.02), resulting in an odds ratio of 5.7 (Fig. 4). Of interest, infarctions that demonstrate MO are associated with late (5 months post-infarction) wall thinning and little functional recovery, while patients without MO demonstrate greater early wall thickness and late (partial) functional recovery [25]. Hombach et al. [29] also identified prognostic value in MO. They studied 110 patients with acute MI at approximately 6 days and then at 6-9 months. They also examined the most severe cases of MO, defined as those patients with persistence of MO (PMO) at 10-15 minutes after contrast injection (not several minutes post-injection, as in other studies). They found that the combined parameters of PMO, infarct size, and infarct transmurality best predicted adverse remodeling. When assessed for major adverse cardiac events (MACE), including death, MI, unstable angina, readmission for congestive heart failure, and revascularization (CABG or PCI), MACE were greater with PMO (21% vs. 8%). Finally, PMO held greater prognostic importance than ejection fraction in predicting MACE.

The evidence from these studies demonstrates that the extent of microvascular obstruction provides a new and important prognostic parameter for predicting cardiac events, beyond quantitation of infarct size alone.

Detection of viability

Determination of viability is vital in the management of ischemic heart disease since LV function may be



Fig. 4. Relationship between the presence of microvascular obstruction (MO) and Event-Free Survival. Event-Free Survival is defined as a lack of cardiovascular death, reinfarction, congestive heart failure, or stroke, and was significantly greater in patients without MO at 2 years post-infarction. Reproduced from Wu KC et al. [28], with permission of *Circulation*

Ryc. 4. Związek pomiędzy obecnością zaburzeń w mikrokrążeniu (MO) a przeżyciem bez nowych epizodów. Przeżycie bez nowych epizodów jest zdefiniowane jako brak zgonów z przyczyn sercowo-naczyniowych, ponownych zawałów, wystąpienia zastoinowej niewydolności serca czy udaru i było znacząco większe u pacjentów bez zaburzeń w mikrokrążeniu 2 lata po zawale. Przedrukowane z: Wu KC i wsp. [28], za zgodą Circulation

improved and survival prolonged with revascularization of dysfunctional but viable myocardium. Methods to assess viability include the evaluation of perfusion and metabolism status and reserve (SPECT and PET), or augmentation of mechanical function (DSE). CMR has likewise been used to evaluate mechanical function (dobutamine MRI±tagging) or perfusion and metabolism (contrast MRI and spectroscopy).

The principle of low-dose DSE is that the mechanical function of viable myocardium will augment with catecholamine stimulation, while nonviable myocardium remains severely hypokinetic or akinetic. DSMR can also detect the augmentation in function in dysfunctional but viable myocardium, perhaps to a greater degree, given its improved spatial resolution and endocardial contour definition. DSMR correlates well with PET, with a sensitivity of 88% and a specificity of 87% [30] for detection of CAD.

DSMR can also predict functional recovery after recent myocardial infarction, as Dendale et al. [31] showed. They studied 37 patients with low dose DSE and low dose DSMR following a recent (4–12 days) myocardial infarction, and at 3 to 6 months post-MI using qualitative wall motion analysis. DSMR and DSE were similar in correctly predicting functional recovery (79% vs. 83%, respectively, p=NS), and were seen as comparable tools in assessing viability early post-infarction.

DSMR with myocardial tagging can provide a more quantitative assessment of mechanical function during stress testing. Sayad et al. compared conventional quantitative left ventricular wall thickening using cine CMR and DSMR with tagging in 10 patients with resting segmental wall abnormalities at baseline and following dobutamine infusion up to 10 µg/kg/min [32]. Images were taken at baseline, at peak infusion rate, and at 4 to 8 weeks after revascularization. End-diastolic and end-systolic (ES) wall thicknesses (WT) in hypokinetic resting segments were compared post-dobutamine, and after revascularization. ESWT with tagging following low-dose dobutamine infusion was the best predictor of functional improvement post-revascularization. There was also no improvement post-revascularization in segments with a resting ESWT of <7 mm. Thus, DSMR with tagging techniques best predicted viability in abnormal myocardial segments.

DSMR with myocardial tagging has also been shown to accurately predict functional recovery in the setting of acute reperfused myocardial infarction. Geskin et al. studied 20 patients with tagged DSMR within four days of reperfused acute infarction [33]. Eight weeks post-revascularization, resting CMR was performed to assess for functional recovery. Greater functional recovery was seen in those patients with a more normal initial intramyocardial circumferential segment shortening.

Conventional resting delayed enhancement CMR is another useful method to assess for viability. On delayed imaging following contrast injection (approximately 10–15 minutes after conventional gadolinium-containing contrast agent), nonviable myocardium demonstrates hyperenhancement due to poor washout (greater volume of distribution) of contrast agent, whereas viable myocardium does not. In patients with stable coronary disease, Ramani et al. demonstrated a strong correlation between contrast CMR with delayed hyperenhancement, SPECT, and DSE in the assessment of viability [34]. In the acute setting in canines, Kim et al. demonstrated that infarcted myocardium hyperenhances, while normal and ischemic myocardium exhibits normal (no delayed) enhancement [35]. In humans, delayed enhancement has been proven to be more sensitive than SPECT for detection of previous nontransmural infarctions [21], which has a major impact on risk stratification and management of patients.

Several recent studies have performed head-to-head comparisons between DSMR and delayed enhancement CMR in order to determine their potential limitations regarding viability assessment. Motoyasu et al. evaluated 23 patients with acute reperfused MI and discovered that DSMR had greater sensitivity, specificity, and accuracy (89%, 80%, 86%) than delayed enhancement (83%, 72%, 79%) [36]. Wellnhofer et al. performed a sub-group analysis and found that DSMR was better at determining functional recovery when the transmural myocardial enhancement was between 1 and 75% of the wall thickness, but sensitivity decreased when transmural enhancement was between 75 to 100% [37]. Thus regional wall motion assessment continues to have an important role in the armamentarium of cardiovascular clinicians and researchers, even in the setting of newer tools.

Conclusions

MRI has the capability to provide important high resolution data noninvasively regarding many aspects of cardiac structure and function. New tools, such as myocardial tagging and the HARP and DENSE methods permit advanced techniques to be used clinically for evaluation of segmental myocardial function in ischemic heart disease. Regional myocardial perfusion may also be determined in the same examination as function and viability, and permits measurement of important tissue characterization properties using cardiac magnetic resonance approaches. Valuable prognostic information may also be obtained from MRI, and the degree of microvascular obstruction and the assessment of membrane integrity have proven to be important determinants of viability.

Nonetheless, segmental myocardial function and its response to injury or stress remains vitally important in the current cardiac evaluation strategy. MRI methods hold promise to contribute significantly to our understanding of cardiovascular physiology and extend our knowledge of the complex and dynamic changes that occur with acute myocardial ischemia and infarction, as well as during the post-infarction remodeling process. Quantitative techniques such as CMR also permit noninvasive serial assessment of the impact of novel treatments such as stem cell or gene therapy, and provide a solid basis of support for multicenter clinical trials of these new approaches to ischemic heart disease.

References

- Pfeffer MA, Braunwald E, Moye LA, et al. Effect of captopril on mortality and morbidity in patients with left ventricular dysfunction after myocardial infarction. Results of the survival and ventricular enlargement trial. The SAVE Investigators. N Engl J Med 1992; 327: 669-677.
- St John Sutton M, Pfeffer MA, Moye LA, et al. Cardiovascular death and left ventricular remodeling two years after myocardial infarction: baseline predictors and impact of long-term use of captopril: information from the Survival and Ventricular Enlargement (SAVE) trial. Circulation 1997; 96: 3294-3299.
- Hochman JS, Choo H. Limitation of myocardial infarct expansion by reperfusion independent of myocardial salvage. Girculation 1987; 75: 299-306.
- Nidorf SM, Siu SC, Galambos G, et al. Benefit of late coronary reperfusion on ventricular morphology and function after myocardial infarction. J Am Coll Cardiol 1993; 21: 683-691.
- Wu KC, Kim RJ, Bluemke DA, et al. Quantification and time course of microvascular obstruction by contrast-enhanced echocardiography and magnetic resonance imaging following acute myocardial infarction and reperfusion. J Am Coll Cardiol 1998; 32: 1756-1764.
- 6. Ito H, Maruyama A, Iwakura K, et al. Clinical implications of the 'no reflow' phenomenon. A predictor of complications and left ventricular remodeling in reperfused anterior wall myocardial infarction. Circulation 1996; 93: 223-228.

- Wu KC, Zerhouni EA, Judd RM, et al. Prognostic significance of microvascular obstruction by magnetic resonance imaging in patients with acute myocardial infarction. Circulation 1998; 97: 765-772.
- Wilke NM, Jerosch-Herold M, Zenovich A, et al. Magnetic resonance first-pass myocardial perfusion imaging: clinical validation and future applications. J Magn Reson Imaging 1999; 10: 676-685.
- Rogers WJ Jr, Kramer CM, Geskin G, et al. Early contrast-enhanced MRI predicts late functional recovery after reperfused myocardial infarction. Circulation 1999; 99: 727-729.
- Clark NR, Reichek N, Bergey P, et al. Circumferential myocardial shortening in the normal human left ventricle. Assessment by magnetic resonance imaging using spatial modulation of magnetization. Circulation 1991; 84: 67-74.
- Young AA, Imai H, Chang CN, et al. Two-dimensional left ventricular deformation during systole using magnetic resonance imaging with spatial modulation of magnetization. Circulation 1994; 89: 740-752.
- Weiss JL, Shapiro EP, Buchalter MB, et al. Magnetic resonance imaging as a noninvasive standard for the quantitative evaluation of left ventricular mass, ischemia, and infarction. Ann N Y Acad Sci 1990; 601: 95-106.
- Lima JA, Jeremy R, Guier W, et al. Accurate systolic wall thickening by nuclear magnetic resonance imaging with tissue tagging: correlation with sonomicrometers in normal and ischemic myocardium. J Am Coll Cardiol 1993; 21: 1741-1751.
- Azhari H, Weiss JL, Rogers WJ, et al. A noninvasive comparative study of myocardial strains in ischemic canine hearts using tagged MRI in 3-D. Am J Physiol 1995; 268: H1918-H1926.
- Denisova O, Shapiro EP, Weiss JL, et al. Localization of ischemia in canine hearts using tagged rotated long axis MR images, endocardial surface stretch and wall thickening. Magn Reson Imaging 1997; 15: 1037-1043.
- Scott CH, Sutton MS, Gusani N, et al. Effect of dobutamine on regional left ventricular function measured by tagged magnetic resonance imaging in normal subjects. Am J Cardiol 1999; 83: 412-417.
- Hundley WG, Hamilton CA, Thomas MS, et al. Utility of fast cine magnetic resonance imaging and display for the detection of myocardial ischemia in patients not well suited for second harmonic stress echocardiography. Circulation 1999; 100: 1697-1702.
- Nagel E, Lehmkuhl HB, Bocksch W, et al. Noninvasive diagnosis of ischemia-induced wall motion abnormalities with the use of high-dose dobutamine stress MRI: comparison with dobutamine stress echocardiography. Circulation 1999; 99: 763-770.
- Garot J, Bluemke DA, Osman NF, et al. Fast determination of regional myocardial strain fields from tagged cardiac images using harmonic phase MRI. Circulation 2000; 101: 981-988.
- Gilson W, Yang Z, French B, et al. Measurement of myocardial mechanics in mice before and after infarction using multislice displacement-encoded MRI with 3D motion encoding. Am J Physiol Heart Circ Physiol 2005; 288: H1491-1497.
- Wagner A, Mahrholdt H, Holly TA, et al. Contrast-enhanced MRI and routine single photon emission computed tomography (SPECT) perfusion imaging for detection of subendocardial myocardial infarcts: an imaging study. Lancet 2003; 361: 374-379.
- Bogaert J, Bosmans H, Maes A, et al. Remote myocardial dysfunction after acute anterior myocardial infarction: impact of left ventricular shape on regional function: a magnetic resonance myocardial tagging study. J Am Coll Cardial 2000; 35: 1525-1534.
- 23. Marcus JT, Gotte MJ, Van Rossum AC, et al. Myocardial function in infarcted and remote regions early after infarction in man: assessment by magnetic resonance tagging and strain analysis. Magn Reson Med 1997; 38: 803-810.
- Gotte MJ, van Rossum AC, Marcus JT. Recognition of infarct localization by specific changes in intramural myocardial mechanics. Am Heart J 1999; 138: 1038-1045.
- Baks T, van Geuns R-J, Duncker DJ, et al. Prediction of left ventricular function after drug-eluting stent implantation for chronic total coronary occlusions. J Am Coll Cardiol 2006; 47: 721-725.
- 26. 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. Grculation 2006; 114: 32-39.
- Gerber BL, Rochitte CE, Melin JA, et al. Microvascular obstruction and left ventricular remodeling early after acute myocardial infarction. Circulation 2000; 101: 2734-2741.

- Wu KC, Zerhouni EA, Judd RM, et al. Prognostic significance of microvascular obstruction by magnetic resonance imaging in patients with acute myocardial infarction. Circulation 1998; 97: 765-772.
- Hombach V, Grebe O, Merkle N, et al. Sequelae of acute myocardial infarction regarding cardiac structure and function and their prognostic significance as assessed by magnetic resonance imaging. Eur Heart J 2005; 26: 549-557.
- 30. Baer FM, Voth E, Schneider CA, et al. Comparison of low-dose dobutamine-gradient-echo magnetic resonance imaging and positron emission tomography with [18F] fluorodeoxyglucose in patients with chronic coronary artery disease. A functional and morphological approach to the detection of residual myocardial viability. Circulation 1995; 91: 1006-1015.
- Dendale PA, Franken PR, Waldman GJ, et al. Low-dosage dobutamine magnetic resonance imaging as an alternative to echocardiography in the detection of viable myocardium after acute infarction. Am Heart J 1995; 130: 134-140.
- Sayad DE, Willett DL, Hundley WG, et al. Dobutamine magnetic resonance imaging with myocardial tagging quantitatively predicts improvement in regional function after revascularization. Am J Cardiol 1998; 82: 1149-1151, A10.
- Geskin G, Kramer CM, Rogers WJ, et al. Quantitative assessment of myocardial viability after infarction by dobutamine magnetic resonance tagging. Circulation 1998; 98: 217-223.
- Ramani K, Judd RM, Holly TA, et al. Contrast magnetic resonance imaging in the assessment of myocardial viability in patients with stable coronary artery disease and left ventricular dysfunction. Circulation 1998; 98: 2687-2694.
- Kim RJ, Fieno DS, Parrish TB, et al. Relationship of MRI delayed contrast enhancement to irreversible injury, infarct age, and contractile function. Circulation 1999; 100: 1992-2002.
- Motoyasu M, Sakuma H, Ichikawa Y, et al. Prediction of regional functional recovery after acute myocardial infarction with low dose dobutamine stress cine MR imaging and contrast enhanced MR imaging. J Cardiovasc Magn Resonan 2003; 5: 563-574.
- Wellnhofer E, Olariu A, Klein C, et al. Magnetic resonance low-dose dobutamine test is superior to SCAR quantification for the prediction of functional recovery. Grculation 2004; 109: 2172-2174.