EDITORIAL POINT OF VIEW

Current clinical relevance of cardiovascular magnetic resonance and its relationship to nuclear cardiology

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In recent years the availability of magnetic resonance (MR) systems has increased enormously. Currently, primary cardiac indications for MR imaging are great vessel disease (aortic dissection, aortic aneurysm), complex congenital heart disease, paracardiac and intracardiac masses, and pericardial disease. Secondary applications are valvular heart disease, cardiomyopathies, congestive heart failure, and myocardial tissue abnormalities. Ischemic heart disease forms a relatively new area of interest for MR imaging that allows the evaluation of myocardial perfusion and function. Major developments in MR coronary angiography suggest an important future role for cardiac MR imaging in daily clinical cardiology practice. In this Editorial Point of View the clinical applications of MR imaging are discussed, and its merits are weighed against the current clinical value of nuclear cardiology.

These MR techniques can be grossly divided into MR imaging, MR angiography, and MR spectroscopy. MR *imaging* provides detailed anatomic and functional images of the cardiovascular system in any desired imaging plane without the limitations inherent to more traditional techniques such as echocardiography, nuclear imaging, cine computed tomography (CT), and X-ray ventriculography. MR imaging techniques reveal 3-dimensional information on anatomy, function, and flow.[1,2] Regional and global heart function can also be evaluated both at rest and under pharmacologic stress.[3-5] High-speed MR imaging techniques allow the assessment of myocardial perfusion.[6] MR tagging is an imaging method that uses a myocardial grid to allow the monitoring of progressive distortion of the myocardium during the cardiac cycle. Specialized MR techniques, such as MR *angiography*, are available to visualize the proximal coronary arteries[7] and to quantitate blood flow velocity and volumes.[8] MR *spectroscopy* offers unique information on cardiac metabolism in a variety of heart diseases.[9]

Recently, the clinical role of MR in cardiovascular disease has been defined in a report instituted by a Task Force of the European Society of Cardiology, in collaboration with the Association of European Pediatric Cardiologists.[10] For several manifestations of heart disease, the MR techniques are already being used as a first imaging modality of choice (Table 1). Before discussing the applications in clinical cardiology, the currently used MR techniques are briefly described.

SPIN-ECHO MRI

Multislice spin-echo MR imaging, with triggering of the image acquisition to the R-wave of the electrocardiogram, is the most commonly used strategy for defining the structure of the heart and great vessels.[11] The flowing blood provides natural contrast, thereby allowing anatomic evaluation of cardiovascular pathology. Slice thickness, image orientation, and image contrast can be selected by the operator, depending on the anatomic structures under investigation. The MR imaging approach provides unlimited access to the chest without the problems of obtaining adequate imaging windows inherent to echocardiography. Spin-echo MR images, however, provide only static information, require relatively long acquisition times, and may be degraded by motion or flow artefacts.

GRADIENT-ECHO MR IMAGING

In contrast to spin-echo sequences, gradient-echo MR imaging provides dynamic information on blood flow and cardiac function.[12] Gradient-echo images display blood flow as a bright signal, whereas spin-echo images show blood flow generally as a dark signal or no signal. Flow disturbances, such as those associated with valvular stenoses and insufficiencies, are visualized

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because of low-signal turbulent jet effects contrasting with the bright signal of normal flowing blood. The images are acquired with high temporal resolution with 20 or more phases per cardiac cycle. They can be displayed in a pseudo-real-time movie loop format to provide a dynamic impression of flow and function. However, gradient-echo acquisitions require electrocardiographic gating and are not real time.

HIGH-SPEED MR IMAGING

Ultrafast MR imaging techniques and real-time echo-planar techniques have recently become available. High-speed MR imaging will reduce image degradation from physiological motion effects such as respiration. Echo-planar imaging operates in a single-shot or multi-shot format, allowing the reduction of acquisition times to 50 msec or less per image.[13] It may become clinically useful in imaging the entire heart with multiple imaging sections within a single breath hold. These fast techniques may be particularly useful in assessing function, flow, and myocardial perfusion. However, echo-planar technology places heavy demands on the MR gradient system and the radiofrequency receiver of the MR imaging machine.

MR ANGIOGRAPHY

MR angiography is based on gradient-echo sequences that allow visualization and quantification of blood flow noninvasively without the use of contrast agents.[14] Such techniques are categorized as time-of-flight or phase-contrast methods. In the resulting angiographic image, the vessels are depicted as a bright signal against a dark background because of the phenomenon of "flow-related enhancement." The phase-contrast method is based on velocity-induced phase shifts of spins in blood flow in the presence of a magnetic field gradient. The measured phase shift is proportional to flow velocity, which allows the extraction of quantitative data on flow velocity and volume. MR flow mapping is widely used to measure blood flow in the aorta, pulmonary circulation, intracardiac flow, native coronary vessels, and coronary artery bypass grafts, as well as a number of other vascular areas throughout the body.

MR SPECTROSCOPY

MR spectroscopy is an exciting tool for evaluation of cardiac metabolism by direct measurement of changes in high-energy phosphates with surface coils directly applied to the surface of the chest wall. Quantification of metabolism, however, is difficult because volumes of interest are relatively large as compared with myocardial wall thickness (minimal sample volume 8 cm^3). Successful preliminary studies have been carried out in control subjects and in patients with coronary artery disease, congestive heart failure, heart transplantation, cardiomyopathy, and left ventricular hypertrophy.[15-18] In our institution, we have focused on the various manifestations of left ventricular hypertrophy such as occurs in patients with hypertension and aortic valve disease, and in highly trained athletes.[19] The long-term clinical value of MR spectroscopy, however, remains to be proven.

Table 1. Current indications for cardiac MR imaging

Primary indications	
	Congenital heart disease
	Great vessel disease
	(Para)cardiac masses
	Pericardial processes
Secondary indications	
	Congestive heart failure
	Myocardial tissue abnormalities
	Valvular heart disease
Research applications	
	Aortocoronary bypass angiography
	Coronary angiography
	Ischemic heart disease

CONGENITAL HEART DISEASE

MR imaging has proven to be a useful tool in preoperative planning of complex cardiovascular malformations and may provide information that cannot be obtained by echocardiography or cardiac catheterization.[20] Its value has been established in the follow-up of patients with a variety of congenital heart disease and great vessel abnormalities.[21] This is partly due to the complexity of the postoperative anatomy and function of the right ventricle in this category of patients. MR imaging is especially well suited to assessing right ventricular structure and function. Left and right ventricular volumetrics can be derived from the MR images, without the need for geometric assumptions. This may hold especially for patients with arrhythmogenic right ventricular dysplasia.[22] Moreover, ventricular volume measurements with MR imaging appear to be more reproducible than those obtained with other imaging modalities. In addition, MR imaging seems to be a useful technique for assessing anatomy and flow of the pulmonary circulation in patients who have undergone surgical procedures to improve pulmonary blood flow.[23] It seems to offer advantages over echocardiography for determining the presence or absence of a confluence of the pulmonary arteries in patients with pulmonary atresia. Obtaining an accurate diagnosis of obstruction in extracardiac conduits, for example, in patients after undergoing Fontan operation,[24] is also possible with MR techniques. MR flow mapping can be used to quantitate pulmonary regurgitation after surgical correction of tetralogy of Fallot.[25,26] In addition, MR flow imaging techniques allow the assessment of diastolic function of the right ventricle after Mustard or Senning repair for transposition of the great arteries.[27]

The use of MR imaging to diagnose vascular rings and other arch anomalies, Marfan's disease,[28] pulmonary artery malformations, and patency of postoperative shunts and conduits has also been well demonstrated. MR imaging can reveal the site and functional severity of narrowing of the distal aortic arch, that is, coarctation of the aorta.[29] MR flow mapping of collateral flow below the coarctation provides direct assessment of the hemodynamic significance of the narrowing, which is critical in planning the surgical procedure.

To summarize, MR imaging is generally superior to other imaging modalities such as echocardiography and nuclear imaging in congenital heart disease. Particularly in patients with complex congenital lesions, MR imaging is developing into a complete tool for the evaluation of presurgical diagnosis and postsurgical sequelae.

ACQUIRED HEART DISEASE

Cardiac Masses

Acquired heart disease such as paracardiac masses, intracardiac masses, and pericardial disease are very well defined by MR imaging, and they are considered to be primary indications for MR imaging.[30] In particular, the use of paramagnetic contrast agents allows the distinction between a cardiac thrombus and a tumor. Obviously, there is no role for nuclear imaging techniques in the detection of cardiac masses.

Great Vessel Disease

A number of large vessel abnormalities can be assessed in considerable detail by use of CT, as well as MR imaging. A comparison of the diagnostic yield of CT, transthoracic and transesophageal echocardiography (TEE), angiography, and MR imaging in patients with suspected aortic dissection has shown that MR imaging provides the most reliable information with regard to the presence and extent of dissection.[31] Currently, TEE and fast spiral CT are the methods of choice in the (hyper)acute phase of aortic dissection, and MR imaging is the preferred tool for diagnosis and follow-up of aortic dissection in more stable patients. Other acquired abnormalities of the aorta such as aneurysms can be well defined and monitored over time by use of MR imaging. The size and extent of aortic aneurysms can be measured in this way and may in time obviate the need for CT or contrast angiography. In summary, great vessel disease is currently accepted as a primary indication for MR imaging, and a combination of echocardiography (acute phase) and MR imaging (subacute phase) may eliminate the need for invasive aortography. Of course, because of its intrinsic high resolution, MR angiography is superior to radionuclide imaging in delineating vessel imaging and vessel flow quantification.

Coronary Artery Disease

Over the past few years, several studies have attempted to validate the use of MR imaging for the detection of coronary artery disease. Most of the studies have focused on function, perfusion, MR coronary angiography, and myocardial viability. Table 2 shows the indications for MR imaging in coronary artery disease on the basis of the previously mentioned Task Force Report.[10] From this report it appears that no class I indication for MR imaging is given in coronary artery disease. Myocardial function has a class III indication, myocardial perfusion and coronary angiography are considered to be investigational, and myocardial viability received a class II indication. This is very much in contrast with the indications for nuclear cardiology as presented in the Guidelines of the American Society of Nuclear Cardiology,[32] whereby almost all aspects of coronary artery disease are given a class I indication. Yet, a considerable amount of important clinical studies have been performed in patients with coronary artery disease by use of MR techniques.

Myocardial Function

Similar to stress echocardiography, the hallmark of myocardial ischemia is the presence of resting or stress-induced wall motion abnormalities. Because physical exercise during MR imaging is difficult to impossible because of motion artifacts and space restriction, pharmacologic stress has been used in these studies. Pennell et al[33] were the first to report on the use of MR imaging in combination with dipyridamole. The authors performed a direct comparison between thallium-201 scintigraphy and MR imaging in 40 patients with coronary artery disease. The sensitivity of dipyridamole MR imaging for the detection of coronary artery disease was 62%; the agreement between reversible Tl-201 defects and wall motion abnormalities was 67%. Hence, dipyridamole did not induce wall motion abnormalities in 33% of the regions exhibiting a perfusion defect on Tl-201

Table 2. Indications for MR imaging in patients with coronary artery disease

Indication	Class
Assessment of myocardial function	III
Detection of coronary artery disease	
Analysis of regional left ventricular function during stress	III
Assessment of myocardial perfusion	Inv
Coronary angiography	Inv
Bypass graft angiography	III
Assessment of coronary flow	Inv
Detection and quantification of acute myocardial infarcts	IV
Sequelae of myocardial infarction	
Myocardial viability	II
Ventricular septal defect	III
Mitral regurgitation	III
Intraventricular thrombus	II

Class I provides clinically relevant information and is usually appropriate; may be used as a first line imaging technique.
Class II provides clinically relevant information and is frequently useful, but similar information may be provided by other imaging techniques.
Class III may provide clinically relevant information but is infrequently used because information from other imaging techniques is usually adequate.
Class IV does not provide clinically useful information.
Inv, potentially useful, but still under investigation.
N.B. No class I indication is provided for magnetic resonance imaging in patients with coronary artery disease.
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imaging. Baer et al[34] using dipyridamole MR imaging showed a sensitivity of 78%. In a subsequent study, Pennell et al[35] compared dobutamine MR with Tl-201 single photon emission computed tomography (SPECT) in 22 patients with coronary artery disease. Twenty-one of the patients showed ischemia on Tl-201 SPECT, with 20 (95%) exhibiting new wall motion abnormalities during dobutamine MR, indicating a high sensitivity for the detection of coronary artery disease. In a subsequent study, Baer et al[36] compared technetium-99m sestamibi SPECT with dobutamine MR imaging and reported comparative sensitivities for MR imaging and Tc-99m sestamibi SPECT: 84% and 87%, respectively

In our institution, Van Rugge et al[37] gained extensive experience with dobutamine MR on the basis of quantitative evaluation of regional and global heart function by use of our homemade MR Analytical Software System (MASS 3.0), which is a dedicated software package for automatic delineation of the epicardial and endocardial borders.[38] Wall motion abnormalities, either induced by pharmacologic stress or after myocardial infarction[39] can be accurately and reliably assessed with the MASS-derived centerline method. With this technique, a sensitivity of 91% and a specificity of 80% were obtained.[37] An overview of the results of the available MR imaging studies in detecting coronary artery disease is presented in Table 3.

Myocardial Perfusion

MR perfusion imaging, with the aid of MR contrast agents, may be used to assess the functional significance of coronary artery stenoses by demonstrating perfusion abnormalities in the myocardial bed distal to the stenoses. Matheijssen et al[40] compared dipyridamole MR imaging with Tc-99m sestamibi SPECT in 10 patients with single-vessel disease. Both SPECT and MR had a 100% sensitivity for detection of coronary artery disease. Agreement in localization of stenosis was 90% between SPECT and MR and 70% between MR and angiography. It should be realized that in most ensuing studies differences in regional perfusion were based on differences in signal intensity rather than on visually judged differences. Therefore radionuclide myocardial perfusion imaging is the current method of choice for the noninvasive assessment of coronary artery disease, whereas MR perfusion imaging is still investigational. Also, radionuclide myocardial perfusion imaging is well recognized for the assessment of prognosis in patients with coronary artery disease, whereas only one MR imaging study

Table 3. Accuracy of MR imaging in the detection of coronary artery disease

Author	Year	No of patients	Stressor	MPI agent	MPI sens	MR sens
Pennell et al[33]	1990	40	Dipyridamole	Tl-201	92%	62%
Baer et al[34]	1992	23	Dipyridamole	—	—	78%
Pennell et al[35]	1992	22	Dobutamine	Tl-201	95%	91%
Baer et al[36]	1994	35	Dobutamine	MIBI	87%	84%
Van Rugge et al[37]	1994	39	Dobutamine	—	—	91%

MPI, Myocardial perfusion imaging; *sens,* sensitivity; *MIBI,* technetium-99m sestamibi; MR, magnetic resonance.

showed prognostic significance. Wu et al[41] recently demonstrated that patients with microvascular obstruction after acute myocardial infarction, as assessed by MR imaging, had a poor prognosis. A potential advantage of MR imaging over myocardial perfusion scintigraphy might be the assessment of both perfusion and function during one study.[42] With the introduction of gated SPECT imaging, however, radionuclide scintigraphy can currently provide similar information.[43] Gated SPECT imaging allows assessment of regional perfusion, wall thickening, wall motion, left ventricular ejection fraction, and volumes in one session. It is likely that gated SPECT imaging will become the state-of-the art technique to evaluate patients with known or suspected coronary artery disease.

MR Coronary Angiography

MR coronary angiography may become a useful screening tool for imaging the main coronary arteries for detecting significant stenoses[44,45] and the abnormal origin and course of the coronary arteries.[46,47] In addition, the evaluation of coronary artery bypass patency by MR flow measurements is an important step forward.[48] The clinical value of MR coronary angiography in daily practice remains to be established, but developments such as high-speed imaging, improved surface coils, intravascular contrast agents, and real-time tracking of diaphragmatic motion to avoid the need for breath-holding indicate a major role for MR coronary artery imaging in the future. In view of the limited spatial resolution of the nuclear imaging techniques, there is obviously no role for nuclear cardiology in delineating the coronary artery tree.

Myocardial Viability

On the basis of the Task Force Report,[10] the clinically most useful approach of MR imaging in coronary artery disease is the assessment of myocardial viability (class II indication, Table 2). Various studies with MR imaging have focused on the assessment of myocardial viability.[49-59] Four markers of viability have been used in these studies: increased signal intensity, end-diastolic wall thickness, systolic wall thickening at rest, and contractile reserve during dobutamine stimulation. The available studies concerning the assessment of myocardial viability with MR imaging are summarized in Table 4.

Comparative studies with radionuclide markers have shown excellent correlations between MR imaging techniques and scintigraphic modalities. Johnston et al[49] evaluated 24 patients with MR and stress-rest Tl-201 scintigraphy. Viability criteria on MR imaging were increased signal intensity and preserved systolic wall thickening. The authors demonstrated that 91% of the patients with redistribution on thallium-201 scintigraphy had preserved increased signal intensity and systolic wall thickening on MR imaging, whereas 46% of the patients with a fixed defect were also classified as viable by MR imaging. It was concluded that MR imaging is capable of detecting myocardial viability and that conventional Tl-201 stress-redistribution imaging underestimated the presence of viable tissue.

Baer et al[50,51] performed two studies evaluating the value of end-diastolic wall thickness (EDWT) and systolic wall thickening (SWT) at rest for defining the presence or absence of viability and compared the results with resting Tc-99m sestamibi SPECT. Both studies indicated segments with EDWT > 2.5 SD below the mean value and absent SWT at rest demonstrated scar on Tc-99m sestamibi SPECT (tracer uptake < 50%). In a more recent study, Baer et al[52] compared MR imaging with fluoro-deoxyglucose positron emission tomography (FDG PET) in akinetic myocardium. Segments were considered viable on FDG PET when the uptake was 50% or more; on MR imaging segments were considered viable when EDWT was ≥5.5 mm (the mean minus 2.5 SD in healthy individuals). FDG uptake correlated with EDWT; considering FDG PET as the gold standard, EDWT had a sensitivity of 72% and a specificity of 89%.

Two studies by Perrone-Filardi et al[53,54] compared FDG PET and Tl-201 reinjection scintigraphy with MR imaging. In one study the authors showed that the major-

Table 4. Experience of MR imaging in the assessment of myocardial viability

Author	Year	No. of patients	Viability	Outcome
Johnston et al[40]	1993	24	ISI, SWT	MR imaging is superior over Tl-201 stress-redistribution for assessment of viability
Baer et al[50]	1992	20	EDWT, SWT	Good agreement between absent SWT or reduced EDWT and scar on MIBI SPECT
Baer et al[51]	1994	55	EDWT, SWT	Good agreement between absent SWT or reduced EDWT and scar on MIBI SPECT
Baer et al[52]	1995	35	EDWT, CR	Comparison with FDG PET; optimal detection of viability by combining EDWT and CR
Perrone-Filardi et al[53]	1992	25	EDWT, SWT	Viable segments on Tl-201 reinjection or FDG PET have preserved EDWT and SWT
Perrone-Filardi et al[54]	1992	25	EDWT, SWT	EDWT and SWT underestimate viability as compared with PET
Baer et al[55]	1998	43	EDWT, CR	CR is superior over EDWT in the prediction of functional outcome after revascularization
Baer et al[56]	1996	43	CR	CR on MR or low-dose dobutamine echocardiography correlates well with viability on FDG PET
Dendale et al[57]	1995	37	CR	CR on MR imaging predicts recovery of function after acute myocardial infarction
Dendale et al[58]	1998	26	CR	Dobutamine MR imaging has an 80% accuracy to predict outcome after myocardial infarction
Lawson et al[59]	1997	24	EDWT	EDWT and SWT correlate with Tl-201 uptake

ISI, Increased signal intensity; *CR*, contractile reserve during dobutamine stimulation; *EDWT*, end-diastolic wall thickness; *FDG*, Fluorodeoxyglucose; *PET*, position emission tomography, *SWT*, systolic wall thickening

ity of segments with viability on FDG PET and thallium-201 reinjection imaging exhibited preserved EDWT and systolic wall thickening at rest.[53] In the other study the authors showed that many regions with reduced EDWT and absent systolic wall thickening at rest were viable on FDG PET, indicating underestimation of viability by the parameters derived from MR imaging.[54] Finally, Baer et al[55] tested the predictive value of end-diastolic wall thickness against outcome after revascularization. In a study comprising 43 patients, EDWT had a high sensitivity (92%) with a low specificity (56%) to predict functional outcome after revascularization. Hence, segments with <5.5 mm EDWT are likely to represent transmural scars and will not recover function after revascularization. On the other hand, segments with preserved end-diastolic wall thickness do not always recover function after revascularization. The most likely explanation for this finding is the presence of subendocardial scars: these segments frequently have a preserved end-diastolic wall thickness but will not improve in function after revascularization.

The last criterion indicating viability that can be derived from MR imaging is the presence of contractile reserve during stimulation with low-dose dobutamine (10 µg/kg/min). Baer et al[56] compared the presence of contractile reserve with MR imaging with FDG PET and dobutamine echocardiography in patients with chronic ischemic left ventricular dysfunction, yielding an excellent agreement between the three approaches. Moreover, the authors showed in a subsequent study that contractile reserve with MR imaging had a sensitivity of 89% with a specificity of 94% for the prediction of functional recovery after revascularization. The number of segments with contractile reserve correlated significantly with the magnitude of improvement of left ventricular ejection fraction after revascularization. Dendale et al[57] studied 37 patients with a recent myocardial infarction and showed that patients with contractile reserve on MR imaging did recover function 3 to 6 months after infarction. In a more recent study,[58] these authors reported an accuracy of 80% of dobutamine MR imaging in predicting functional outcome after myocardial infarction. Lawson et al[59] showed a good correlation between end-diastolic/systolic wall thickness and Tl-201 uptake in patients with acute and healed infarcts. In conclusion, different markers for viability can be derived from MR imaging, and it seems that assessment of contractile reserve during dobutamine MR imaging provides the most accurate information on the presence/absence of viability. Currently, very limited data are available concerning the accuracy of MR imaging for the prediction of functional recovery after revascularization. This is in contrast to the extensive number of studies performed with radionuclide imaging. As a result, radionuclide imaging is presently the imaging modality of choice for the evaluation of myocardial viability.

To summarize, nuclear cardiology techniques remain the first modalities of choice in patients with coronary artery disease because of (1) long-lasting experience, (2) multiple choice of tracers, (3) assessment of ischemia during conventional exercise, (4) gated SPECT imaging, and (5) evidence-based prognostic value. It is hoped that MR imaging techniques will get a more clearly defined clinical role in patients with coronary artery disease in the near future.

The clinical role of cardiovascular MR imaging is unequaled in congenital heart disease and abnormalities of the great vessels. The role of MR imaging in coronary artery disease is not fully matured, and at present nuclear cardiology techniques are superior in any field of coronary artery disease except MR coronary angiography. In the near future, the replacement of multiple diagnostic tests with one single MR test may become a major asset for MR imaging, although the advent of gated SPECT imaging (simultaneous assessment of perfusion and function) has been a major breakthrough in nuclear cardiology. The time has come to institute adequate studies with comparative imaging modalities to have a better insight in the true relative value of MR techniques in clinical cardiology.

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