INVITED PAPER

Magnetic Resonance Imaging in Cardiomyopathies

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INTRODUCTION

Cardiomyopathies are chronic progressive myocardial diseases with distinct morphological, functional, and/or electrophysiological characteristics. On clinical, morphological, and histological grounds, they have been classified into four categories: dilated cardiomyopathy (DCM), hypertrophic cardiomyopathy (HCM), restrictive cardiomyopathy (RCM), and arrhythmogenic right ventricular cardiomyopathy (ARVC) (1).

Although originally understood as "primary" or "idiopathic," several etiological factors leading to the phenotype have been identified for each cardiomyopathy. A genetic predisposition with a possible additional effect of inflammatory or toxic injuries of the myocardium may contribute to the development of DCM (2) and ARVC (3). Genetic defects are made responsible for HCM (4). RCM may be idiopathic but also may be due to infiltrative systemic diseases such as amyloidosis, which is also often inherited.

The diagnosis of cardiomyopathies must be established by exclusion of other cardiovascular etiologies, and the specific type of cardiomyopathy must be confirmed. Therapy is guided by the individual stage and hemodynamic relevance of the disease, which is frequently a long-term management problem. Thus, imaging techniques are of paramount importance for both diagnosis and therapy. The modalities frequently used in these diseases are echocardiography, conventional an-

Received December 8, 1998; Accepted September 8, 1999 Address correspondence to M. G. Friedrich. giography, radionuclide ventriculography, and magnetic resonance imaging (MRI).

ROLE OF OTHER DIAGNOSTIC MODALITIES IN CARDIOMYOPATHIES

Echocardiography and conventional left ventricular (LV) angiography are the tools routinely used for function analysis. Transthoracic echocardiography serves as the standard technique to assess LV parameters, including M mode, two-dimensional (2D), and Doppler methods. The technique is widely available, noninvasive, fast, and easily performed in most patients. However, obtained results feature substantial interstudy and interobserver variability, which is a limiting factor in their use (5-8). Because of the poor ultrasound transmission of adjacent tissues such as pulmonary air and sternal or costal bones, the echocardiographic fields of view may be restricted. Consequently, echocardiography is susceptible to angular errors of the ultrasonic plane and diameters, resulting in underestimation of (especially systolic) intraventricular dimensions and subsequent overestimation of the ejection fraction (9). The use of newer techniques such as acoustic quantification (10), automated border detection (11), or three-dimensional postprocessing (9) may improve this state of affairs to a minor degree. However, their value in clinical cardiology is not yet established. Transesophageal echocardiography (12) is semiinvasive,

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uncomfortable, and not free of risks for cardiovascular patients (13).

One of the most important limitations of echocardiographic (as well as other "ray" modalities) is the lack of techniques to analyze tissue pathology itself. Despite the initial hope to identify specific pathology-related changes of echogenicity (14), results to date have generally been disappointing.

LV angiography after intraventricular injection of contrast media reveals an accurate projection of the contracting LV. Biplane data acquisition is possible with a high temporal and high in-plane spatial resolution. The technique provides reliable information on cardiac volume and ventricular function (15). The investigation of coronary vessels in the same session is important to exclude coronary artery disease. As a strong limitation of the method, invasive angiography poses substantial risks to the patient, including vessel injury, plaque disruption, volume overload, and arrhythmia, leading to an overall mortality of 0.14% (16). Further limitations include radiation and adrenergic stimulation of the patient's cardiovascular system (17).

MRI IN CARDIOMYOPATHIES: GENERAL ASPECTS

MRI noninvasively visualizes LV and right ventricular (RV) morphology and function with a very high degree of accuracy and reproducibility (18,19). MRI is superior to 2D echocardiography in determination of ventricular mass (5,20) and volumes (21). In the last few years, the upsurge of cardiac MRI as the in vivo gold standard for identifying the phenotype of cardiomyopathies in the diagnosis and follow-up of these patients is increasingly apparent.

The power of MRI to obtain visual information on the pathological processes of the myocardium and to perform tissue analysis in cardiomyopathies has not yet been fully exploited. This task will be easier in the future because of faster and stronger gradient systems currently available and a wider spectrum of sequences. The MRI tecnique will most likely overcome the limitations of density projections, such as x-ray or analysis of reflected ultrasound. Because proton relaxivity depends on the chemical environment, pathological processes with a more or less destinct local chemistry may allow a specific identification of diseased tissue. This principle was recognized rather early on and will incresingly be exploited (22, 23). MRI is contraindicated when metallic objects may harm the patient during exposure to the B_0 field. This factor must be considered in the case of implanted pacemaker electrodes or projectiles due to trauma, whereas surgical implants (exceptions include metallic devices with magnetic properties rarely used in vessel surgery), valve prostheses, and state-of-the-art coronary stents are harmless and are *not* a contraindication to MRI. Claustrophobia occurs in about 5% of the patients but can be managed by careful sedation before moving the patient into the device. Other limitations are the lack of wide availability of scanners, costs, and limited knowledge and personal experience of cardiologists with this technique.

MRI APPROACH TO THE PATIENT WITH CARDIOMYOPATHY

Morphology and Function

Cardiomyopathies are characterized by specific alterations of ventricular and myocardial geometry and/or function. To assess volumes and mass, generally white blood gradient echo sequences are applied with 10 to 30 phases per heartbeat (Fig. 1). Breathholding techniques with acquisition times of 15 to 20 sec reduce blurring of the endocardium-blood border and are preferred, although a small shift of the heart's position between the breathhold studies may occur. Developments of breathhold multislice techniques covering the entire ventricles are under way. To cover the whole diastolic phase, techniques exist with continuous data acquisition and retrospective gating (24). Whereas under routine clinical circumstances a biplanar approach (long-axis and shortaxis view) may be sufficient (25), entire coverage of the left ventricle with short-axis views from the mitral plane to the apex is preferable for accurate measurements of volume and mass (26).

Total coverage is especially important in the followup after therapeutic interventions. Reliable angulation of the images by a series of at least three angulated scouts is crucial, because the anatomical axis of the heart is not perpendicular to any of the orthogonal planes of the magnetic field. Slice thickness should not exceed 10 mm; in case of circumscribed or subtle global changes it should be reduced adequately. It is important to notice a substantial shortening of the ventricular long axis (27) leading to a smaller number of slices covering the heart in systole as compared with diastole (28). Small doses of gadolinium enhance image quality in patients with arrhythmia or other causes of a low contrast-to-noise ratio (29). In

MRI in Cardiomyopathies



Figure 1. Dilated cardiomyopathy. Gradient-echo images (TE 4.6 msec) in a long-axis view (left) showing extensive global dilatation of the left ventricle. The end-diastolic diameter is 88 mm. Diastolic (middle) and systolic (right) gradient-echo image in a shortaxis view revealing global hypokinesie with septal akinesia.

the future, automated edge detection may facilitate the evaluation process in clinical routine (30).

A frequent finding in patients with cardiomyopathies is mild to moderate mitral regurgitation. Promoting factors are dilatation of the mitral valve ring (DCM, infiltrative cardiomyopathies) and papillary muscle dysfunction due to infiltration (sarcoidosis, amyloidosis, hemochromatosis, or tumor). Because mitral valve competence is of prognostic value, it should be assessed using gradientecho sequences (with adjusted TE) or phase-contrast techniques. If quantification of mitral regurgitation is required for therapeutic decision-making, an established technique using flow analysis should be performed (31,32). "Eyeball" quantification of the regurgitant jet, as used in ventriculography or evaluation of the jet size performed in echocardiography (33), may be misleading and should be used with great caution.

Tissue

For delineation of cardiac anatomy, "black-blood" T1-weighted spin-echo techniques are preferable, because of the excellent contrast between the myocardium and adjacent structures such as epicardial fat and intracavital blood. Slice orientation depends on the question being posed to the MR study; however, the orientation should include views orthogonal to the anatomical axis of the heart. Gadolinium administration followed by a repeat T1 study may be helpful in infiltrative and infiammatory myocardial disease. T2-weighted image quality has markedly improved by short T1 inversion recovery techniques, and fluid accumulation such as edema and effusion in inflammatory or malignant diseases may be sensitively visualized. Cardiomyopathic tissue transformation can be identified, including granulomatous infiltrates in sarcoidosis or iron deposits in hemochromatosis. However, MRI still lacks reliable techniques to detect intramyocardial fibrosis as a frequent type of pathology with prognostic relevance. Preliminary studies with contrast-enhanced MRI suggest that the increase of interstitial space in fibrotic tissue may be reflected by gadolinium accumulation (34); however, clinical and controlled data are not available.

Metabolism

MR spectroscopy (MRS) has generally relied on ¹H and ³¹P and has been applied in several studies of cardiomyopathy. Changes of high-energy phosphates as studied by ³¹P-MRS in cardiomyopathy were reported for DCM (35,36) and HCM (37). However, MRS remains an experimental approach for several reasons. ¹H-MRS is limited by a strong signal from water-bound protons and difficulties in spectral interpretation. ³¹P-MRS is limited by the weakness of the phophorous signal. Thus, voxels must be sufficiently large to cover circumscribed myocardial regions, and spectra are often altered by blood or adjacent tissue (e.g., skeletal muscle). Newer techniques feature irregularly shaped voxels and a significantly lower degree of spectral contamination (38). This approach may allow reproducible acquisition of reliable and highly informative myocardial spectra and even identify local pathology. However, MRS techniques require extensive experience, strong support from an MR physicist, highly sophisticated hardware and software, and a close collaboration with the manufacturer. Thus, the number of centers with access to this promising tool is currently limited.

DILATED CARDIOMYOPATHY

DCM is characterized by a progressive dilatation of the heart with loss of contractile function. Its etiology is not clarified in about half of the cases (39); however, the typical pattern may be the final result of a disease process initiated by various insults, including myocardial inflammation, toxic agents like alcohol or anthracyclines, or genetic disorders (2). The histological hallmark of DCM is a progressive interstitial fibrosis with a numerical decrease of contractile myocytes. In advanced stages, DCM is also associated with at least relative wall thinning.

Main targets of MRI studies in DCM are LV morphology and function, and gradient-echo sequences are suitable. MRI has been proven to have a low interobserver and intraobserver variability of LV mass and volume measurements (18,40), with a good correlation to results obtained with radionuclide ventriculography (41). It is superior to echocardiography (20,42). MRI was also used to analyze wall thickening in DCM (43), visualize impaired fiber shortening (44), and calculate end-systolic wall stress that may be a very sensitive parameter for changes of LV function (45). The right ventricle is also frequently affected in DCM, and its morphology and function is accurately assessed by MRI (46,47). Using three-dimensional MRI, atrial volumes and function were approached (48), and in patients with DCM, enlargement and reduction of the atrial ejection fraction were found (49). Cardiac MR may be the method of choice for a longitudinal follow-up in patients with DCM under pharmacological interventions (50) or after cardiomyoplasty (51). MRI-derived parameters also serve for reliable end point definitions in clinical studies of DCM (52). In a retrospective analysis of a study in patients with DCM, the estimated sample size needed to detect LV parameter changes in a clinical trial on pharmacological interventions was by far lower when MRI was chosen instead of 2D echocardiography (21). Thus, costs could be reduced markedly and time could be saved in clinical research.

However, the application of MRI as a method with a higher sensitivity to subtle changes should not be confined to scientific considerations. The extremely high accuracy enables the physician to adequately adjust the therapy. Moreover, inconsistency in the results is much less likely to occur. Both improvements in therapy and reduction in hospital admissions for repeat studies are likely to overcome the additional costs of an MRI study. However, an analysis of cost effectiveness has not yet been prospectively conducted.

Spectroscopic studies have shown that high-energy phosphate metabolism is altered in dilated cardiomyopathy (53). A low ratio of phosphocreatine to ATP as assessed by MRS was shown to be of prognostic value in DCM (36). A study with a similar technique related these changes to a reduction of creatine kinase activity (54). Future studies will shed more light on these exciting field of research, and further clinical studies are warranted.

Investigating the early onset of DCM is an important undertaking. The incidence of inflammation-induced forms of DCM is unclear (2); however, a substantial proportion of DCM patients may in fact suffer from viral myocarditis (55). In a series of endomyocardial biopsies in patients with clinically suspected hypertrophic and dilated cardiomyopathy, the proportion of inflammatory changes as detected in biopsy material was as high as 25% (56). Inflammation may serve as a trigger to initiate myocardial tissue transformation. Autoimmunological mechanisms and persistence of active viruses are currently under active investigation. In these cases, an ongoing inflammatory process is likely to be present. In a recent study, contrast media-enhanced T1-weighted MR images visualized reversible myocardial signal changes in acute myocarditis (57). The increase of gadolinium accumulation and subsequent signal increase were presumably caused by a combination of increased inflow (inflammatory hyperemia), slow interstitial wash-in/washout kinetics (capillary leakage and edema), and diffusion into cells (necrosis). Long-term follow-up revealed persisting changes in patients with clinical and functional evidence for ongoing inflammation (58). Signal enhancement was also found to be increased in patients with Chagas myocarditis (59).

There is evidence for similar changes in chronic DCM (60). Associated edema during acute inflammation may be detected by conventional and breathhold T2-weighted MRI (61,62). Contrast-enhanced MRI could also increase the sensitivity of endomyocardial biopsy by visualization of inflammatory areas and preinterventional definition of the biopsy site (63). Regional changes of contrast media may also occur when the myocardium is involved in systemic vasculitis (Fig. 2). Thus, MRI may be a very help-ful tool for the diagnosis and noninvasive follow-up of patients with inflammatory myocardial disease presenting as DCM. However, further studies are needed to enhance the specificity of contrast-enhanced MRI by additional or improved imaging techniques and to assess the prognostic value of these changes. Moreover, similar ap-



Figure 2. Myocardial involvement in systemic lupus erythematodes in a patient with known disease and new onset of angina, tachycardia, ST segment changes, arrhythmia, and small pericardial effusion. T1-weighted spin-echo image after application of Gd-DTPA. Subendocardial contrast media accumulation (arrow) and a suspected septal focus.

proaches are warranted in toxic injuries to the myocardium.

Progressive fibrotic replacement of the myocardium characterizes advanced stages of the disease. In a pilot study, the attempt was made to visualize myocardial fibrosis by contrast-enhanced MRI (34), but further results have to be awaited before firm conclusions can be drawn.

HYPERTROPHIC CARDIOMYOPATHY

HCM features inappropriate myocardial hypertrophy with loss of diastolic function and a narrowing of the LV outflow tract (LVOT). The condition is a common cause of sudden death in young people (64). Histologically, areas of hypertrophy reveal a pattern of myofibrillar disarray and patchy areas of necrotic tissue due to relative coronary insufficiency.

Echocardiographic findings include wall thickening and accelerated flow in the LVOT in obstructive HCM. For the clinical follow-up, the pressure gradient is estimated from measurements of velocity and according to a modified Bernoulli formula. In a small series of patients, the correlation with direct catheter measurements was adequate (65). However, there is an unacceptably high intraindividual variation of results, probably due to the susceptibility of flow velocities to the hemodynamic status (66). Moreover, the pressure gradient may be overestimated easily (67). Thus, although frequently used, echocardiography has substantial limitation in defining the morphology and hemodynamics in individual HCM.

MRI studies have been applied to morphology, mass, function, tissue characterization, and hemodynamic relevance of obstruction. Because of its high sensitivity of detecting regional morphological changes and its noninvasive character, MRI may be of special importance in screening families of index patients.

MRI reliably quantifies LV mass and is superior to 2D echo (20), which seems to overestimate LV mass (68). Also, MRI is more accurate than 2D echo to assess regional hypertrophy patterns (69,70) and is an excellent tool to determine different phenotypes of this disease (e.g., apical forms) (71) or cases associated with other diseases (72). Postsurgical changes after myectomy can be reliably monitored and quantified (73). Standard gradient-echo sequences are suitable for functional studies, visualization of turbulent flow in LVOT obstruction, and mass quantification (Fig. 3).

The turbulent jet during systolic LVOT obstruction is easily detected when suitable echo times (about 4 msec for typical blood flow velocities) are used. The systolic anterior motion of the anterior mitral valve leaflet may



Figure 3. Hypertrophic obstructive cardiomyopathy. Systolic gradient-echo in a long-axis view, including the LVOT (TE 4 msec). The increase of flow velocity and subsequent signal loss due to LVOT obstruction is easily detected.

contribute significantly to the LVOT obstruction and is a typical feature of obstructive HCM. The phenomenon is detectable by MRI (74) and best visualized in the fourchamber view or a short-axis view through the valvular plane. Mitral valve regurgitation, probably due to a pathological change of leaflet geometry, is frequent and should be included in an MRI workup.

MRI may be helpful in the exclusion or verification of hypertrophy due to extracardiac causes such as amyloidosis (75). Preliminary studies indicate that hypertrophic tissue may reveal native signal heterogeneities (76). The tissue signal of HCM-associated hypertrophy may also differ from normal myocardium in contrastenhanced MRI studies (77).

MR techniques have been established to investigate phosphate metabolism in HCM. Myocardial phosphocreatine/ATP ratio and the signal of phosphomonoesters reveal changes in patients with HCM (37,78), and the decrease of myocardial energy reserve related to high-energy phophate metabolism correlates to diastolic dysfunction (79). Phosphorous metabolism was also found to be altered in skeletal muscles of HCM (80).

Blood flow analysis in the coronary sinus using MR is feasible, and a preliminary study suggested alterations of coronary flow reserve in patients with HCM (81). A promising approach to assess the hemodynamic relevance of LVOT obstruction may be the noninvasive measurement of the effective outflow tract area by MRI planimetry of transplanar flow in the LVOT during systole (82). This method may overcome the problem of pressure recovery with subsequent overestimation of the pressure gradient (67) and the high interstudy variability of pressure gradient measurements by echocardiography (66), which is presumably also a feature of invasive studies.

Diastolic function (or dysfunction) is a powerful clinical and prognostic factor in hypertrophy but is not part of the routine MRI. Preliminary clinical results suggest that the analysis of the early untwisting motion of the myocardium may be a helpful tool to assess early diastolic function in hypertrophic heart diseases (83). Other functional changes detected by the use of myocardial tagging are a reduction of posterior rotation, a reduced radial displacement of the inferior septal myocardium (84), heterogeneities of regional function (85), and reduced 3dimensional myocardial shortening (86). These findings may be more sensitive in the detection and quantification of functional impairment than conventional parameters such as mitral valve inflow patterns in echocardiography. Future studies will have to show the feasibility and practicability of these approaches in clinical routine.

MRI may also be very important in the follow-up of patients after surgical (74) or pharmacological interventions. A long-term follow-up is sensitive to morphological changes during the natural course of the disease (87). The acute and chronic morphological and functional changes due to interventional ablation of a septal artery in obstructive HCM are easily detected by T1-weighted images (Fig. 4).



Figure 4. Effect of septal artery ablation in severely symptomatic hypertrophic cardiomyopathy. T1-weighted spin-echo images (TE 25 msec, non-breathhold, acquisition time ≈ 6 min) in axial orientation after administration of Gd-DTPA. Left: 3 days after the intervention there is contrast media accumulation in the thickened septum. Right: 6 months later the septum shows a significant involution with subsequent reduction of LVOT obstruction (images not shown).

ARRHYTHMOGENIC RV CARDIOMYOPATHY

ARVC is characterized by a progressive degeneration of the RV and to a lesser extent the LV myocardium with localized disturbance of myocardial function. Morphological features include fibrous and/or fatty replacement of myocardial tissue, extensive wall thinning, and atypical arrangement of trabecular muscles. The associated morphological spectrum ranges from subtle changes to extensive fibrofatty dysplasia of the right ventricle (88,89).The clinical course is generally determined by ventricular arrhythmias with a substantial risk of sudden cardiac death (90). The morphological substrate to ventricular arrhythmias probably are fibromuscular bundles isolated from each other by fatty tissue, leading to reentry phenomena (91).

Echocardiography is able to show regional or global changes of myocardial contractility (92) and thus may be very helpful in detecting the disease during a routine study. However, visibility of the apex and the RV outflow tract (RVOT) are limited, areas of wall thinning may be very difficult to detect, and fat does not provide any specific signal to diffentiate it from surrounding tissue or fluid. Studies have shown a limited accuracy compared with electrocardiographic and angiographic criteria (93). So, echocardiography is a useful tool to detect findings leading to a further diagnostic workup but lacks the power to rule out or confirm the diagnosis of ARVC.

MRI noninvasively visualizes ventricular cavities and

walls with an excellent depiction of myocardial anatomy. A slice thickness of less than 6 mm is obligatory. T1weighted spin-echo studies visualize fatty infiltration, wall thinning, and dysplastic trabecular structures (Fig. 5). Orthogonal image planes (axial and sagittal) and additional short-axis views reveal the best results. The addition of a saturation band over the atria in T1-weighted images may reduce slow-flow aritfacts of inflowing blood and thereby enhance the image quality at the endocardial border of the RV apex (94). Standard gradient-echo sequences detect regional wall motion changes such as global or local hypokinesia localized early diastolic bulging or, more specifically, circumscribed sacular aneurysmatic outpouchings (Fig. 6). Several studies have been published on this issue (94-99). Frequent findings include increased RV volumes and a lower RV ejection fraction in patients with inducible ventricular tachycardia compared with those without an inducible tachycardia (76). Additionally, wall thinning and regional functional abnormalities may be detected, the latter of special value due to its high specificity. However, the sensitivity of MRI to detect intramyocardial fat was lower compared with that of endomyocardial biopsy, and fibrosis is not visualized (99). Recently, the specificity of singular findings typical for ARVC has been questioned. On the other hand, the sensitivity and specificity are good when findings such as wall thinning and regional loss of contractility are combined (100).

Recently, morphological and functional abnormalities were also detected by MRI in up to 76% of patients with



Figure 5. Arrhythmogenic right ventricular cardiomyopathy. Left: Spin-echo in the short-axis view (TE 40 msec, TR 1882 msec, slice thickness 5 mm). There is a marked RV dilatation (arrow), wall thinning, and possible myocardial fatty infiltration. Right: Systolic gradient-echo image in the same slice orientation showing extensive right ventricular dyskinesia.



Figure 6. Arrhythmogenic right ventricular cardiomyopathy. Systolic gradient-echo image in a sagittal view. There are several small dyskinetic areas of the diaphragmal right ventricular wall (arrows).

idiopathic RVOT tachycardia (101–104). The results concerning the incidence of regional wall motion abnormalities are conflicting; however, such abnormalities were found in up to 97% of patients (104). The etiological and pathophysiological relation of idiopathic RVOT tachycardia with its favorable prognosis to ARVC is under discussion. MRI will play an important role as the tool of choice for follow-up studies in ARVC.

RESTRICTIVE CARDIOMYOPATHY

Primary infiltration of the myocardium by fibrosis or other tissues leads to the rare entity of RCM. The condition is characterized by a severe diastolic dysfunction, biatrial dilatation, preserved LV size, and usually normal systolic function. Atrial thrombi occur. The main differential diagnostic consideration is constrictive pericarditis, which must be excluded in a patient with suspected RCM.

MRI studies in RCM should focus on myocardial morphology and function and on the exclusion of constrictive pericardial disease. LV size and wall thickness are quantified in gradient-echo image sets. Long-axis views are obligatory. Biatrial dilatation is easily visualized by Friedrich

means of a four-chamber view. MR volumetry of the enlarged atria may be recommended (105). Although MRI might be at least as powerful as echocardiography to assess atrial thrombi (106), slow-flowing blood in the atria may lead to false-positive results when spin-echo techniques are used (107). The choice of a longer TE, saturation of inflowing blood, and combination with gradientecho sequences may be helpful. Concomitant mitral regurgitation should be visualized. The exclusion of relevant pericardial thickening rules out constrictive pericarditis and may prevent unnecessary operative exploration of the pericardium (108). This exclusion is possible by T1 weighted spin echo-techniques (109,110).

SARCOIDOSIS

The incidence of myocardial involvement in systemic sarcoidosis is about 20-30% (111), although the heart was involved in about half of the cases in a large Japanese autopsy series (112). Up to 50% of deaths in sarcoidosis may be related to cardiac involvement (113), primarily due to sudden death and congestive heart failure. Histological findings are granulomas that are often transmural. Sarcoid lesions may lead to different signal intensity behaviors, possibly because of different stages of disease activity. Muscular sarcoidosis was reported as high signal intensity areas in T2-weighted MRI (114). In another study of skeletal muscle sarcoidosis, the granulomatous nodules exhibited a central region with low signal intensity in T1- and T2-weighted imaging but were surrounded by a high signal ring (115). Gadolinium gadopentetate dimeglumine (Gd-DTPA) seems to accumulate in sarcoid lesions of the brain (116). This behavior may be compatible with fibrotic nonactive granulomatous nodules with inflammatory response of the surrounding tissue. Similar findings were reported in several cases of sarcoid infiltration of the heart (117-120). Thus, T2weighted followed by T1-weighted spin-echo techniques in short and long axis before and after Gd-DTPA may be useful to detect or exclude suspected granulomas (Fig. 7). Occasionally, the MRI findings could be used to "guide" endomyocardial biopsy (118).

Because follow-up is very important to guide therapy, MRI may be very helpful in these patients. However, sufficient data sets and standardized protocols must still be generated.

AMYLOIDOSIS

Infiltration of the heart by amyloid deposits is found in almost all cases of primary amyloidosis and in about



Figure 7. Cardiac involvement in sarcoidosis in a patient with clinical signs of heart failure, nonspecific electrocardiographic changes, and invasive exclusion of coronary artery disease. Diastolic T1-weighted short-axis view before (left) and after (rightl) administration of Gd-DTPA (TE 23 msec, TR 635 msec). There is a circumscribed area of increased gadolinium uptake in the lateral segment, including the papillary muscle (arrow). The arrowhead marks the central region of an extensive posterolateral hypokinesia.

one fourth of familial amyloidosis (121), leading to a loss of atrial (122) or LV function and congestive LV failure (123). There are only a few reports on MRI in cardiac amyloidosis (75,124). Similar to sarcoidosis, the MRI approach is directed toward the detection of signal changes after Gd-DTPA administration. At present, it is unclear how to differentiate between different infiltrative diseases. Because of the rather low incidence of these diseases, the difficulties to enroll a sufficient number of patients are obvious. Furthermore, the underlying mechanisms of a change in magnetization and relaxation have to be clarified and standard protocols have to be developed.



Figure 8. Cardiac involvement in hemochromatosis. Left: T2-weighted short T1 inversion recovery, TE 68 msec, TR 1552 msec). Right: T1-weighted fast spin-echo (TE 23 msec, TR 768 msec). Both techniques show a low intensity appearence of the liver and an area with signal reduction in the anterolateral myocardium (arrows)

HEMOCHROMATOSIS

Hemochromatosis of the myocardium is characterized by sometimes extensive iron deposits, leading to wall thickening, ventricular dilatation, progressive loss of function with congestive heart failure, and subsequent death. Because of a predominantly subepicardial deposition of iron, endomyocardial biopsy may fail to confirm the diagnosis (125).

The MRI approach is directed toward the detection of iron deposits as the specific marker for the disease. Iron has very strong paramagnetic properties, and myocardial deposits imply an extensive signal loss in native T1Friedrich

weighted, but also T2- and T2*-weighted, imaging of different regions of the body (126,127). Similar findings were also reported for cardiac hemochromatosis (128) (Fig. 8). The pattern of focal signal loss in a dysfunctional myocardium combined with a ''dark'' liver may be sufficient to confirm the diagnosis of cardiac hemochromatosis by MRI alone. LV function should be carefully assessed.

Because an intensified therapy may improve LV function (129), MRI is an ideal tool to follow-up infiltrations and LV parameters in these patients. The highly specific detection of typical tissue changes are especially an example of the diagnostic power of MRI.



Figure 9. Endomyocardial fibrosis in a patients with a variant of Churg-Strauss vasculitis. (a) T1-weighted spin-echo in an axial orientation (TE 25 msec, TR 821 msec) crossing the apex. There is an apical wall thickening of intermediate signal intensity with a subsequent reduction of left ventricular stroke volume. (b) Left: Gradient-echo images in a long-axis view of the left ventricle (LV) and the left atrium (LA). Right: Right ventricle (RV) and right atrium (RA). Ventricles are small and both atria are dilated due to the restrictive ventricular physiology.

ENDOMYOCARDIAL FIBROSIS

Endomyocardial fibrosis is related to two forms, one occuring in the tropics and the other in temperate climate, termed Löffler's endocarditis. Both conditions lead to primarily posterobasal concentric wall thickening followed by extensive subendocardial fibrosis and frequent apical thrombus formation. Both ventricles may be affected. The course is determined by progressive diastolic dysfunction and decreased stroke volume.

The morphological and functional features can be visualized and quantified by MRI (130,131) (Fig. 9). Fibrosis or calcifications may be visible as a dark rim in bright bloodprepared gradient-echo sequences but may also reveal an intermediate signal intensity (132). Thus, there is a certain lack of accuracy to assess fibrosis (low sensitivity and specificity) and calcifications (low specificity). Differentiation from apical infarction is easy by visualization of the preserved (or increased) wall thickness and the v-shaped outer form of the apex in the long-axis views.

SUMMARY

The emerging role of MRI for the understanding and treatment of cardiomyopathies cannot be overestimated. Establishing the diagnosis is generally possible by a single noninvasive MRI study. The follow-up examination is sensitive to even small changes. MRI data on ventricular morphology, volumes, and function are very reliable, and the use of MRI-derived end points in clinical studies may lead to a substantial decrease in subjects needed to test a given hypothesis. In addition to established approaches, MRI analysis of myocardial tissues should be the focus in future studies. If MR coronary angiography will be available in a routine clinical setting, a single MR study could provide a complete and comprehensive diagnostic procedure in patients with cardiomyopathies.

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