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CHAPTER SIX

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Magnetic resonance imaging assessment of left ventricular remodeling later after restrictive mitral annuloplasty in early stages of dilated cardiomyopathy

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Abstract

Objective: Magnetic resonance imaging was used to evaluate left ventricular reverse remodeling at long-term follow-up (3–4 years) after restrictive mitral annuloplasty in patients with early stages of nonischemic, dilated cardiomyopathy, and severe mitral regurgitation.

Methods: Twenty-two selected patients (eligible to undergo magnetic resonance imaging) with mild to moderate heart failure (mean New York Heart Association class 2.2±0.4), dilated cardiomyopathy (left ventricular ejection fraction 37±5%, left ventricular end-diastolic volume 215±34 mL), and severe mitral regurgitation (grade 3–4+) underwent restrictive mitral annuloplasty. Magnetic resonance imaging was performed 1 week before surgery and repeated after 3 to 4 years.

Results: There was no hospital mortality or major morbidity. Two patients died during follow-up (9%), and 2 patients could not undergo repeat magnetic resonance imaging because of comorbidity. New York Heart Association class improved from 2.2±0.4 to 1.2±0.4 ($P<0.05$). Mitral regurgitation was minimal at late echocardiographic follow-up. There were significant decreases in indexed (to body surface area) left atrial end-systolic volume (from 84±20 mL/m^2 to 68±12 mL/m^2, $P<0.01$), left ventricular end-systolic volume (from 42±14 mL/m^2 to 31±12 mL/m^2, $P<0.01$), left ventricular end-diastolic volume (from 110±18 mL/m^2 to 80±17 mL/m^2, $P<0.01$) and left ventricular mass (from 76±21 g/m^2 to 66±12 g/m^2, $P=0.03$). Forward left ventricular ejection fraction improved from 37±5% to 55±10% ($P<0.01$). Indexed left atrial end-diastolic volume did not show a significant decrease (from 48±16 mL/m^2 to 44±10 mL/m^2, $P=0.15$)

Conclusions: Magnetic resonance imaging confirms sustained significant reverse left atrial and ventricular remodeling at late (3–4 years) follow-up in patients with nonischemic, dilated cardiomyopathy, and mild to moderate heart failure after restrictive mitral annuloplasty.

Magnetic resonance imaging (MRI) is currently considered the gold standard for the assessment of left ventricular (LV) function and volumes.[1] Advantages of MRI over echocardiography are the superior image quality and the 3-dimensional quantification possibilities with high reproducibility, implying that smaller sample sizes are needed to prove statistical significance of changes in LV volumes after therapy.[2] MRI may therefore be the most appropriate imaging technique for the evaluation of surgical treatments for heart failure. In a previous study, we presented MRI data on short-term follow-up after restrictive annuloplasty in patients with nonischemic, dilated cardiomyopathy and severe mitral regurgitation (MR).[3] Significant left atrial (LA) and LV reverse remodeling were noted 2 months after surgery. Moreover, LV ejection fraction (LVEF) improved significantly. However, whether these beneficial effects are sustained at long-term follow-up is not clear.[4] In the current study, the persistence of reverse remodeling at long-term follow-up after restrictive mitral annuloplasty is evaluated with MRI. Twenty-two selected patients with nonischemic, dilated cardiomyopathy, mild to moderate heart failure, and severe MR were evaluated by MRI within 1 week before restrictive mitral annuloplasty, and repeat imaging with MRI was performed at 3 to 4 years after surgery.

Methods

Patients

Twenty-two selected patients (18 male, 4 female, mean age 57±15 years) with mild to moderate heart failure and dilated cardiomyopathy (New York Heart Association [NYHA] class 2.2±0.4, LV end-diastolic dimension 61±5 mm, forward LVEF 37±5%, LV end-diastolic volume [LVEDV] 215±34 mL) who were scheduled for restrictive mitral annuloplasty were included. All patients presented with nonischemic, dilated cardiomyopathy (coronary artery disease excluded on coronary angiography) and severe functional MR on echocardiography. The patients had 3+ to 4+ MR (central jet) secondary to LV and annular dilatation and systolic restrictive motion of mitral leaflets (Carpentier type IIIb). All patients were receiving optimized medical therapy and kept on an optimal regimen during the study period.

Patients selected for this study had to be eligible to undergo repeat MRI examination. Therefore, in addition to general MRI exclusion criteria (i.e., pacemakers/defibrillators, intracranial clips, pregnancy, claustrophobia), disease-related specific criteria were applied. These included the presence of (supra)ventricular arrhythmias or an existing indication for postoperative (biventricular) pacemaker/defibrillator implantation. To maintain uniformity of surgical intervention in this small patient group, additional valve surgery, including tricuspid valve repair, was another exclusion criterion. These factors inevitably limited the patient selection to those with relatively mild heart failure, a group of patients representing the better part of our heart failure program. None of the patients had pulmonary hypertension, and all patients had preserved right ventricular function. MRI was performed within 1 week before surgery and repeated 3 to 4 years later (43±8 months). At follow-up, a routine transthoracic echocardiographic examination was performed.

Surgery

All surgical procedures were performed via midline sternotomy under normothermic cardiopulmonary bypass with intermittent antegrade warm blood cardioplegia. The mitral valve was exposed through a vertical transseptal approach along the right border of the foramen ovale, leaving the roof of the left atrium untouched. Ring size (Carpentier-Edwards Physio ring, Edwards Lifesciences, Irving, CA) was determined after careful measurement of the intercommisural distance and height of the anterior leaflet, and then downsizing by two ring sizes (i.e., size 26 when measuring 30). All patients had intraoperative transesophageal echocardiographic assessment of valve function. Mitral valve repair was considered successful if there was no residual MR and a leaflet coaptation length of at least 8 mm at the A2-P2 level was achieved on intraoperative echocardiography.

Magnetic Resonance Imaging

MRI was performed using a 1.5 T MRI scanner (ACS-NT15 Gyroscan with the Powertrack 6000 gradient system; Philips Medical Systems, Best, The Netherlands). The body coil was used for transmission and a 5-element phased-array synergy cardiac-coil was placed on the chest for signal reception. Standard 2- and 4-chamber long-axis series and a complete set of short-axis cine acquisitions were performed (conform standard cardiac MRI protocols[5] using steady-state free-precession[6]) with the patient performing a breath hold in end-expiration. Imaging parameters of the 2- and 4-chamber long-axis and for the short-axis series were as follows: TE/TR = 1.52/3.0, flip angle = 50 degrees, field of view = 350 mm, scan matrix = 192 ×153, slice thickness = 8 mm, and gated cardiac triggering with retrospective reconstruction of 30 phases. For the short-axis series, 10 to 12 parallel oriented slices were acquired with a 2-mm slice gap, 1 slice during each breath hold. LVEDV and LV end-systolic volume (LVESV) (from short-axis MRI[7]) and LAEDV and LAESV (from measuring biplane area-length in orthogonal long-axis 2- and 4-chamber views[3]) were obtained by manual segmentation. Image analysis was performed blinded with respect to echocardiographic data.
In the presence of significant MR, LVEF does not represent the true forward blood flow (through the aortic valve) because a substantial part of the blood volume leaks back into the left atrium. To correct for this effect, we have recently used the "forward LVEF," which was derived by calculating the ratio of the forward stroke volume and the EDV.[3] The forward stroke volume was obtained from aortic flow measurements derived from velocity-encoded MRI.[8] QMass and QFlow software (Medis, Leiden, The Netherlands)

were used for image analysis. MRI examination was repeated at 3 to 4 years follow-up, and similar parameters were assessed. Significant reverse remodeling was defined as a volume reduction exceeding 15%. An increase in forward LVEF of 5% or more and a decrease in LV mass 10 g or more were considered significant.[3] The medical ethics committee of our institute approved all examinations. All patients gave informed consent.

Statistical Analysis

Continuous data were expressed as mean ± standard deviation and compared using the Student t test for paired data.

Results

Clinical Outcome

All patients underwent successful mitral valve repair. The median annuloplasty ring size was 26. Intraoperative transoesophageal echocardiography showed a mean coaptation length of 8±1 mm. Residual MR was trivial in 4 patients and absent in the remaining patients. None of the patients had mitral stenosis, and systolic anterior movement of the anterior leaflet was not observed on echocardiography. There was no in-hospital or 30-day mortality, and no major complications occurred.

During follow-up, 2 patients died (9%) of refractory heart failure before repeat MRI. In 2 additional patients, follow-up MRI could not be performed because of comorbidity (Alzheimer's disease and amyotrophic lateral sclerosis). There were no cases of endocarditis or thromboembolic events.

At late follow-up (43±8 months) NYHA class was 1.2±0.4 (P<0.05 vs. baseline), and transthoracic echocardiography showed minimal MR (mean grade 0.6±0.5), with a mean leaflet coaptation length of 8±3, without mitral stenosis.

Reverse Remodeling on Magnetic Resonance Imaging

Figure 1 shows the LA and LV reverse remodeling assessed by MRI. The MRI results are summarized in Table 1. Although $LAEDV_i$ ('i' indicating indexation to body surface area) did not decrease significantly (predefined by a volume reduction ≥15%) (from 48±16 mL/m^2 to 44±10 mL/m^2, P=0.15), significant LA reverse remodeling for EDV occurred in 56% of the patients. Individual data are presented in Figure 2A. $LAESV_i$ decreased significantly from 84±20 mL/m^2 to 68±12 mL/m^2 (P<0.01), with significant LA reverse remodeling for ESV occurring in 67% of (Figure 2B). $LVEDV_i$ decreased significantly from 110±18 mL/m^2 to 80±17 mL/m^2 (P<0.01). Significant reverse remodeling of LVEDV occurred in the majority of patients (89%); individual data are shown in Figure 3A. $LVESV_i$ significantly decreased from 42±14 mL/m^2 to 31±12 mL/m^2 (P<0.01), with 72% of patients showing significant reverse remodeling of LVESV (Figure 3B). Overall, 2 patients (11%) did not show any (LA or LV) reverse remodeling.

Forward LVEF increased significantly over time: from 37±5% at baseline to 55±10% (P<0.01). Of note, 94% of patients showed a significant increase in forward LVEF (predefined as an increase of ≥5% in forward LVEF); individual results are shown in Figure 4A. Indexed LV mass showed a statistically significant decrease (predefined as a mass reduction ≥10 g): from 76±21 g/m^2 to 66±12 g/m^2 (P=0.03). In addition, 83% of the patients showed a significant decrease in LV mass (Figure 4B).

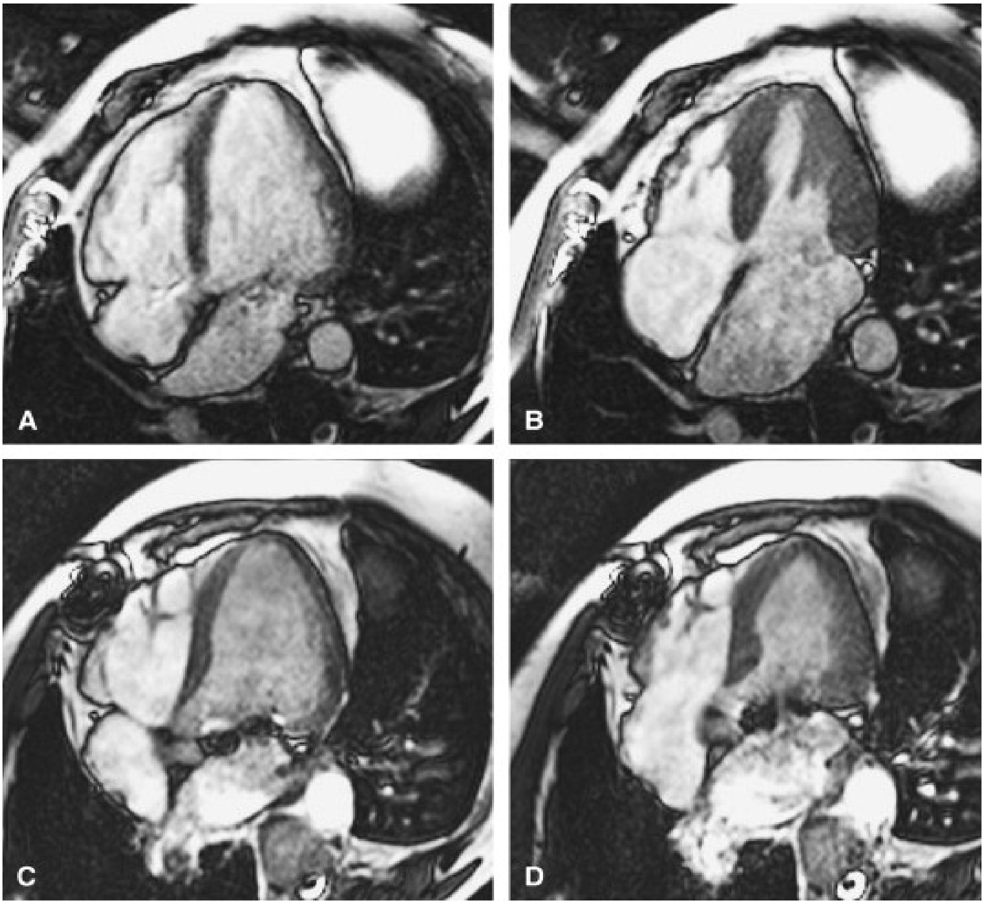

Figure 1. *Patient example illustrating reverse remodeling of the left atrium and left ventricle 43 months after mitral valve repair. Four-chamber views during end diastole (A) and end systole (B) before surgery show severe dilatation of the left atrium (LAEDV 128 mL, LAESV 216 mL) and left ventricle (LVEDV 311 mL, LVESV 90 mL) caused by volume overload secondary to severe MR. The 4-chamber views during end-diastole (C) and end-systole (D), 43 months after surgery, show a reduction in LA volumes (LAEDV 88 mL, LAESV 145 mL) and LV volumes (LVEDV 210 mL, LVESV 89 mL). A restrictive semirigid ring is implanted in the mitral annulus, resulting in signal loss because of paramagnetic material inside the ring.*

Table 1.

MRI Results: Pre-surgery and at 43±8 Months Follow-up.

	Presurgery	43±8 months' follow-up	*P* value
LAESV (mL)	165±43	132±20	<0.01
$LAESV_i$ (mL/m²)	84±20	68±12	<0.01
LAEDV (mL)	95±32	85±19	0.14
$LAEDV_i$ (mL/m²)	48±16	44±10	0.15
LVESV (mL)	82±25	60±22	<0.01
$LVESV_i$ (mL/m²)	42±14	31±12	<0.01
LVEDV (mL)	215±34	157±32	<0.01
$LVEDV_i$ (mL/m²)	110±18	80±17	<0.01
Forward LVEF (%)	37±5	55±10	<0.01
LV mass/BSA (g/m²)	76±21	66±12	0.03

LAESV, Left atrial end-systolic volume; *LAEDV*, left atrial end-diastolic volume; *LVESV*, left ventricular end-systolic volume; *LVEDV*, left ventricular end-diastolic volume; *LVEF*, left ventricular ejection fraction; *LV*, left ventricular; *BSA*, body surface area; *i*, indexation to body surface area.

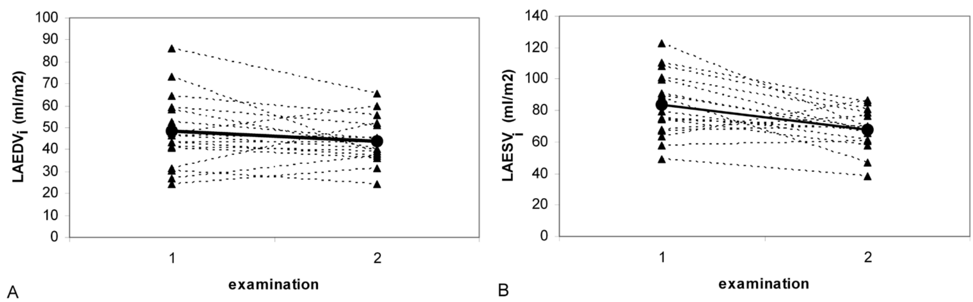

Figure 2. *Individual data of patients demonstrating the changes over time in LAEDVi(A) and LAESVi(B). Examination 1 concerns MRI before surgery; examination 2 concerns MRI at 43±8 months follow-up. Mean values (circular data points and solid line); individual data (triangles and dotted lines).*

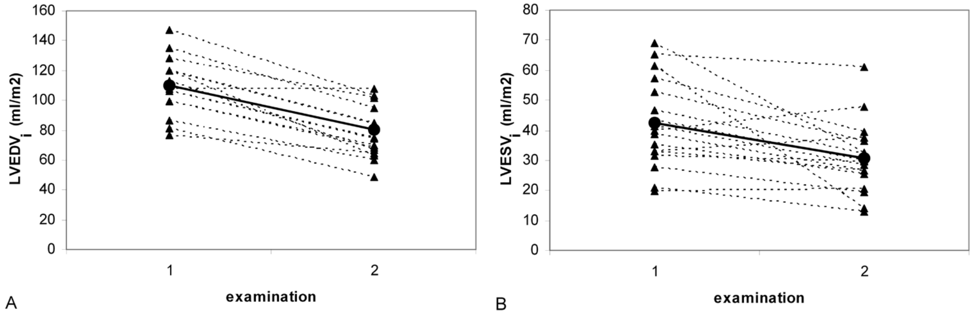

Figure 3. *Individual data of patients demonstrating the changes over time in LVEDVi (A) and LVESVi (B). Examination 1 is MRI before surgery; examination 2 is MRI at 43±8 months follow-up. Mean values (circular data points and solid line); individual data (triangles and dotted lines).*

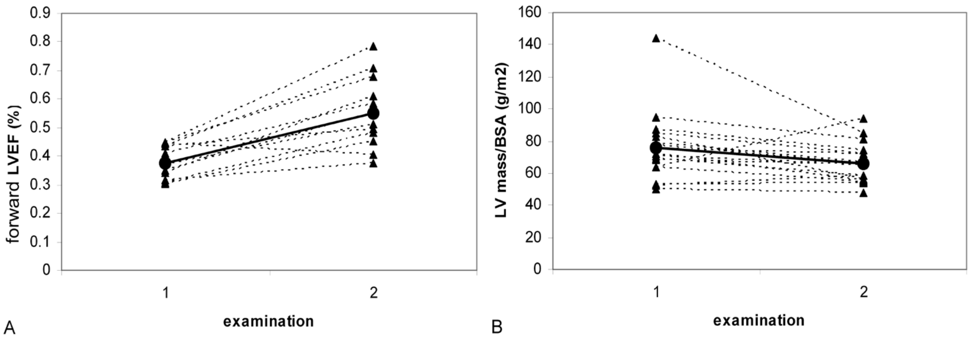

Figure 4. *Individual data of patients demonstrating the changes over time in forward LVEF (A) and LV mass indexed by body surface area (B). Examination 1 is MRI before surgery; examination 2 is MRI at 43±8 months follow-up. Mean values (circular data points and solid line); individual data (triangles and dotted lines).*

Discussion

This study demonstrates the ability of MRI to report in a detailed fashion on various aspects of the LV reverse remodeling process (forward LVEF, LV and LA volumes). All previous studies on improvement in LVEF and LV reverse remodeling after restrictive mitral repair in patients with dilated cardiomyopathy used echocardiography, which is limited by substantial intra– and interobserver variations and geometric assumptions needed for quantification of LVEF and LV volumes. The same measurements done with MRI have been reported to be highly accurate and reproducible.[3,7] MRI has a superior image quality compared with echocardiography and is not hampered by technical limitations, such as suboptimal acoustic windows.

Moreover, MRI has the advantage of acquiring every arbitrary double obliquely oriented imaging plane in 3 dimensions. Accordingly, MRI is considered the gold standard for assessment of LA and LV volumes, and its noninvasive nature and high reproducibility make this technique ideal for follow-up studies after therapy.[9] The high reproducibility allows for smaller study sample sizes to prove statistical significance. For example, to demonstrate a 10 mL difference in LVEDV with a P value less than .05 and a power of 90%, evaluation of only 12 patients is needed when MRI is used, compared with 121 patients when echocardiography is used.[2] Indeed, in the current study, significant LA and LV reverse remodeling were statistically significantly proven with only 18 patients. Moreover, MRI permits easy correction for the influence of MR on LVEF by the use of the forward stroke volume (reflecting true forward blood flow through the aortic valve), as applied in the current study. This approach also permits a better appreciation of the true effect of mitral valve surgery on forward blood flow, reflected in the current study by a significant increase in forward LVEF.

However, the use of MRI for follow-up purposes is still limited by technical factors, and, as explained before, the patient group presented here represents the better part of our heart failure program. Currently, all patients with heart failure undergo MRI before surgery, but only those not requiring implantation of an epicardial LV lead or a pacemaker/defibrillator and those without (supra)ventricular arrhythmias are eligible to undergo follow-up MRI. These contraindications currently hamper widespread use of MRI in patients with heart failure. It is expected that these technical limitations of MRI will be overcome in the near future, which will greatly increase the possibilities of follow-up imaging in patients with heart failure.

In the current study, the beneficial effects of restrictive mitral annuloplasty in a selected group of patients with mild to moderate heart failure was shown. Currently, not much information on the effects of restrictive mitral annuloplasty in this patient category is available. Acker et al[10] recently reported initial results from the Acorn trial. In this study, a subgroup of patients with mild heart failure (NYHA class II and relatively preserved LVEF and functional MR) underwent isolated mitral valve surgery, similar to the patients in the current study. The outcome of this subset of patients was not reported separately, making direct comparison with the current findings impossible.

Another conclusion that can be drawn from the present study is that treatment of functional MR in nonischemic dilated cardiomyopathy by restrictive annuloplasty alone eliminates MR and leads to LA and LV reverse remodeling in the majority of this selected patient population. It has been questioned whether LV reverse remodeling is maintained over longer follow-up periods. Our current results confirm that LV reverse remodeling is indeed present at long-term follow-up. These favorable results may be related to the fact that only patients with milder heart failure were included (mean NYHA class 2.2±0.4 and mean forward LVEF 37±5%), reflecting the less ill patients in our heart failure program. In addition, only patients with preserved right ventricular function and without pulmonary hypertension or significant tricuspid regurgitation were selected. For reference, in our institution patients with more advanced stages of heart failure undergo tricuspid annuloplasty when significant tricuspid regurgitation or severe annular dilatation (annular diameter ≥40 mm) is present. When LV end-diastolic diameter exceeds 65 mm, an external cardiac constraint device (CorCap cardiac support device; Acorn Cardiovascular, St Paul, Minn) is also applied. These patients have a 6% operative mortality, and long-term results are currently being evaluated. When LV end-diastolic dimension exceeds 80 mm, surgical LV restoration is considered as described by Isomura et al.[11]

The current results strengthen the hypothesis that grades 3 to 4+ functional MR can be successfully treated by restrictive mitral annuloplasty in patients with LV dilatation but relatively mild heart failure (NYHA class II to III). On a patient basis, 89% and 72% of patients exhibited a significant reduction in LV volumes. These observations are clinically relevant because LV function and volumes have been demonstrated to be important predictors of long-term outcome in patients with LV dysfunction.[12,13]

Also, LA dimensions have been shown to provide prognostic information.[14,15] In the present study, LA volume in end-systole showed a significant decrease, although LA volume in end-diastole did not exhibit a decrease in the entire study population.

On the basis of the reverse remodeling observed in the current study, one could speculate that the point of no return (irreversible LV dilatation) was not yet reached in this patient category, suggesting that mitral valve surgery may be considered at an earlier stage in patients with nonischemic dilated cardiomyopathy. Further prospective studies are needed to confirm the benefit of early surgical intervention in patients with mild heart failure.

Conclusions

MRI provides a powerful tool for the evaluation of the LV and LA reverse remodeling process in patients with mild heart failure with functional MR and nonischemic dilated cardiomyopathy who underwent isolated restrictive annuloplasty. At late (3–4 years) follow-up, sustained significant LV and LA reverse remodeling was demonstrated using MRI. It should be emphasized that the current findings have been obtained in a highly selected patient population and that further MRI experience in patients with more advanced stages of heart failure is needed.

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