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EVALUATION OF SURGICAL INTERVENTIONS

Early Regression of Left Ventricular Hypertrophy After Aortic Valve Replacement by the Ross Procedure Detected by Cine MRI

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ABSTRACT

Aim. The primary objective of our study was to assess the time course of left ventricular remodeling after the Ross procedure with the use of cine magnetic resonance imaging (MRI). *Methods.* In a prospective study, 10 patients with isolated aortic valve disease were examined prior to aortic valve surgery, as well as at early follow-up (mean 4 weeks) and at late follow-up (mean 8 months) after pulmonary autograft aortic valve replacement (Ross procedure). The heart was imaged with a 1.5 T MR scanner along the short and long axes using a breath-hold, electrocardiogram (ECG)-triggered, cine gradient-echo sequence (FLASH). Myocardial mass and ventricular function were assessed. *Results.* After aortic valve replacement, left ventricular myocardial mass (LVM) decreased by 13% (261±74 g to 230±65 g, $p<0.05$) in the early postoperative period and by a further 16% in the late postoperative period to 192±31 g ($p<0.05$). In addition, left ventricular end-diastolic and end-systolic volumes decreased from preoperative 187±89 mL (LV EDV) and 73±59 mL (LV ESV) to 119±55 mL and 56±42 mL, respectively, in the early postoperative period. In the late postoperative period, there was a further decrease to 98±30 ($p<0.05$) and 33±19 mL, respectively. Ejection fraction did not change markedly after surgery (preoperatively 61±13% vs. 56±14% postoperatively). Patients with leading aortic stenosis were characterized by predominant regression of LVM and patients with leading aortic regurgitation by predominant regression of LV EDV (each $p<0.05$). *Conclusion.* Cine MRI allows accurate assessment of left ventricular structure

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and geometry before and after aortic valve replacement with pulmonary autograft and is very sensitive in detecting relatively small changes of left ventricular myocardial mass and volumes early after hemodynamic relief as well as during serial assessment.

Key Words: Heart; Aortic valve disease; Ross procedure; Cine MRI; Left ventricular hypertrophy.

INTRODUCTION

Cine magnetic resonance imaging (MRI) has been shown to provide highly accurate and reproducible measures of ventricular mass and volume, stroke volume, and ejection fraction (Debatin et al., 1992; Heusch et al., 1999). In fact, several authors have established cine MRI as the standard of reference for assessing ventricular function (Debatin et al., 1992; Higgins, 1992). Magnetic resonance imaging estimates of left ventricular (LV) mass have been shown to be closely correlated to actual heart weights determined at autopsy in both animal (Aurigemma et al., 1991; Caputo et al., 1987) and human models (Katz et al., 1988; Sechtem et al., 1987).

In patients with chronic aortic valve (AV) disease, the left ventricular wall is known to hypertrophy. Being an independent cardiac risk factor, left ventricular hypertrophy (LVH) is associated with a higher incidence of cardiovascular clinical events and death (Levy et al., 1990). Regression of hypertrophy has been observed after AV replacement (Henry et al., 1980; Monrad et al., 1988). Mass regression after AV replacement is a marker of favorable LV remodeling, and exact assessment of the extent of postoperative mass regression may provide a functional assessment of the hemodynamic characteristics associated with an AV replacement.

Postoperative assessment of LV structure and geometry by MRI is usually not always possible after AV replacement with mechanical valves. In contrast, MRI is possible after replacement with pulmonary autograft valves as introduced by Ross (1967).

The Ross procedure, first described in 1967 (Ross, 1967), involves replacement of the diseased aortic valve (AV) with a pulmonary autograft and implantation of a cryopreserved pulmonary homograft to reestablish right ventricle–pulmonary artery continuity. After the Ross procedure, patients do not require anticoagulation, and the potential growth of the pulmonary autograft has led to expanded indications for the Ross procedure. Because of these attributes, the pulmonary autograft is an attractive alternative to mechanical, porcine, and homograft valves in the treatment of AV disease. Although mechanical valves provide a satisfactory hemodynamic result, they require lifelong anticoagulation, and hemorrhage and thromboembolism remain important complications (Schenck et al., 1993). Porcine bioprotheses, which do not require anticoagulation, deteriorate rapidly in the aortic position and have limited durability (Al-Khaja et al., 1991). Several reports have documented the effective use of the Ross procedure for isolated AV disease (Gerosa et al., 1991; Kouchoukos et al., 1994; Schoof et al., 1994).

The primary objective of our study was to assess the time course of left ventricular remodeling after the Ross procedure with the use of cine MRI.

METHODS

Patient Population

Ten patients (nine male and one female) who underwent the Ross procedure between June 1999 and May 2001 were included in this study. The median age of the patients was 43.7 years at the time of surgery (range 31 to 55 years). The primary indication for surgery was severe, isolated, aortic valvular disease in all patients: isolated aortic stenosis (AS; n = 2), combined aortic stenosis/regurgitation with leading stenosis (AS/AI; n = 3), isolated aortic regurgitation (AR; n = 4), and combined aortic regurgitation/stenosis with leading regurgitation (AR/AS) (n = 1). For all of the patients the Ross procedure was their first cardiac surgical procedure. All patients were symptomatic for dyspnea [New York Heart Association (NYHA) function class III or IV]. Patient characteristics are listed in Table 1.

All subjects underwent a preoperative, transthoracic echocardiography examination to assess the severity of AV disease and to exclude the presence of another valve disease. Each subject of the study population underwent left heart catheterization to rule out the presence of coronary artery disease.

All patients were followed up prospectively with serial MR imaging performed preoperatively, between

Table 1. Selected preoperative patient characteristics.

Initials	Age	Sex	NYHA	Echocardiographic diagnosis
S.O.	37	M	III	AR
B.H.	49	M	III	AR
S.A.	44	M	IV	AR
A.R.	52	M	IV	AR
B.H.	31	M	III	AR/AS
E.K.	42	M	III	AS
W.H.	48	M	III	AS
O.J.	45	M	III	AS/AR
W.S.	55	F	III	AS/AR
S.K.	34	M	III	AS/AR

Abbreviations: AR=aortic regurgitation, AS=aortic stenosis, AR/AS=combined aortic valve disease with leading aortic regurgitation, AS/AR=combined aortic valve disease with leading aortic stenosis. Mean age: 43.7±7.8.

2 and 6 weeks (mean 4 weeks) postoperatively (early follow-up), and at 6 to 9 months (mean 8 months, late follow-up).

All patients provided written, informed consent, and the protocol for implantation and patient follow-up was reviewed by the local institutional review board.

Operative Technique

The Ross procedure was performed as previously described (Ross, 1967). Under general anesthesia, cardiopulmonary bypass was instituted through a medial sternal approach. Myocardial preservation was by crystalloid cardioplegia. The pulmonary autograft was inserted into the aortic anulus as a free standing root. For each patient a pulmonary homograft was implanted as a pulmonary root, based on MRI and/or echocardiographic estimation of the pulmonary anulus. Mean aortic cross clamp and cardiopulmonary bypass times were 123±36 and 152±42 minutes, respectively.

MR Imaging

The MR images were acquired with a 1.5 T superconductive MR imager (Magnetom Symphony; Siemens Medical Solutions, Erlangen, Germany) transmitting with a circularly polarized (cp) body coil, receiving with a cp four-element, phased-array, body coil.

Volumetric data were estimated using images acquired in the cardiac short-axis plane. Short- and long-axis cine MR images were obtained with a fast low-angle shot (FLASH) sequence, which was an electrocardiographically, prospectively triggered gradient-echo sequence with a 195 Hz/pixel bandwidth and a gradient arrangement to compensate dephasing due to first-order motion. Acquiring nine Fourier lines per heart beat per cardiac phase led to a measurement time of 15 heart beats for the utilized 126×256 matrix size during suspended respiration. Section thickness was 8 mm with a gap of 2 mm between sequentially acquired slices. The true measurement of the central k-space segment with echo sharing of adjacent phases for higher k-space frequencies provided a true temporal resolution (TR) of 56 ms. The TR was 13 msec and the gradient motion rephasing (GMR) arrangement allows an echo time (TE) of 6 ms. Field of View (FoV) was $350\times$ 260 mm (0.75), leading to a spatial resolution of $2.08\times 1.37\times 8$ mm. A 20° excitation angle has been utilized.

Determination of Myocardial Mass and Global LV Function

Volumetric data were extracted by feeding these images into the semiautomatic ARGUS evaluation program, which is part of the commercially available

Table 2. Individual changes of LV mass (g) and LV mass index (g/m^2) divided in the two subgroups (AR and AS) before the Ross procedure and in the early and late follow-up periods.

Initials	Preoperative	Early follow-up	Late follow-up
a) AR group			
S.O.	236 (113)	195 (99)	188 (96)
B.H.	232 (130)	220 (121)	218 (112)
S.A.	234 (110)	175 (84)	158 (75)
A.R.	213 (120)	204 (109)	193 (107)
B.H.	239 (124)	222 (117)	186 (95)
Mean	231±10 (119±8)	203±19 (106±14)	188±27[a] (97±16)
b) AS group			
E.K.	218 (108)	206 (103)	167 (83)
W.H.	193 (93)	184 (88)	156 (76)
O.J.	341 (177)	292 (155)	216 (111)
W.S.	266 (175)	207 (141)	179 (119)
S.K.	441 (209)	393 (167)	255 (119)
Mean	292±101 (152±49)	256±87 (131±34)	195±41[a] (102±21)
Both groups	261±74 (136±38)	230±65[a] (118±28)	192±31[a] (99±17)

[a]P<0.05 compared to preoperative values.

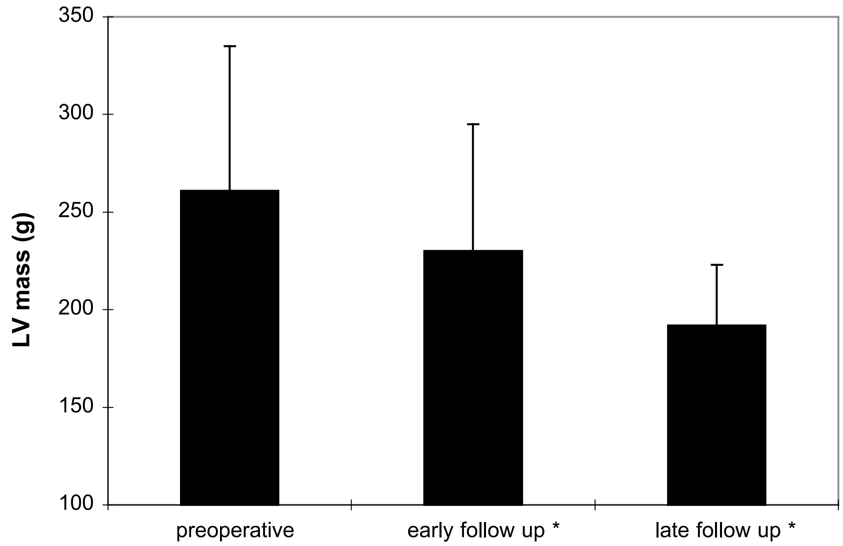

Figure 1. Changes of LV mass before the Ross procedure and in the postoperative follow-up. Data are mean values (±SD) of 10 patients. *p<0.05 compared to preoperative value.

cardiac package of the scanner software. A long axis scan was acquired using the same imaging technique and was later used to confirm a complete coverage of the cardiac chamber with the short axis acquisitions. As previously reported, the most basal section was defined as the section in which the left ventricular myocardium extended over at least 50% of the circumference on the end-diastolic and end-systolic images (Barkhausen et al., 2001).

Manual segmentation was performed in all cases. The end-diastolic frame was represented at the beginning of the QRS-complex as the frame with the largest intraventricular area. The end-systolic frame was represented at the end of the T wave as the frame with the smallest intraventricular area. The evaluation program estimated automatically LV end-diastolic volumes (LVEDV) and LV end-systolic volumes (LVESV), as well as derived stroke volumes (SV), by summing up the areas for each slice multiplied by slice thickness, considering a correction of the interslice gap. The LV ejection fraction (EF) was calculated as (LVEDV − LVESV)/LVEDV. The LV myocardial mass was calculated at end-diastole after additional detection of epicardial borders of the LV by subtraction of endocardial volume from epicardial volume multiplied by 1.05 g/cm^3. Cardiac output was calculated as SV × 60 sec/min/CL (cycle length).

Statistical Analysis

Results are given as mean ± SD. Differences between preoperative and early and late postoperative data were tested for significance by t-test with Bonferroni correction. A p value <0.05 was considered statistically significant.

RESULTS

Preoperative Data

Clinical data of the 10 patients under study are summarized in Table 1. Mean age was 43.7±7.8 years. Before entering the study, all patients underwent a preoperative transthoracic echocardiography examination where the severity of AV disease was confirmed (AR, n=4; AR/AS, n=1, i.e., AR group, n=5; AS, n=2; AS/AR, n=3, i.e., AS group, n=5) and the presence of another valve disease was excluded. Each subject underwent left heart catheterization where the presence of coronary artery disease could be ruled out.

Cine-MRI could be performed in all 10 patients and resulted in a mean left ventricular mass of 261± 74 g (range 441–193 g), mean LVEDV of 187±89 mL, mean LVESV of 73±58 mL, mean SV of 100±33 mL, and mean EF of 61±13%. Eight of 10 patients showed a normal EF > 50% (range: 53–78%). Two patients with severe aortic regurgitation showed preoperatively a slightly reduced EF of 40% and 43%, respectively. Mean cardiac output (CO) was 7.3±2.2 L/min.

Postoperative Data

Early follow-up ranged from 2 to 6 weeks (mean 4 weeks) and late follow up ranged from 6 to 9 months

Table 3. Mean values of left ventricular volumes and systolic function divided in the two subgroups (AR and AS) before the Ross procedure and in the early and late follow-up periods.

	Preoperative	Early	Late
LVEDV (mL), both groups	187±89	119±55	98±30[a]
AR group	258±63	150±65[a]	112±36[a]
AS group	117±37	88±15	84±16
LVESV (mL), both groups	73±59	56±42	33±19
AR group	121±59	82±42	43±24
AS group	35±12	30±6	23±2
LV SV (mL), both groups	100±33	63±20[a]	65±16[a]
AR group	122±27	68±26[a]	69±16[a]
AS group	82±30	58±13	61±16
LV EF (%), both groups	61±13	56±14	67±9
AR group	52±12	47±13	63±10
AS group	70±5	66±6	72±7
CO (L/min), both groups	7.3±2.2	5.7±0.9	4.6±0.8[a]
AR group	8.8±1.3	5.9±1.1[a]	4.4±0.3[a]
AS group	6.1±2	5.4±0.7	4.7±1.2

Abbreviations: LV EDV=left ventricular end-diastolic volume, LV ESV=left ventricular end-systolic volume, LV SV=left ventricular stroke volume, LV EF=left ventricular ejection fraction, CO=cardiac output.
[a]P<0.05 compared to preoperative values.

(mean 8 months). All patients showed a considerable symptomatic clinical improvement (7 to NYHA functional class I and 3 to functional class II). Postoperatively, only one major complication occured. In the early postoperative period one patient suffered from a mediastinal bleeding located at the aortic anastomosis, which was successfully stopped during reexploration.

Mean LV myocardial mass decreased in the early follow up by 13% to 230±65 g, $p<0.05$, and in the late follow-up by a further 16% to 192±31 g, $p<0.05$) (Figure 1). The individual changes of LV mass in all patients as well as both subgroups are summarized in Table 2. The LVEDV and LVESV became normal. In the early follow-up LVEDV decreased to 119±55 mL and in the late follow-up to 98±30 mL ($p<0.05$). Basically, the AS group showed a predominant regression of LVM, whereas the AR group showed a predominant regression of LVEDV. The LVESV decreased to 56±42 and to 33±19 mL. The LVSV decreased to 63±20 mL ($p<0.05$) in the early follow-up and to 65±16 mL in the late follow-up ($p<0.05$). The EF slightly decreased to 56±14% in the early follow-up, whereas it increased to 67±9% in the late follow-up. The EF in the two patients with the preoperatively reduced EF (40% and 43%) decreased further in the early postoperative follow-up to 38% and 31%, respectively, but recovered to normal values (52% and 54%, respectively) in the late follow-up. Cardiac output normalized postoperatively because of a predominant reduction in the AR group. The left ventricular volumes and systolic function in all patient and in the both subgroups are summarized in Table 3.

DISCUSSION

In the present study, we show that cine MRI is very sensitive in detecting small changes in left ventricular myocardial mass and is suitable for serial assessment of LV structure and function. As a model we chose patients with single aortic valve disease and consecutive left ventricular hypertrophy who underwent surgery with the Ross procedure. Despite the small number of patients (n=10), cine MRI was able to detect a reduction of left ventricular hypertrophy in the early and late follow-up after the operation.

The Ross procedure has emerged as the operation of choice for young individuals with aortic root pathology not amenable to repair (Kouchoukos et al., 1994). The pulmonary valve´s structural similarity to the aortic valve probably explains the excellent clinical results and the low mortality risk (Marino et al., 1999; Ross et al., 1991). Freedom from thrombosis in the absence of long-term anticoagulation provides additional support for its application. The mean age for patients undergoing the Ross procedure is currently 28, with the majority between 11 and 50 years of age. Although the mean age is not significantly different from Ross's early series (28 years vs. 27 years), the range has broadened considerably (1 day to 73 years) (Oury, 1996). In our study mean age was 43.7 years and ranged from 31 to 55 years.

The aim of our study was to assess the time course of left ventricular remodeling after the Ross procedure with the use of cine MRI. Cine MRI is now considered the most accurate clinical method for assessing ventricular volumes and mass (Aurigemma et al., 1991; Caputo et al., 1987; Debatin et al., 1992; Heusch et al., 1999; Higgins, 1992; Katz et al., 1988; Sechtem et al., 1987). Based on this method, MRI estimates of left ventricular mass would be useful to monitor regression of LVM for the individual patient. In contrast to angiographic volumetric analysis, the cross-sectional nature of cine MRI makes it independent of geometric assumptions. Thus, all ventricular shapes can be accurately measured. Lack of radiation or any other

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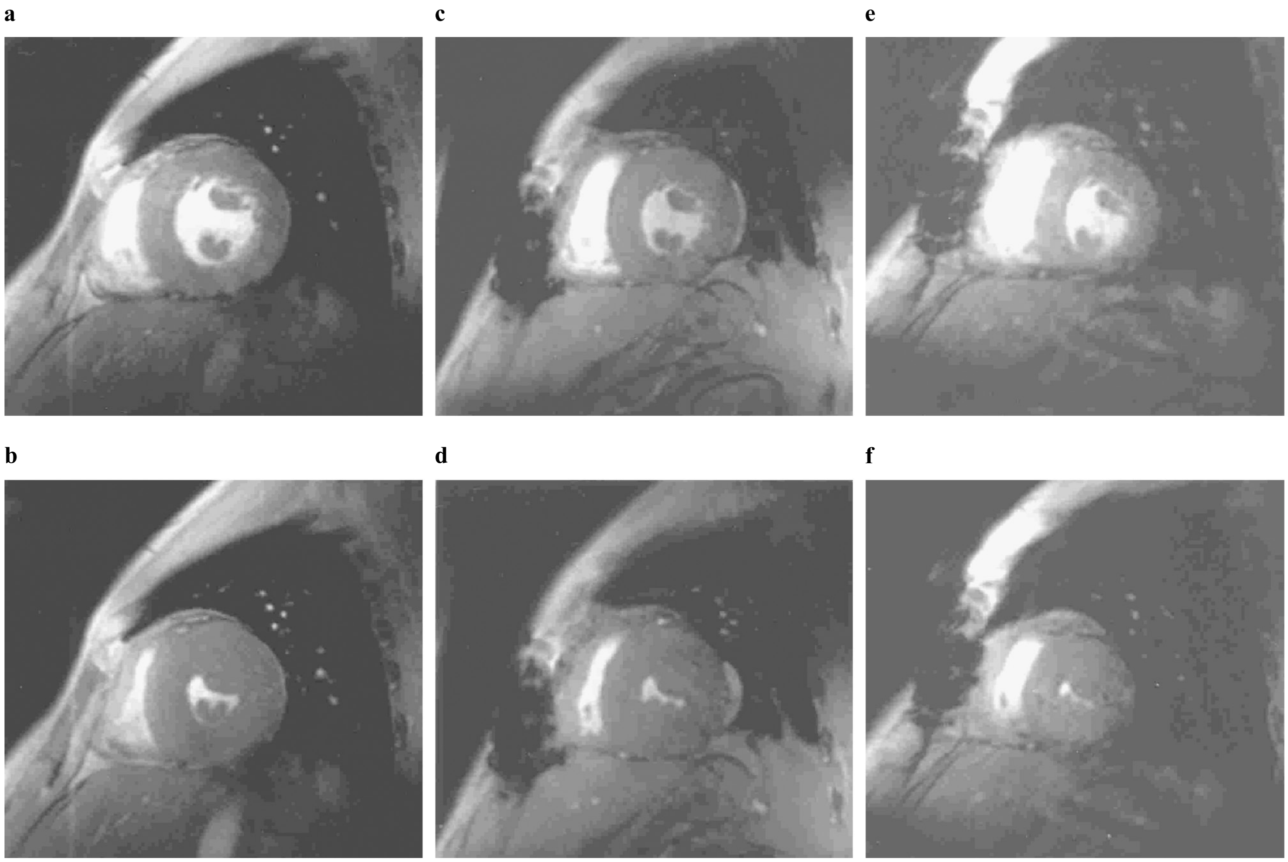

Figure 2. Time changes of LV mass in Patient S.K. documented by cine MRI in oblique sagital short-axis orientation during the preoperative, early (after 3 weeks) and late study (after 6 months). The figures show mid-ventricular slices through the left ventricle at end-diastole (a,c,e) and end-systole (b,d,f). (a and b) preoperative slices: LV mass (g) and LV mass index (g/m^2) were calculated as 441 g and 209 g/m^2, respectively. LV EDV and LV ESV were 151 mL and 33 mL, respectively. (c and d) early follow-up slices: LV mass (g) and LV mass index (g/m^2) decreased significantly compared to preoperative data and were calculated as 393 g and 167 g/m^2, respectively. LV EDV and LV ESV were 98 mL and 27 mL, respectively. (e and f) late follow-up slices: LV mass and LV mass index (g/m^2) decreased further and were calculated as 255 g and 119 g/m^2, respectively. LV EDV and LV ESV were 90 mL and 22 mL, respectively.

harmful side effects, coupled with better spatial resolution, make cine MRI superior to nuclear medicine techniques (Debatin et al., 1992). Better distinction between myocardium and ventricular cavity and operator independence are important advantages of cine MRI over echocardiography (Heusch et al., 1999). The FLASH sequence we used is a spoiled gradient-echo sequence, where blood pool vs. myocardium contrast is dependent on blood flow, which results in reduced contrast in areas with low velocity caused by saturation (Chien and Edelman, 1991). Since all our patients showed a normal EF or in two cases only a slightly reduced EF, there were no problems with low velocities. Thus, drawing the epicardial and endocardial contours on all end-diastolic and end-systolic images could be done manually without problems in all patients, due to good blood pool vs. myocardium contrast.

Regresssion of left ventricular hypertrophy after successful aortic valve replacement for aortic valve disease has previously been documented by the use of echocardiography or left ventriculography. Monrad et al. reported on the time course of regression of left ventricular hypertrophy after aortic valve replacement in 1988 (Monrad et al., 1988). They used an invasive method (contrast left ventriculography) and showed that left ventricular mucle mass index fell by 31% 1.6±0.5 years after surgery and by a further 13% after 8.1±2.9 years. Pantely, Morton, and Rahimtoola found similar regression of left ventricular hypertrophy (Pantely et al., 1978). Kennedy, Doces, and

Stewart, while observing a significant reduction in left ventricular muscle mass, found that 1.5 years postoperatively there still remained significant hypertrophy compared with control (Kennedy et al., 1977). Roman et al. showed in an echocardiography study reversal of left ventricular dilatation and hypertrophy by valve replacement in aortic regurgitation (Roman et al., 1989). In the majority of their patients, nearly complete reversal of both dilatation and hypertrophy had occurred by the time of the first postoperative study (9±6 months).

Our study confirms and extends these observations as it demonstrates a marked reduction in LV mass and volume already very early after valve surgery (mean 4 weeks), as well as a sustained and further reduction at late follow-up (mean 9 months). To our knowledge this is the first study using cine MRI to show a regression of left ventricular hypertrophy after aortic valve repair in the early postoperative period. Determination of left ventricular mass and its change with therapy remains an important clinical goal, and the capability of MR to detect these changes indicates the appropriateness of this method, if available.

The definition of LVH remains a critical issue, since it varies considerably according to the diagnostic method and the formula used to calculate volumes. However, the inclusion of our patients was only based on the fact that they had isolated aortic valve disease, which required an operation due to their clinical symptoms for dyspnea (NYHA functional class III–IV).

We employed the manual border detection method to quantify LV volumes and mass. Although several automated and semiautomated border detection methods have been developed in the past, it is known that automatic segmentation in FLASH imaging results in overestimation of systolic volumes and underestimation of ejection fractions. This bias is likely caused by failed delineation of the left ventricular borders on systolic images during automatic segmentation. Thus, we chose the more exact but time-consuming manual border detection. Data on intra- and interobserver variation published previously demonstrate the feasibility of the manual method we used (Globits et al., 1992; Semelka et al., 1990).

CONCLUSION

Cine MRI is very sensitive in detection of early regression of left ventricular hypertrophy after the Ross procedure in aortic valve disease. In the present study cine MRI detects a reduction of LV mass and a normalization of left ventricular function within the early postoperative period (mean 4 weeks).

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