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MYOCARDIAL FUNCTION

Myocardial Mass and Volume Measurement of Hypertrophic Left Ventricles by MRI—Study in Dialysis Patients Examined Before and After Dialysis

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ABSTRACT

Techniques to reliably quantify left ventricular myocardial mass (LVMM) are mandatory for monitoring therapy in patients with left ventricular hypertrophy (LVH). The purpose of this study was to measure LVMM and volumes by cine magnetic resonance imaging (MRI), and to assess acute changes through hemodialysis as a model for different loading states. Seven dialysis patients with LVH were examined before and immediately after hemodialysis. All MR imaging was done with a steady-state free precession (SSFP) cine sequence (TrueFISP; TR, 3.2 ms; TE, 1.6 ms; flip angle, 60°; slice thickness, 8 mm). LV volumes, ejection fraction (EF), and LVMM were determined by slice summation after manual planimetry in short axes. A significant reduction of end-diastolic volume (EDV) (mean pre, 140 mL; post, 109 mL; $p < 0.01$), end-systolic volume (ESV) (49 mL → 42 mL; $p < 0.05$), and stroke volume (91 mL → 66 mL; $p < 0.01$) through dialysis was revealed by MRI. Ejection fraction did not change significantly. A slight decrease in LVMM was detected in all patients (mean pre, 184 g; post, 177 g; $p < 0.05$). Intra- and interobserver variability for EDV, ESV, and LVMM were 1.3 ± 6.2 mL, -0.9 ± 4.1 mL, -1.4 ± 3.9 g, and 3.3 ± 7.5 mL, 2.6 ± 5.0 mL, -2.4 ± 4.6 g, respectively. Standard error of estimation (SEE) was ± 2.3 mL, ± 2.0 mL, ± 1.6 g, and ± 2.6 mL, ± 2.1 mL, and ± 2.0 g for intra- and interobserver variability. In conclusion, cine MRI is a reliable technique for LVMM measurement that is independent of LV loading status. This method allows for detection of small changes, which is crucial for accurate therapy monitoring in LVH. Left ventricular myocardial mass and volumes decrease significantly during hemodialysis.

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Key Words: Magnetic resonance imaging; TrueFISP cine imaging; Cardiac MRI; Left ventricle; Myocardial hypertrophy; Dialysis.

INTRODUCTION

Left ventricular hypertrophy (LVH) is one of the most frequently encountered consequences of end-stage renal disease (ESRD) that affects the cardiovascular system. It is found in over 70% of patients even at the onset of hemodialysis (Foley et al., 1995b), and progresses rapidly as renal function further declines (Levin et al., 1996). In general, abnormalities of left ventricular (LV) size, shape, or function remains present in 70–80% of patients undergoing chronic hemodialysis (Foley et al., 2000). In this context, chronic volume and pressure overload seem to alter neurohumoral pathways resulting in LV dilatation and LVH (London et al., 1994), which has been proven to be strongly predictive of developing cardiac failure and higher mortality (Foley et al., 1995a).

Chronic changes in LV volumes and particularly myocardial mass (LVMM) should be carefully monitored in dialysis patients in terms of blood pressure and anemia therapy (Devereux et al., 1997). Acute hemodynamic changes through dialysis have been reported to decrease LV dimensions by lower preload and afterload conditions and to improve cardiac function (Blaustein et al., 1986; Ireland et al., 1981). Different ventricle sizes and loading states have been shown to lead to inaccuracies in LVMM measurement when using techniques based on geometric models (Chuang et al., 2000; Harnett et al., 1993; Missouris et al., 1996; Soler et al., 1999; Stewart et al., 1999). Due to its wide availablility, relative simplicity of use, and rapid acquisition, two-dimensional echocardiography remains the method of choice for assessing LV myocardial mass clinically despite its limitations.

Cardiac cine magnetic resonance imaging (MRI) overcomes these limitations and has been proven feasible for LVMM and volume measurement. Thus, it now serves as the standard of reference in this respect (Bottini et al., 1995; Pattynama et al., 1993; Sakuma et al., 1993). Recent developments in cine sequences using the steady-state free precession (SSFP) technique have been shown to accurately assess LVMM rapidly and with low interobserver variability while maintaining high reproducibility (Jaffe et al., 2001; Plein et al., 2001).

We hypothesize that MRI estimates LVMM independently from the actual LV loading status. The purpose of this study was to assess the reliability of LVMM and volume measurements in MRI by assessing the LV geometry before and after hemodialysis in chronic dialysis patients with left ventricular hypertrophy.

METHODS

Seven patients who were on chronic hemodialysis for more than four years (4.2 $\pm$ 1 year) were enrolled (58 $\pm$ 10 years, 5 male, 2 female) for this study. Two had clinical symptoms of heart failure, all had echocardiographically proven LV myocardial hypertrophy according to the American Society of Echocardiography recommendations for quantitation of the left ventricle (Park et al., 1996; Schiller et al., 1989). Table 1 shows clinical characteristics of the patients before and after dialysis. All patients gave written informed consent.

Table 1. Patient characteristics. Values for body weight, noninvasive blood pressure, and heart rate are given before and immediately after hemodialysis.

Patient no.	Gender	Age (yrs)	Body weight (kg)		Blood pressure (mmHg)		Heart rate (bpm)	
			Before	After	Before	After	Before	After
1	f	65	81.7	80.8	190/90	185/90	92	92
2	f	47	82.5	81.4	180/100	125/80	80	100
3	m	73	100.3	97.3	170/80	140/80	80	80
4	m	42	83.6	80.1	150/80	130/80	104	84
5	m	60	86.6	86.5	180/90	150/75	76	72
6	m	60	78.4	76.3	175/90	160/80	88	84
7	m	62	74.2	72.9	200/100	150/80	92	84

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Exclusion criteria were the standard contraindications for MRI such as metal implants [cardiac pacemakers, automated implantable cardioverter/defibrillator (AICD)] and claustrophobia.

Patients were examined by MRI before hemodialysis (time between end of exam and onset of dialysis, 14 ± 7 min) and immediately after (time delay, 22 ± 10 min) hemodialysis.

MRI Image Acquisition

All MRI examinations were performed on a 1.5 T whole body scanner (Magnetom Sonata; Siemens Medical Systems, Erlangen, Germany) equipped with high-performance gradients (maximum amplitude, 40 mT/m, slew rate, 200 mT/m/msec). Patients were placed in supine position and a body-phased array coil was placed over the chest. Standard horizontal and vertical long-axis cine MR images were obtained with a segmented steady-state free precession (SSFP) sequence (TrueFISP, Siemens; TR, 3.2 ms; TE, 1.6 ms; flip angle, 60°; no. of segments, 15; bandwidth, 975 Hz per pixel) using prospective ECG-triggering. An in-plane data acquisition matrix of 166×256 was used with a rectangular field of view of 400 mm, which rendered an in-plane pixel size of $2.0 \times 1.6\,mm^2$. Image acquisition time was about 11 R-R intervals per section, temporal resolution was 45 msec. After acquisition of the long axis slices, the entire left ventricle was imaged in contiguous, short-axis slices without intersection gaps using the same sequence and a section thickness of 8 mm. End-diastole was defined as the first phase within the cine cardiac cycle as prospective ECG triggering started with the R-wave; end-systole was defined as the phase with the smallest LV volume in all orientations.

Data Analysis

Evaluation of LV volumes and LVMM was performed by manually drawing the endocardial and epicardial contours on all short-axis, end-diastolic and end-systolic images using the commercially available ARGUS® software (Siemens Medical Systems, Germany). Planimetry was done by two independent radiologists blinded to the pre- or postdialysis conditions in random order. According to the American Heart Association (AHA), the first section next to the mitral anulus, which contains myocardium in all 360°, is defined as the most basal section (Cerqueira et al., 2002). During manual tracing, the papillary muscles were included in the left ventricular chamber volume (Chuang et al., 2000; Hahn et al., 2000; Lee et al., 2002; Miller et al., 2002; Zandrino et al., 2000). End-diastolic (EDV) and end-systolic (ESV) volumes were calculated by summation of the single-slice volumes ($V_{total} = \sum area_d \times slice\ thickness_d$), and stroke volume (SV) was calculated following the equation $SV = EDV - ESV$. Ejection fraction (EF) calculation was done using the equation: $EF = (SV/EDV)$. Left ventricular myocardial mass was calculated as the difference of epi- and endocardial volumes multiplied by the specific gravity of myocardium ($1.05\,g/cm^3$) and was displayed as the mean of the end-diastolic and end-systolic measurements. The left ventricular mass index (LVMI) is defined as the LVMM divided by the body surface area. The body surface area was calculated according to DuBois and DuBois (1915) [$S = M^{0.425} \times H^{0.725} \times 71.84$; S, body surface area ($cm^2$); M, body weight (kg); H, body height (cm)].

Statistical Analysis

The SPSS (Version 11.0, SPSS Inc., Chicago, IL) statistics package was used for the statistical analysis.

Changes in MR measurements of LV volumes and mass before and after dialysis were compared using a two-tailed t-test for paired samples as all data had normal distribution. Correlations among the changes, throughout dialysis, in body weight and MRI measurements of EDV, ESV, SV, EF, and LVMM were tested using the Pearson's test. A statistical level of $p < 0.05$ was considered significant for all comparisons. Not significant results were designated by "n.s." All measurement values were presented as the mean $\pm$ SD, unless otherwise stated.

For the assessment of intraobserver variability, the coefficient of repeatability was determined for two evaluations of the same predialysis data set performed by one observer. In the same way, interobserver variability for the predialysis measurements was tested in a comparison of evaluations performed by two observers.

RESULTS

Manual border detection of the entire LV endocardial and epicardial surface and consecutive measurement of LV volumes and myocardial mass in MRI were possible in all patients. The acquisition time for the MRI examination, which depended on the patient's LV size, was 21 ± 3 min. Time for postprocessing was 10 ± 2 min.

Measurements Before and After Dialysis

LV Volumes and Function

Predialysis EDV ranged from 59 mL to 181 mL (mean, 140 ± 39 mL) and decreased to between 56 mL and 136 mL (mean, 109 ± 27 mL) post dialysis ($p < 0.05$). Predialysis ESV was 49 ± 19 mL (range, 22.4 mL to 79 mL) and decreased to 42 ± 15 mL (range, 20 mL to 64 mL) post dialysis ($p < 0.05$). Ejection fraction did not change significantly through dialysis (mean pre, 65 ± 8%; range, 56% to 77% → mean post, 62 ± 10%; range, 47% to 77%; n.s.), since the stroke volume (SV) decreased correspondingly to EDV (mean pre, 91 ± 28 mL; range, 37 mL to 130 mL → mean post, 66 ± 24 mL; 35 mL to 104 mL; $p < 0.05$). Figure 1a–c shows the changes in LV volumes and function through dialysis measured by MRI. Figures 2 and 3 give a patient example of MRI.

LV Myocardial Mass

The LVMM and LVMI significantly decreased through the course of dialysis in all patients (Fig. 1d). Mean LVMM immediately before and after dialysis was 184 ± 23 g (range, 153 g to 214 g) and 177 ± 27 g (range, 148 g to 209 g; $p < 0.01$), respectively (Fig. 1d). The mean LVMI, correspondingly, decreased from 118 ± 17 g/m^2 to 114 ± 17 g/m^2 ($p < 0.001$).

Intra- and Interobserver Variability of MRI Measurements

For repeated measurements by one observer (intraobserver variability) of EDV, ESV, and LVMM measurements before and after dialysis, we found a mean difference of 1.3 ± 6.2 mL, −0.9 ± 4.1 mL, and −1.4 ± 3.9 g, respectively; standard error of estimation (SEE) was ± 2.3 mL, −2.0 mL, and ± 1.6 g. For the interobserver measurements of EDV, ESV, and LVMM by MRI, a mean difference of 3.3 ± 7.5 mL, 2.6 ± 5.0 mL, and −2.4 ± 4.6 g was found; SEE was ± 2.6 mL, ± 2.1 mL, and ± 2.0 g.

Relation Between the Changes in Body Weight and MRI Measurements

Mean body weight decreased by 2.0 ± 1.3% (range, 0.1% to 4.2%) after dialysis (Table 1) due to net volume loss. The mean decrease in EDV, ESV, SV, and EF measured by MRI was 20.4 ± 11.4% (range, 5.3% to 33.5%), 11.9 ± 12.1% (range, −10.8% to 23.4%), 25.5 ± 16.6% (range, 3.8% to 47.2%), and 4.8 ± 6.6% (range, −3.2% to 16.7%), respectively. The mean decrease in LVMM was 3.7 ± 2.0% (range, 0.8% to 6.3%). According to the Pearson's test, the correlation between body weight change and the changes in both LVMM and volumes was not statistically significant.

DISCUSSION

This study, where changes in LV volume and mass during dialysis were measured using MRI, carries three messages:

1. Although EDV, ESV, and SV significantly decreased throughout the course of dialysis, MRI accurately quantified LVMM independently of LV loading status and, therefore, seems to allow for monitoring of even small changes in LVMM.
2. MRI measurements of LV volumes and mass reveals low intra- and interobserver variability.
3. An anticipated small decrease in LVMM through dialysis can be detected by the investigated imaging technique.

Cardiovascular diseases are responsible for about half of the deaths in ESRD patients (USRDS, 1997). In these patients, a high prevalence of myocardial hypertrophy is found even in the predialysis time course. It has been shown that LVH and its evolution is of utmost clinical importance for the outcome in patients undergoing chronic hemodialysis (Devereux et al., 1997; Foley et al., 1995a, b; Locatelli et al., 1998). In respect of high therapy costs of chronic antihypertensive and anemia treatment in dialysis patients, the need for accurate LVMM measurements, in terms of therapy planning and monitoring, has emerged.

MRI Measurements of LV Volumes and Mass

For the last decade, cardiac cine MRI has been serving as the reference standard in measuring cardiac function, LV volumes, and myocardial mass, since it is independent of geometric assumptions when using the disk summation method in short axes. However, due to technical difficulties and long scan times, it has not yet been widely applied in clinical routines. Recently developed techniques such as SSFP have replaced formerly used gradient echo sequences to overcome major limitations. Upcoming, novel developments

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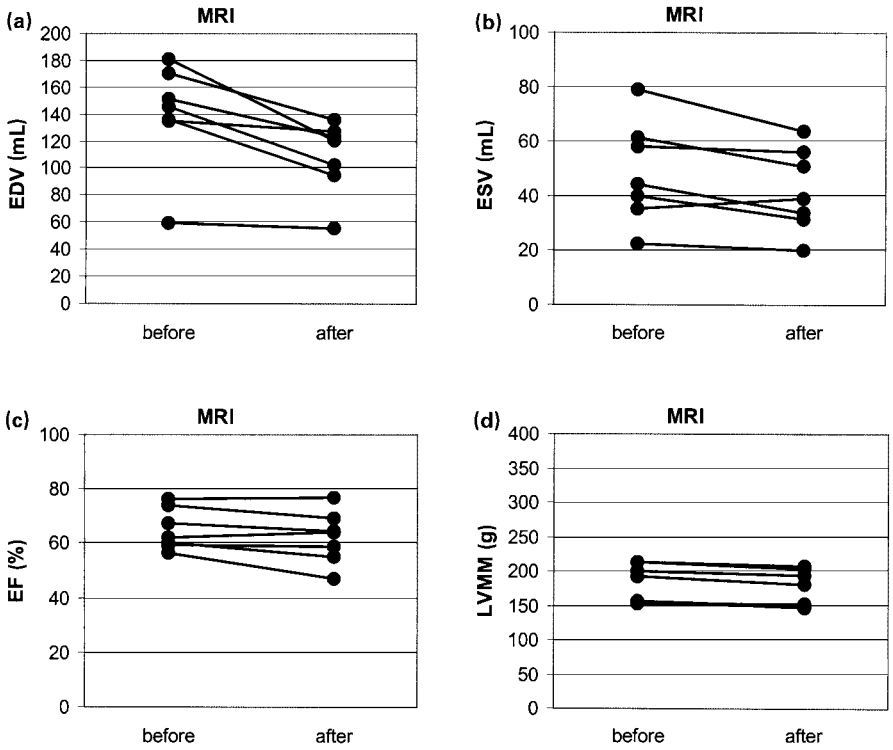

Figure 1. Cine MRI measurements of LV end-diastolic volume (a), end-systolic volume (b), ejection fraction (c), and myocardial mass (d) before and immediately after hemodialysis

include real-time imaging, which would shorten the overall scan time by covering the entire ventricle within one breath hold (Barkhausen et al., 2002; Lee et al., 2002). Parallel acquisition techniques (PAT) may yet enforce the feasibility of MRI in assessing LV parameters by accelerating the acquisition time. In view of postprocessing, reliable, automated border detection of the epi- and endocardium by new software tools in combination with higher image signal-to-noise ratio (SNR) is expected to improve the capabilities of cardiac MRI.

Several animal (Jaffe et al., 2001) and human (Pattynama et al., 1993; Shapiro, 1994) studies have proven the accuracy of MRI in LVMM estimation. An autopsy-controlled ex vivo MRI study showed excellent agreement ($r = 0.99$) of the MRI estimation with the actual LVMM (Bottini et al., 1995). The data presented in this study suggest that an accurate MRI measurement of LVMM is possible irrespective of the actual vascular and cardiac loading status represented by the LV volumes. As the LV volumes decreased significantly with only a small but consistent decrease in LVMM, it can be stated that LVMM estimations are not influenced by loading conditions. This finding has not yet been reported. Although the population of examined patients was small, our MRI measurements showed a statistically significant decrease in LVMM throughout dialysis. The mean decrease in LVMM was 3.7% and could be explained by the loss of interstitial volume through dialysis treatment. These small changes in LVMM estimation are statistically significant in our study, although they were within the same order of magnitude as was the measured interstudy variability (intra- as well as interobserver). Our findings are in agreement with literature results in terms of interstudy variability (Stewart et al., 1999). To our knowledge, no data have been published describing the acute volume or mass changes of myocardium or skeletal muscle throughout dialysis.

Physiological Background of the Findings

In animal experiments, Morgenstern et al. (1973) found that the left ventricular myocardial mass depends greatly on the intramyocardial blood flow. They found that up to 15% of the LVMM is related to the intramyocardial blood. In view of the significant loss of interstitial volume by dialysis leading to a decreased stroke volume and cardiac output, the concomitant slight

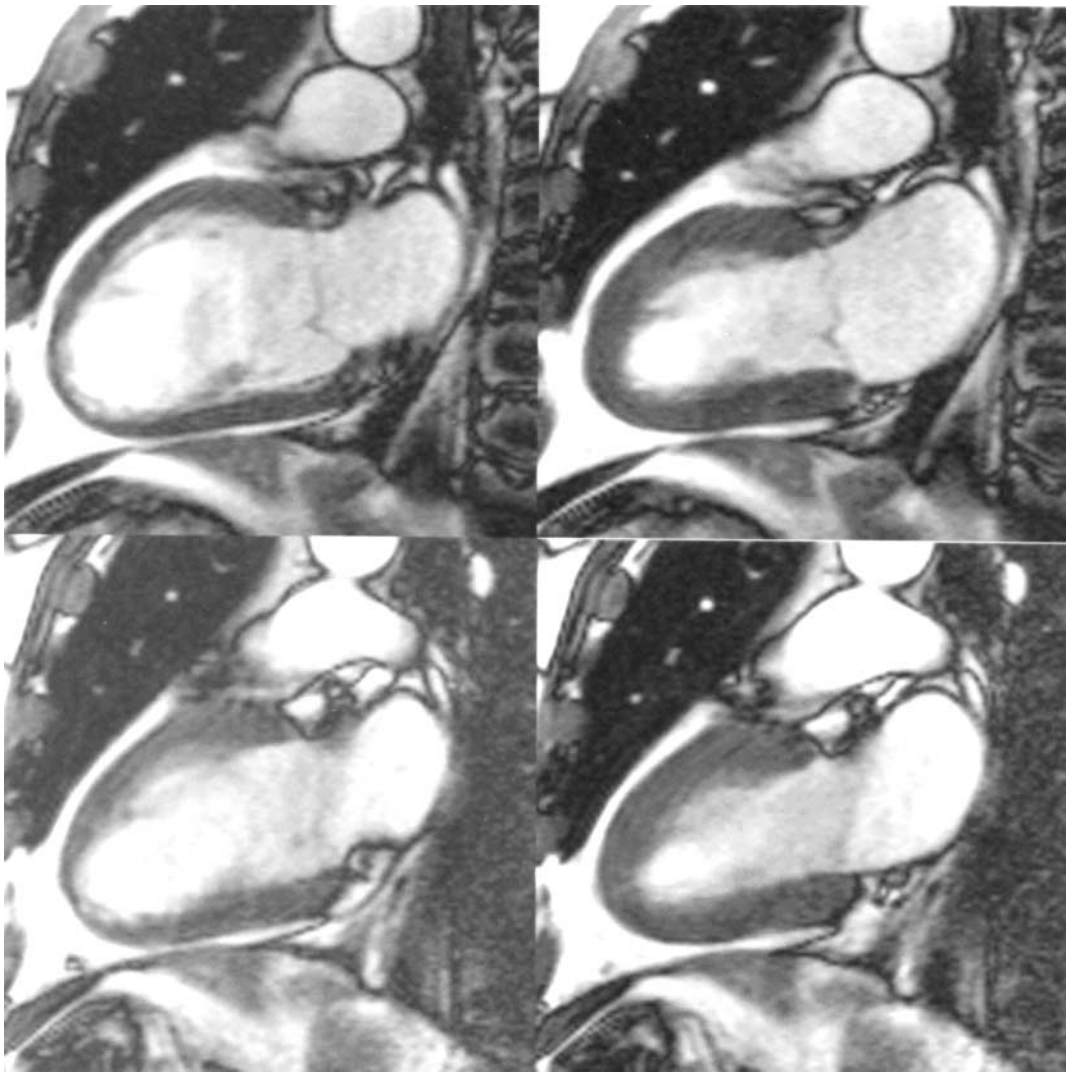

Figure 2. A 42-year-old man with end-stage renal disease on chronic hemodialysis. Vertical, long-axis cine MR images in end-diastole (left) and end-systole (right). Above: before dialysis; below: immediately after dialysis treatment. Mild concentric LV myocardial hypertrophy is present (LVMM, 157 g; LVMI, 103 g). The difference in EDV (left column) between the scans before (EDV_{pre}, 181 mL) and after dialysis (EDV_{post}, 120 mL) is obvious. ESV also decreases through the dialysis from 79 mL to 64 mL.

"loss of LVMM" in the described order of magnitude seems plausible from a pathophysiological point of view. This has been shown experimentally, however, to our knowledge, has not yet been proven by imaging techniques.

Comparison to Echocardiography Studies

During dialysis, LV volumes and EF in our study changed in the way it has been published in echocardiographic studies. Both by M-mode (Blaustein et al., 1986) and 2DE (Nand et al., 1997), LV dimensions have been described to decrease in hypertrophic left ventricles with normal function. However, M-mode and 2D techniques depend on geometric assumptions for determining LV volumes and mass, which causes difficulties in measurement of asymmetric ventricles myocardial mass arising from the unidimensional nature of the technique (Missouris et al., 1996; Schiller et al., 1989). This leads to false results, especially in asymmetric ventricle shapes (Reichek et al., 1983). The major limitation of echo in ESRD patients is its dependency on

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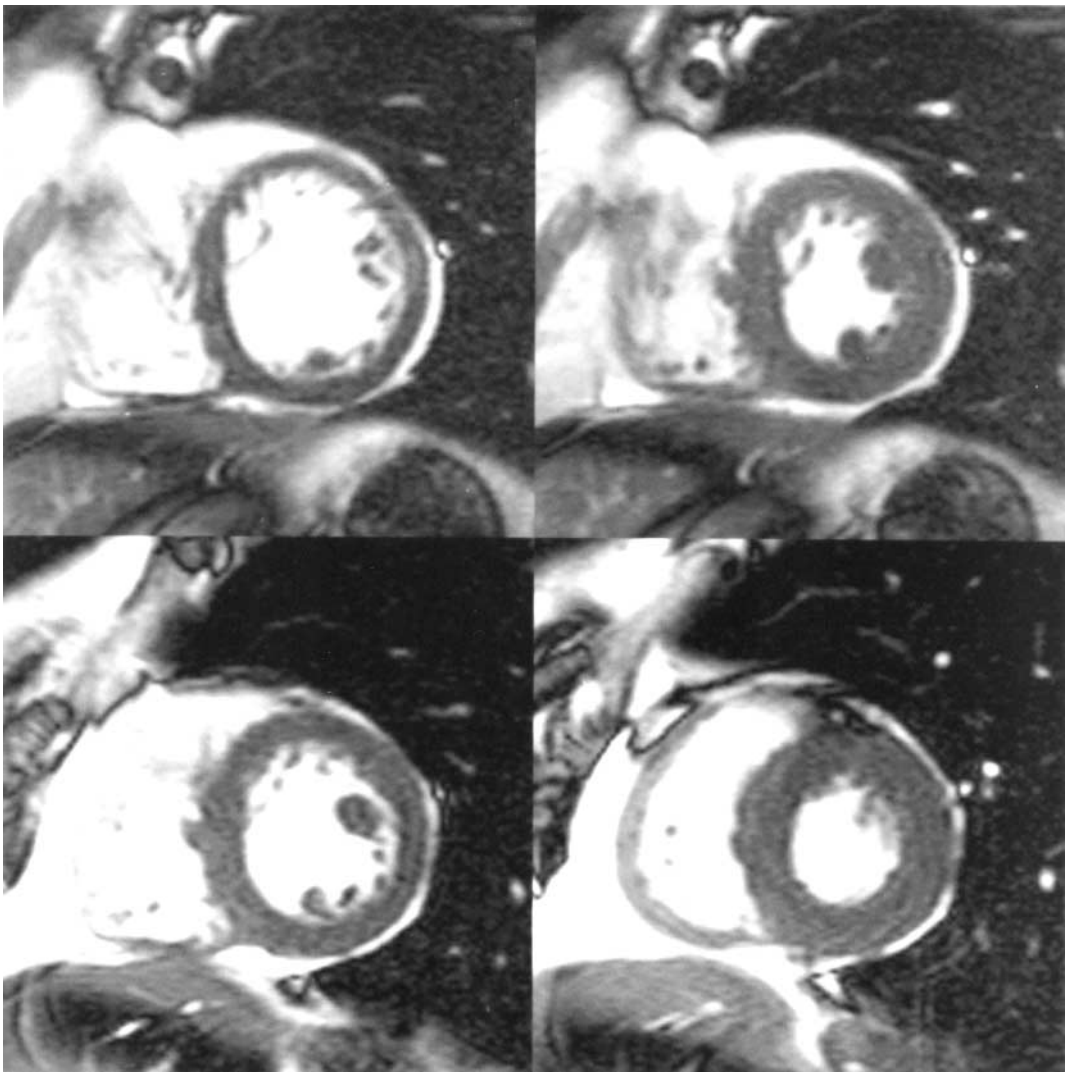

Figure 3. Same patient as Fig. 2: Comparable end-diastolic (left) and end-systolic, (right) short-axis, cine MR images, on which the volume evaluation was based. Above: before dialysis; below: after dialysis treatment. Note the decrease in left ventricular diameter after dialysis and the larger shift of the end-systolic image towards the valvular plane (no papillary muscles depicted) due to the shortened long-axis diameter of the ventricle with lower volumes.

loading conditions and geometry of the LV. Stewart et al. showed a systematic overestimation of LVMM by 2DE compared to MRI (Stewart et al., 1999). The degree of overestimation clearly correlated with the LV size. The major impact of LV size and timing of the echo exam in relationship to dialysis sessions has been shown previously (Harnett et al., 1993). Recent three-dimensional techniques may overcome these problems; however, these have not been established so far.

Clinical Implications

Magnetic resonance imaging, using recent SSFP cine sequences, accurately measures LVMM and LV volumes with a low interstudy variability. Cine MRI is a feasible, robust, and fast technique in a clinical environment as it is independent from cardiac fluid loading status. Therefore, it seems to allow reliable detection of changes in LVMM, which is crucial for

therapy monitoring with regard to LVH. The need for proper LVMM assessment in chronic dialysis patients is obvious. Thus, for serial LVMM measurement of hypertrophic left ventricles, MRI should be recommended as the technique of choice.

ABBREVIATIONS

LVH	left ventricular hypertrophy
ESRD	end-stage renal disease
LV	left ventricle/left ventricular
LVMM	left ventricular myocardial mass
SSFP	steady-state free precession
AICD	automated implantable cardioverter/defibrillator
TR	repetition time
TE	echo time
EDV	end-diastolic volume
ESV	end-systolic volume
SV	stroke volume
LVMI	left ventricular myocardial mass index
SEE	standard error of estimation

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