ORIGINAL ARTICLE

Ventricular Function

Left Ventricular Remodeling Subsequent to Reperfused Myocardial Infarction: Evaluation of a Rat Model Using Cardiac Magnetic Resonance Imaging

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ABSTRACT

Purpose: This study characterized the time course of ventricular remodeling subsequent to reperfused myocardial infarction (MI) in a rat model using cardiac magnetic resonance (MR) imaging.

Methods and Results: Short axis cine MR imaging was used to measure left ventricular ejection fraction (LVEF) and left ventricular volumes in Lewis rats at baseline, 1, 2, 4, 6, 8, and 10 weeks post-MI. Ventricular pressure and myocardial mass were evaluated at the 10 week time point.

Results: Measurements of LVEF showed a significant decrease in cardiac function immediately after MI with no significant changes over the remainder of the time course. Measurements of left ventricular end-systolic volume (LVESV) showed significant increases over the first 4 weeks after MI with no significant changes over the remainder of the time course. Statistical analysis of the MR measurements of LVESV yielded a repeatability standard error of 3.3%, an inter-observer standard error of 3.3%, and an intra-observer standard error of 1.6%.

Conclusion: This study indicates that cine MRI can be used to longitudinally evaluate changes in ventricular structure and function in a rat model of left ventricular remodeling. In this animal model, preliminary results indicate that the majority of remodeling is completed by 4 weeks and no significant changes in LVEF

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are seen after the first week. The repeatability values indicate that cardiac MR could be used for evaluating new therapies for mitigating the effects of LV remodeling after reperfused MI.

Key Words: *Magnetic resonance imaging; Ventricular remodeling; Myocardial infarction; Reperfusion; Heart failure*

INTRODUCTION

Left ventricular (LV) remodeling as a result of large anterior myocardial infarction (MI) is characterized by wall thinning at the site of infarction and progressive dilatation of the remaining ventricular chamber. Severe LV remodeling can give rise to the clinical condition of heart failure where the heart is either no longer able to meet baseline metabolic demands of the body, or can meet these demands only under increased filling pressures. Decreased left ventricular ejection fraction (LVEF), increased end-systolic and end-diastolic ventricular volumes, elevated arterial pressures, and elevated plasma renin are all indicative of heart failure.[1−4]

The rat model of LV remodeling subsequent to *permanent* coronary ligation has been used extensively in the study of the pathophysiology of LV remodeling and heart failure, and in evaluating new treatments. Using this model, progressive increases in LV volume associated with heart failure have been demonstrated, the relationship of the initial infarct size to ventricular function and survival has been developed, and the benefits of ACE-inhibitor therapy for heart failure were first demonstrated.[5−7] However, animal models based on permanent coronary ligation may not offer the closest comparison to current patient treatment regimens, as most patients receive revasularization to ensure patency of the infarct-related artery. Animal models of LV remodeling subsequent to *reperfused* MI may be more relevant to modern clinical practice. Studies in a rat model of reperfused MI have shown that late reperfusion (>1 hr occlusion) does not alter the size of the infarct, but does limit the extent of ventricular remodeling at 2−3 weeks.[8−10] However, the progression of LV remodeling in rat models of reperfused MI has not been well-characterized past the 2−3 week end-point, primarily because most previous studies were conducted by euthanizing a portion of the cohort at regular intervals post-MI. The effects of remodeling on LVEF are also not well established in the rat model because of the difficulty in accurately and reproducibly assessing LVEF over the entire time course of LV remodeling. A complete time course of these events is important in designing studies to evaluate new genetic and pharmocologic approaches to controlling LV remodeling post-MI.[11,12]

The purpose of this study was to: 1) characterize the time course of LV remodeling in a rat model subsequent to reperfused MI using cine MR imaging to measure factors clearly identified with the progression of heart failure, such as decrease in LVEF, and increase in LV end-systolic and end-diastolic volumes, and 2) perform a statistical analysis of these measurements to determine repeatability, inter-observer and intra-observer variability, and to confirm the accuracy of LV mass measurement prudent.

METHODS

Animal Model

This study conforms with the "Guide for the Care and Use of Laboratory Animals" published by the National Institutes of Health and was performed with the approval of the Institutional Animal Care and Use Committee at the University of Virginia. For baseline MR scans, 11 Lewis rats were sedated with 12 mg/kg of intraperitoneal (IP) diazepam for imaging of the LV. Pilot studies in our laboratory established that this dose of diazepam had minimal effects on blood pressure and heart rate. Although sedated, it should be noted that the rats remained conscious under the effects of diazepam during all imaging sessions.

One day after baseline MRI scans, the left coronary artery of each animal was occluded for 2 hr followed by reperfusion in order to induce MI. The protocol for animal surgery described below was modified from a mouse protocol described previously by Yang et al.[13] Animals were anesthetized with 100 mg/kg of sodium pentobarbital IP. Surgery was performed with the animals placed in a supine position with their paws and tails taped to the operating table. The head was retracted with a thin rubber band fastened to the upper incisors. The upper portion of the trachea was exposed through a 5 mm long middle incision in the neck and the

pretracheal muscles were bluntly dissected. A black-tipped endotracheal tube, made with PE-200 tubing was inserted orally into the trachea with the black tip placed 10 mm below the thyroid cartilage. The incision was then closed with a suture. The rat was turned laterally (right-side down) and the upper and hind paws re-fixed with tape. Artificial respiration was maintained through the use of a respirator with an FIO_2 of 0.89, a frequency of 70 strokes/min, and a tidal volume of 6.0 mL to maintain normal arterial PaO_2, $PaCO_2$, and pH. The connection between the ventilator and the endotracheal tube was intentionally left somewhat loose to guard against lung overexpansion. A 1.5 cm long incision was made parallel to the rib cage, centered over the heart. The left pectoris major muscle and the muscle beneath it were dissected longitudinally, without cutting these muscles, to expose the left third and fourth ribs. A parasternal incision was made to open the chest by cutting the left third and fourth ribs and intercostal muscles with a cautery pen (Pefectemp #0231, SSI, Nashville, TN). A 6-0 silk suture was passed with a tapered needle underneath the LAD at the level between the right ventricular outlet and the left atrium. Coronary ligation was achieved by tightening the suture over a piece of PE-200 tubing. Successful coronary occlusion and reperfusion were confirmed by significant ECG changes (e.g., widening of the QRS complex and elevation of ST segment) as well as color changes in the area at risk. ECG was monitored with a BioAmp connected to a PowerLab physiological data recording unit (ADInstruments, Mountain View, CA). Reperfusion was achieved by removing the PE-200 tubing. Once the reperfusion was initiated, the chest was closed in layers. The rat was weaned from the respirator, and the endotracheal tube was removed when the animal recovered spontaneous breathing and began to move. Body temperature was monitored with a rectal probe and was maintained between 36.5 and 37.5°C. Hemodynamic studies were conducted by cannulating the right common carotid artery so that blood pressures could be monitored with a pressure-transducing catheter connected through a Bridge Amp to the data recording unit (ADInstruments, Mountain View, CA).

MR Imaging

Images of the LV were obtained at baseline (one day prior to MI), 1, 2, 4, 6, 8, and 10 weeks post-MI. The MRI scans were performed in a 1.5 T Siemens Magnetom Vision (Siemens Medical Systems, Iselin, NJ) using a quadrature wrist coil (Medical Advances, Milwaukee, WI). The ECG signal from the rats was obtained using Ag/AgCl surface leads (Invisitrace, Conmed Corp., Utica, NY) in conjunction with an external ECG monitoring system (Omni-Track 3100, In Vivo Research Inc, Orlando, FL).

An ECG-triggered, 2D Cine FLASH sequence was used with TR = 32 msec, TE = 15 msec, FOV = 90 mm, rectangular FOV = 3/4. Matrix size was 192×256, yielding an in-plane resolution of $0.35 \times 0.35\,mm^2$. Slice thickness was 3.0 mm. Rat heart rates varied from approximately 250–350 beats/min, thus limiting the number of phases that could be obtained. This imaging sequence typically yielded six phases over the cardiac cycle, which has been adequate for determining LVEF.[14] Five contiguous slices covering the entire LV were obtained in the short axis orientation at each imaging session. Using both sagittal and coronal orientations from initial survey images, the short axis slices were aligned in an oblique orientation perpendicular to the central long axis of the LV. Additionally, 2- and 4-chamber long axis images were obtained following acquisition of the short axis images.

LVEF and LVESV Measurements

Calculation of LVEF and LVESV from the short axis images was performed using the cardiac image analysis package Argus WIP2.4 (Siemens Medical Systems, Chicago, IL). Endo- and epi-cardial boundaries were manually traced at both end-systole and end-diastole for all slices. These tracings identified the LV blood pool for semi-automated calculation of LVEF. LVEF was determined as the difference in end-diastolic and end-systolic volumes divided by the end-diastolic volume. The number of pixels within the endo-cardial contour were then counted and multiplied by the volume of an individual voxel ($0.3675\,mm^3$) in order to obtain LVESV.

Repeatability and Variability Analysis

A statistical repeatability analysis of the LVEF data was performed by repeating eight imaging sessions a second time immediately following the normal procedure. The repeated sessions included two baseline sessions, and two sessions at each of the following time points; 2, 4, 6, and 8 weeks. All animals participated in at least one of the repeated studies. The animals were removed from the scanner, repositioned, and imaged a second time. These repeated images were analyzed in the same manner as all other data and results were compared

using a one-way random effects model as outlined by Fleiss.[15]

Inter- and intra-observer statistical analysis of the LVEF data only required the repetition of data analysis. A sample of eight imaging sessions from various time points within the study was selected for analysis. For inter-observer analysis, a second observer, trained in the method of manually tracing endocardial boundaries performed the data analysis procedure for comparison with that performed by the primary observer. For intra-observer analysis, the primary observer re-analyzed the selected images, one month after initial analysis of the same image data. The guidelines for inter- and intra-test comparison from Fleiss were followed for the statistical analysis.[15]

LV Pressure Measurement

Upon completion of the final MR imaging session conducted 10 weeks post-MI, the rats were removed from the scanner and immediately taken to a lab for an invasive procedure to measure mean arterial and LV pressures. Each rat was anesthetized with pentobarbital (50 mg/kg, IP). ECG leads were attached to two forelimbs and one hindlimb. A middle skin incision was made in the neck and bleeding was stopped with a cautery pen. The right common carotid artery was bluntly dissected between the right sternocleidomastoid muscle and pre-trachea muscles without damaging the vagus nerve. The carotid artery was suture-ligated distally and occluded with a mini-clamp proximally. A hole was cut in the artery between the two occlusions and a blunt-ended catheter fashioned from PE-10 tubing was inserted into the artery and fixed by a suture. The PE-10 tubing was connected to a pressure transducer by an extension of saline-filled PE-50 tubing. After removing the mini-clamp, the arterial pressure was monitored through a BridgeAmp coupled to a PowerLab data recording unit (ADInstruments, Mountain View, CA). After recording the peripheral arterial pressures, the PE-10 tubing was advanced into LV so that LV pressures and developed pressure (dP/dt) could be recorded simultaneously along with the rat's ECG. The position of the catheter in the LV was indicated by a typical LV pressure wave and was confirmed after euthanasia at autopsy.

Three additional rats, not included in the main study, underwent the pressure measurement procedure immediately after baseline MRI scans to provide a normal comparison for the rats that were assessed 10 weeks post-MI.

Plasma Renin Activity

Plasma samples were isolated from five additional (noninfarcted) rats not included in the main study and from the rats that completed the 10 weeks post-MI follow-up scans. These samples were assessed for plasma renin activity by radioimmunoassay (DiaSorin, Stillwater, MN) according to the manufacturer's protocol.

Infarct Extent and LV Mass Measurements

After euthanasia at the end of the 10 week follow-up period, the extent of MI in each heart was determined by standard methods.[8] In brief, the excised hearts were sequentially perfused with saline and a 1% solution of triphenyltetrazolium chloride (TTC) in phosphate buffer (pH 7.4). Each heart was then frozen to facilitate sectioning into 6–7 transverse, short-axis slices. The individual slices were fixed in neutral-buffered formalin for digital photography. The infarcted area in each slice was calculated by determining the percent of the total area containing scar tissue and multiplying by slice thickness. Finally, the total percent of the LV wall involved in MI was calculated by summing the results from the individual slices.

LV mass at 10 weeks post-MI was determined by using endocardial and epicardial contours obtained at end-systole. The number of pixels within the contours were counted and the endocardial sum was subtracted from the epicardial sum in order to obtain the pixel count for the LV in each slice. The number of pixels was then multiplied by the volume of the individual voxel (0.3675 mm^3) in order to obtain the LV myocardial volume. The LV mass was calculated by multiplying the LV myocardial volume by the density of myocardium (1.03 g/cm^3). After the final imaging session at 10 weeks post-MI, each animal was euthanized, the heart was weighed for comparison to LV mass calculations from the MR data.

RESULTS

Of the 11 animals scanned at baseline, seven completed the 10 week study. Three of the rats expired during the course of the study and one was excluded after cardiac MR analysis and histological follow-up determined that it had not been successfully infarcted. Only the data from the seven animals that completed the study were included in the final results. In all animals, LV

structure and function over the 10 week time course following acute MI showed significant changes from baseline measurements. Figure 1 shows end-systolic and end-diastolic mid-ventricular short axis MR images taken from one animal at baseline and at 10 weeks post-MI. Increased end-systolic and end-diastolic volumes as well as thinning in the anterolateral wall are evident in the post-MI images.

LVEF and LVESV Measurement

Left ventricular ejection fraction was shown to decrease from an average of $79 \pm 4\%$ at baseline (mean $\pm$ SEM) to an average of $38 \pm 3\%$ at one week post-MI ($p < 0.01$). A trend of continued decrease in LVEF was observed over the remainder of the time course reaching a value of $30 \pm 5\%$ at 10 weeks post-MI (Table 1). However, no session-to-session changes between weeks 1 and 10 reached the level of statistical significance at a p-value of 0.01. Figure 2 shows average values and standard deviations for LVEF over the 10 week study period.

Left ventricular end-systolic volume increased from an average value of $44 \pm 10 \mu L$ at baseline to an average value of $224 \pm 23 \mu L$ at one week post-MI ($p < 0.01$). A second significant increase from $260 \pm 41 \mu L$ at 2 weeks to $337 \pm 36 \mu L$ at 4 weeks post-MI was also observed ($p < 0.01$). A trend of continued increase in LVESV was observed over the remainder of the time course, reaching a value of $354 \pm 53 \mu L$ at 10 weeks post-MI. However, no changes from week 4 to week 10 reached the level of statistical significance at a p-value of 0.01. Similar results were seen for LVEDV. Figure 3 shows average values and standard deviations for LVESV and LVEDV over the 10 week study period.

Repeatability and Variability Analysis

A repeatability analysis of LVEF measurement was performed by repeating eight of the imaging sessions. Statistical analysis of LVEF repeatability data yielded a standard measurement of error of 3.3%. A 95% confidence interval on the LVEF data is, therefore, observed within 6.7% of individual measurements. An
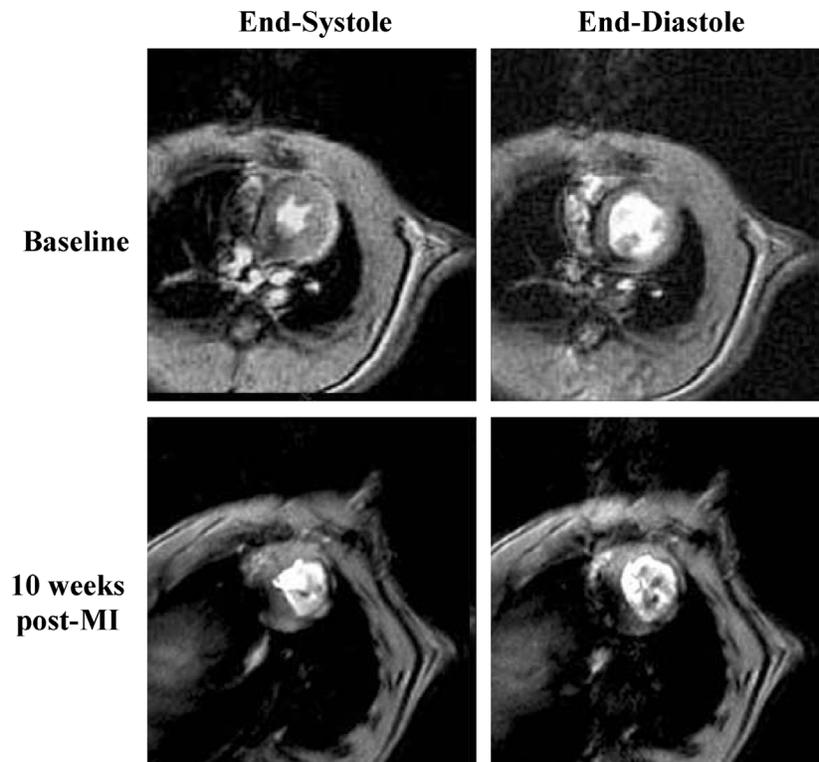

End-Systole   **End-Diastole**

Baseline

10 weeks post-MI

Figure 1. End-systolic (left) and end-diastolic (right) short axis images at baseline (top row) and at 10 weeks post-MI (bottom row). The heart at 10 weeks post-MI shows increased LVESV and LVEDV, as well as marked thinning of the anterolateral wall.

Table 1

Global LV Function, Histologic, and Hemodynamic Data in Baseline/Normal Rats and in Rats 10 Weeks Post-MI (All Values Reported as Mean ± SEM)

	Measurement Method	Normal/Baseline	10 Weeks Post-MI
LV end diastolic volume (μL)	MRI	209 ± 35	497 ± 84[a]
LV end systolic volume (μL)	MRI	44 ± 10	354 ± 53[a]
LV ejection fraction (%)	MRI	79 ± 4	29 ± 5[a]
Infarct extent, %LV area	TTC stain	0 ± 0	36 ± 2[a]
Heart to body weight (%)	Lab scale	0.25 ± 0.01	0.30 ± 0.01[a]
Mean arterial press (mmHg)	Pressure cath	114 ± 8[b]	101 ± 5
LV systolic press (mmHg)	Pressure cath	135 ± 5[b]	120 ± 4[a]
LV end diastolic press (mmHg)	Pressure cath	− 2.2 ± 0.8[b]	3.0 ± 0.6[a]
+dP/dt max, (mmHg/sec)	Pressure cath	11084 ± 1249	6231 ± 556[a]
− dP/dt max, (mmHg/sec)	Pressure cath	6210 ± 611	5074 ± 566
Heart rate (bpm)	Lab monitor	440 ± 6	383 ± 4[a]
Plasma renin (ng AngI/mL hr)	Lab analysis	9.9 ± 2.2	61 ± 9[a]

[a] Denotes $P < 0.05$ vs. Baseline.
[b] Baseline pressure values were obtained on a separate group of three animals not in the study group.

inter-observer analysis of LVEF measurement was performed on eight of the image sets. Statistical analysis of LVEF data yielded a standard measurement of error of 3.3%. A 95% confidence interval on the LVEF data is, therefore, observed within 6.5% of individual measurements. An intra-observer analysis of LVEF measurement was performed on eight of the image sets. Statistical analysis of LVEF data yielded a standard measurement of error of 1.6%. A 95% confidence interval on the LVEF data is, therefore, observed within 3.2% of individual measurements.

LV Pressure Measurement

An invasive measurement of LV pressures was performed on all rats immediately after the MR imaging session conducted 10 weeks post-MI. Additionally, a group of three normal (noninfarcted) Lewis rats were subjected to invasive pressure measurement for comparison with the rats in the heart failure group. Hemodynamic data from the two groups are presented in Table 1. Mean arterial pressure in the post-MI group (101 ± 5 mmHg) tended to be lower than in the normal
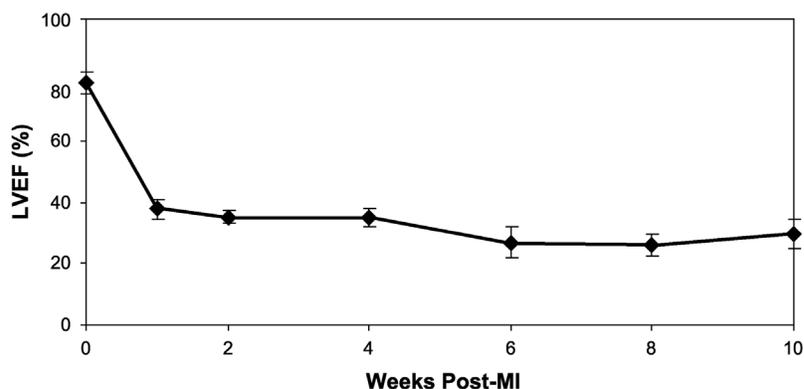

Figure 2. Left ventricular ejection fraction (LVEF) over the 10 week study. Average values ± standard error are plotted for the seven animals that completed the study. The LVEF decreased by half after MI, but there were no other significant changes over the remainder of the study.
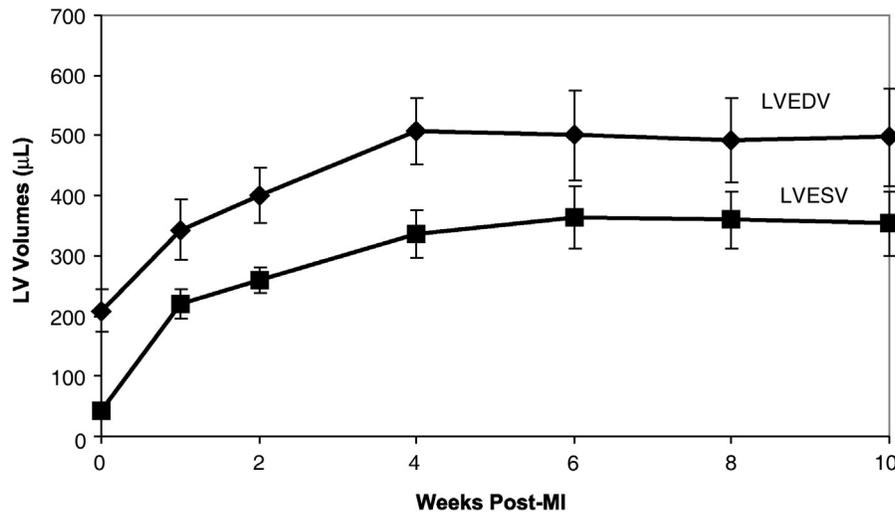
Figure 3. Left ventricular end-systolic volume (LVESV) and end-diastolic volume (LVEDV) over the 10 week study. Average values ± standard error are plotted for the seven animals that completed the study. The LVESV quadrupled in the first week after MI, and continued to rise until four weeks post-MI.

group (114 ± 8 mmHg), but this difference did not achieve statistical significance at a p-value of 0.05. The LV systolic pressure in the post-MI group was 120 ± 4 mmHg, which was significantly reduced relative to the value of 135 ± 5 mmHg seen in the normal group, $p < 0.05$. Furthermore, LV diastolic pressure in the post-MI group (3.0 ± 0.6 mmHg) was significantly elevated relative to the normal group (−2.2 ± 0.8 mmHg), consistent with the progression of heart failure. The mean $+dP/dt$ max in the post-MI group (6231 ± 556 mmHg/sec) was significantly reduced relative to the normal group (11,084 ± 1249 mmHg/sec). The mean LV $−dP/dt$ max in the post-MI group (5074 ± 566 mmHg/sec) tended to be lower than that in the normal group (6210 ± 611 mmHg/sec); however, this trend failed to reach statistical significance at a p-value of 0.05. Finally, heart rate in the post-MI group was 383 ± 4 bpm and this was significantly reduced relative to the value of 440 ± 6 bpm seen in the normal group, $p < 0.05$. The small variations in heart rate are probably due to the fact that Lewis rats are an inbred strain with minimal genetic variations between individual animals.

Plasma Renin Activity

Mean plasma renin activity in rats 10 weeks post-MI (61 ± 9 ng AngI/mL hr) was significantly elevated relative to normal values (9.9 ± 2.2 ng AngI/mL hr), con-sistent with neurohormonal activation in response to MI, $p < 0.05$.

Infarct Extent and LV Mass Measurements

Figure 4 shows a histological short-axis section from an excised heart next to the corresponding end-diastolic frame selected from the MR cine acquired from the same animal. The MR image shows excellent anatomical correspondence, including delineation of the anterolateral wall thinning in the infarct zone. In the group of rats assessed 10 weeks post-MI, quantitative analysis of infarct extent revealed that 36 ± 2% of the LV wall contained scar tissue as a result of MI (Table 1).

LV mass was determined from short-axis MR images and compared to the weight of the excised heart. Table 2 shows the results for all animals. The mean LV mass by MRI was 0.50 ± 0.09 g and the mean LV mass by weight was 0.49 ± 0.06 g. A Bland–Altman analysis was done on the heart mass data in Table 2. The mean error was small, but the variability was high. Two standard deviations (95% confidence interval) were 0.18 g, or 36% of the mean value.[16]

Total body weights were also recorded at the end of the 10 week study for calculation of the heart to body weight ratios. For comparison, a group of normal (noninfarcted) Lewis rats ($n = 5$) were analyzed in the same manner. As anticipated, the heart to body weight ratio in the group of rats assessed 10 weeks post-MI (0.30 ± 0.01) was
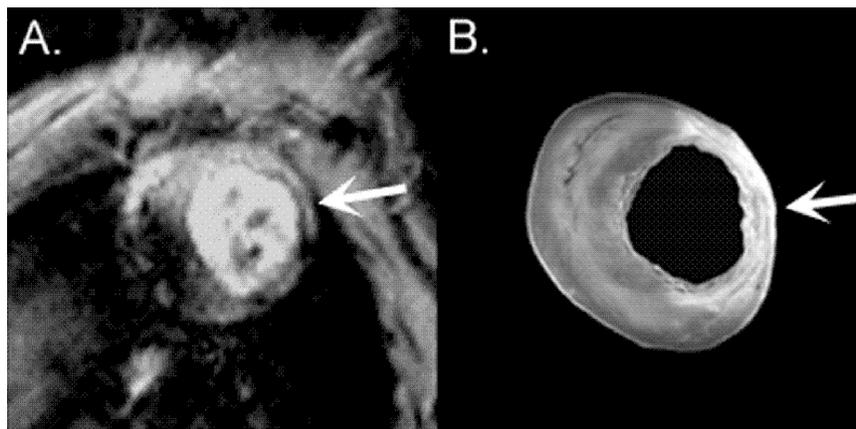
Figure 4. A mid-ventricular section of the excised left ventricle (right, B) compared with a mid-ventricular end-diastolic frame from the short axis cine image (left, A). The MR images give excellent anatomical depiction of the remodeled LV, including the thinning of the anterolateral myocardial wall (arrow).

significantly elevated relative to normal rats of similar body weight (0.25 ± 0.01, Table 1), $p < 0.05$.

DISCUSSION

This study found that cine MR imaging could monitor LV structure and function serially over a 10 week evaluation period in a rat model of LV remodeling subsequent to reperfused MI. LVEF was shown to decrease significantly from baseline to the first measurement at one-week post-MI. LVEF remained

Table 2

Left Ventricular Mass at Ten Weeks Post-MI by Wet Weight vs. Cardiac MRI

Rat	Mass by Wet Weight (g)	Mass by MRI (g)
1	0.54	0.46
2	0.56	0.67
3	0.42	0.44
4	0.48	0.50
5	0.55	0.43
6	0.47	0.57
7	0.42	0.46
Mean	0.49	0.50
SD	0.06	0.09

A Bland–Altman analysis revealed that although the mean error was small, the variability was high. The 95% confidence interval was 0.18 g, or 36% of the mean value.

stable at this level, and did not change significantly over the remainder of the 10 week evaluation period. LVESV was shown to increase significantly from baseline to one-week post infarction and again between the two- and four-week time points post-MI. LVESV did not change significantly over the remainder of the 10 week evaluation period. Left ventricular remodeling was readily apparent as visual changes in cardiac structure including decreased wall thickness, loss of apical definition, and increased LV volume.

Previous studies have examined the effect of reperfusion on acutely infarcted myocardium in a rat model over the first 3 weeks after MI.[8,10] These studies showed the effect of reperfusion on limiting infarct expansion and accelerating infarct healing. However, these studies focused entirely on histologic parameters associated with ventricular remodeling, and did not employ noninvasive measures of cardiac structure and function to assess LVESV or LVEF in vivo. Additionally, previous studies were terminated at 3 weeks post-MI, and thus did not characterize the full time course of remodeling and did not assess the long-term effects of reperfused MI as the rats progressed toward heart failure.

The observed serial changes in LVESV seen in this study are consistent with previously reported findings. It has been shown in both patients and in rat models that LVESV increases over time following an acute MI as a function of infarct size.[5,6] Furthermore, LVESV has been identified as the primary determinant of survival after recovery from MI,[17] making it an extremely valuable endpoint in the study of heart failure. Ventricular dilation after MI can be viewed as a global

response to the regional contractile dysfunction present within the infarcted myocardium. Dilation of the LV can restore stroke volume despite decreased LVEF. This dilation augments wall stress, however, resulting in the stimulation of further ventricular enlargement. LV enlargement is accompanied by wall thinning and further reduction in contractile function, probably due to rearrangement of the myofibrils across the ventricular wall.[5] Although our first post-MI time point was taken one week after MI, it is clear that the precipitous drop in LVEF measured at that time actually accompanied MI. Thus the dramatic decline in LVEF that occurs at the time of coronary occlusion represented the majority of the loss in LVEF that occurred over the entire 10 week period.[18] The lower heart rates seen post-MI may be due to the negative chronotropic effects of excessive nitric oxide, probably resulting from the induction of iNOS expression post-MI.

Repeatability and Variability Analysis

Statistical analysis of repeatability, inter- and intra-observer error demonstrated the ability of MRI to consistently and reproducibly measure cardiac function over time. Accurate, noninvasive, and serial measurements of cardiac structure and function are critical in evaluating the efficacy of novel approaches in the treatment of heart failure. MR evaluation of cardiac structure and function over time after MI in the rat model of LV remodeling may provide an accurate means for evaluating new therapeutic modalities including the assessment of drug and gene therapy. Although the sample size in this study was small, the variability and repeatability analysis presented may help in determining the number of animals necessary to obtain a statistically significant difference between treated and nontreated groups.[19] Despite the small size of the rat LV, the repeatability, intra- and inter-observer statistical analyses yielded standard error of measurements consistent with previously reported measurements of error in LVEF in patients evaluated by MR.[19] The low variability and excellent repeatability of the measurements is due in part to the small pixel size and high SNR provided by the quadrature wrist coil. The number of pixels across the myocardium at end-diastole was typically four, similar to the number seen in human studies using breath-hold cine MRI.

Limitations

A clinical 1.5 T MR system was chosen for the current study because similar scanners are widely available to researchers throughout the world. However, inherent limitations exist in the use of a whole body MR system to examine small animals. The small size of the area of interest in the rat model creates difficulties in obtaining images at high spatial and temporal resolutions. In this study, we obtained high spatial resolution ($0.35 \times 0.35 \, mm^2$ in-plane resolution) at the expense of a long echo time (15 msec) and a long repetition time (32 msec), which in turn limited the number of cardiac phases that could be acquired. The rapid heart rate of the sedated rats combined with the long repetition time limited our ability to obtain high temporal resolution images. Furthermore, the rapid heart rate in combination with the relatively long echo time often resulted in flow de-phasing artifacts within the LV blood pool.[20] Nevertheless, the limited number of cardiac phases obtained in this study was adequate for reproducible LVEF determinations.[14] However, no direct evaluation of the accuracy of LVEF was acquired in this study.

In conclusion, the current study demonstrates that cine MR imaging can be used to characterize a rat model of LV remodeling subsequent to reperfused MI. Cine MRI can assess the progression of LV remodeling through measurement of LVESV in a longitudinal study. In this study of a rat model of reperfused MI, we found that the majority of LV remodeling was completed by 4 weeks post-MI and the reduction in LVEF is largely complete, soon after MI. The sensitivity and reproducibility of cardiac MR for longitudinal studies should expedite future studies evaluating the efficacy of novel therapeutic approaches by potentially reducing the number of animals required to obtain statistically significant results.

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