Determination of Left Ventricular Mass by Magnetic Resonance Imaging in Hearts Deformed by Acute Infarction

Edward P. Shapiro, MD, Walter J. Rogers, BSc, Rafael Beyar, MD, Renate L. Soulen, MD, Elias A. Zerhouni, MD, Joao A.C. Lima, MD, and James L. Weiss, MD

Measurement of left ventricular (LV) mass by magnetic resonance imaging (MRI) is accurate in normal hearts. Because determination of mass by MRI does not require assumptions about ventricular shape, this method may be well suited for evaluating hearts distorted by infarction. To test this hypothesis, gated MRI was performed in 15 dogs before and after acute myocardial infarction. The LV mass of each dog was calculated from five short-axis images acquired at end systole, when shape distortion is greatest, at end diastole, and also from slices at varying phases of the cycle with a multiphase mode that required only one acquisition. Correlation was excellent between actual mass and end-systolic mass before infarction ($p < 0.001$, $r = 0.98$, and $\text{SEE} = 5.1$ g) and after infarction ($p < 0.001$, $r = 0.97$, and $\text{SEE} = 6.6$ g). Likewise, values correlated closely at end diastole before ($p < 0.001$, $r = 0.96$, and $\text{SEE} = 6.7$ g) and after infarction ($p < 0.001$, $r = 0.94$, and $\text{SEE} = 8.7$ g). Surprisingly, measurements of mass by a multiphase mode were also very accurate before ($p < 0.001$, $r = 0.98$, and $\text{SEE} = 5.1$ g) and after ($p < 0.001$, $r = 0.95$, and $\text{SEE} = 6.49$ g) infarction. Therefore, at the same phase and at multiphases of the cardiac cycle, MRI permits accurate determination of LV mass in distorted hearts. (Circulation 1989;79:706–711)

Changes in left ventricular mass can indicate disease progression and regression in hypertensive, valvular, hypertrophic, congenital, and possibly ischemic heart disease.1–6 A variety of noninvasive techniques for determining left ventricular mass have been proposed and tested.7–12 Of these methods, echocardiography and single-photon emission computerized tomography with thallium scanning are the most practical and widely available. However, these methods cannot be applied easily in measuring mass of hearts with ischemic involvement. Accuracy of echocardiographic methods is dependent on symmetry of left ventricular shape, which may not be present after infarction,13 and accuracy of radionuclide methods is dependent on coronary flow distribution, which is altered in ischemic heart disease.

Previous investigators14–16 demonstrated the accuracy of magnetic resonance imaging (MRI) in determining left ventricular mass in normally shaped, nonischemic hearts but not in hearts deformed by myocardial infarction or other diseases that alter ventricular shape. Because almost the entire heart can be included in a set of parallel tomographic magnetic resonance images and because assumptions about shape are, therefore, unnecessary, we postulated that MRI may be well suited for measuring left ventricular mass in abnormally shaped hearts distorted by acute myocardial infarction. In addition, because MRI is noninvasive, serial studies can be performed. In this study, we determined the accuracy of MRI measurements of left ventricular mass in in vivo canine hearts with shape abnormalities induced by acute myocardial infarction. In addition, we sought to determine whether or not multislice acquisition, which requires a minimum of scanning time, is accurate in left ventricular mass determination.

Methods

Experimental Protocol

All animal experiments were performed within guidelines established by the National Institutes of
Health, with a protocol approved by The Johns Hopkins Animal Services Committee, Johns Hopkins University, Baltimore, Maryland. Fifteen mongrel dogs weighing 20–25 kg were anesthetized with sodium pentobarbital (35 mg/kg body wt i.v., augmented as necessary during the experiment), were intubated and connected to a Harvard respirator (South Natick, Massachusetts), and ventilated with room air. A thoracotomy was performed through the fifth intercostal space, the heart was exposed, and the pericardium was opened. A femoral arterial line was placed to monitor systemic blood pressure. A heart sound sensor (Gould, Cleveland, Ohio) was sewn into place adjacent to the aorta for determination of the timing of the second heart sound and, therefore, end systole. The left anterior descending coronary artery or the left circumflex coronary artery was inspected, and a site for occlusion was dissected free from the myocardium. In 10 dogs, a long snare was attached so that coronary occlusion could be performed later without removing the animal from the magnet. The hearts of all dogs were imaged in the preinfarction state. In the 10 dogs with snares, coronary ligation was then performed (five left anterior descending, five left circumflex) to produce areas of systolic bulging. The five other dogs were moved out of the magnet but kept in position on the MRI couch, and infarction was created by injecting a biologically inert, nonresorbable polysulfide polymer (Perplastic, Kerr, Romulus, Michigan) ("dental rubber") into the left anterior descending coronary artery. Dental rubber is a viscous polymer that occludes anterograde and retrograde collateral flow into the risk region and results in dense transmural infarction.17 In this model, regional infarct dilation occurs rapidly, resulting in systolic and diastolic shape distortion within 1 hour of infarction. The dogs were then returned to the magnet. After 60–90 minutes, the heart was again imaged. The dogs were killed by injecting Monastral blue, 15 ml, into the left atrium. The right ventricle, the atria, the valves, and any large deposits of epicardial fat were then removed, and the isolated left ventricle was weighed. The left ventricle was sectioned into five short-axis slices of equal thickness. The sections were traced onto transparencies and then outlined on a computerized digitizing board (Diasonics CRC4, Milpitas, California) for determining myocardial area. Areas of Monastral blue nonstaining were considered ischemic and were outlined and expressed as a percentage of total area.

**Image Acquisition**

All images were acquired on a Resonex RX4000 (Sunnyvale, California) instrument with a 0.38 Tesla iron core resistive magnet with a flexible, single-turn solenoidal coil, a 25-cm field of view, and a 128 × 128 matrix with an in-plane resolution of 2 mm. Four excitations were averaged. The system can image in oblique planes, and after we obtained an axial and long-axis scout view, the short-axis plane was identified. In a previous study of excised nonbeating hearts,18 we showed that five slices were adequate for accurate mass determination. Accordingly, in the present study, we imaged five 1-cm thick short-axis slices obtained from each heart, and the interslice gap was adjusted to space the images equally from the base to the apex. The adjusted interslice gap ranged from 1 to 3 mm. The center of the first slice was positioned 5 mm below the actual left ventricular base as determined from the long-axis scout view. The most apical slice typically showed little cavity. Images of each beating heart were acquired in two ways; first, with a multislice method, and second, in 10 dogs, with a sequential method in which end-diastolic and end-systolic images were obtained for each slice. With the multislice method (Figure 1, top panel), TR was equal to the RR interval, and TE was 30 msec. In this mode, the first slice was imaged in end diastole, triggered by the R wave, and subsequent slices were acquired throughout systole at 54-msec intervals. The entire heart was imaged in one acquisition that took 4–7 minutes, depending on the heart rate, but each slice was recorded at a different phase in the cardiac cycle.

To obtain a set of short-axis images, each timed to end diastole and end systole, end diastole was marked by the R wave. We defined end systole as the time of the first high-frequency deflection of the second heart sound because this corresponds closely to the time of peak negative Dp/dt and minimal cavity dimension,19 which are well-accepted markers of end systole. We used two ways to obtain end-diastolic and end-systolic images (Figure 1, middle and bottom panels). The first method was a variation of the multislice mode in which the TE was shortened to 15 msec, and the slices were packed but spaced to ensure that the final slice corresponded to the second heart sound. To record each slice at end diastole and end systole required five iterations, in which slice order was changed each time. This took 20–35 minutes and produced the typical short-axis view on which the blood pool appeared as a black flow void. Alternatively, the same slice was imaged twice within the same RR interval with diastole defined by the R wave and with end systole defined by S2. The TR for end systole was thus equal to the interval between the QRS complex and S2, and the TR for end diastole was equal to the interval between S2 and the QRS complex. This also took 20–35 minutes but produced short-axis views with a bright white blood pool.

**Left Ventricular Mass Calculations**

Left ventricular mass was calculated with a simplified Simpson’s reconstruction according to the following formula:

\[
LV \text{ mass} = \sum (\text{EPI} - \text{ENDO}) \times (\text{THK} + \text{GAP}) \times (1.05)
\]

where LV is left ventricular, mass is in grams, EPI is the area enclosed by the epicardium, ENDO is
the area enclosed by the endocardium, THK is the slice thickness, GAP is the interslice gap, and 1.05 represents the density of myocardium (g/ml). Areas were obtained by digitizing the MRI images with Resonex on-line software. The papillary muscles were included in the area traced, and the epicardial fat excluded.

To document the presence of apical expansion in dogs injected with dental rubber, the ratio of slice area at the base (slice 1) to that near the apex (slice 4) was calculated before and after infarction.

Statistical Analysis

Left ventricular mass determined by MRI was compared with actual left ventricular mass by linear regression. Differences in slice area at different times in the cardiac cycle were determined by analysis of variance. Values are mean±SD.

Results

Fifteen dogs were studied with multislice MRI. The software required for MRI at end systole was not available for the first five dogs, so only 10 dogs had both multislice and systolic and diastolic MRI performed. Of those, two died shortly after coronary occlusion.

Hearts weighed from 72 to 143 g. Coronary ligation resulted in systolic bulging in all 10 dogs, and hearts in all survivors had areas of Monastral blue nonstaining in the distribution of the ligated coronary artery. Injection with dental rubber produced visible diastolic expansion in all five dogs (Figure 2). The ratio of basal to apical slice area decreased in all these dogs, from 2.26±0.9 to 1.40±0.2, because apical expansion distorted the usual taper of the left ventricle toward the apex. For all 15 dogs, the ischemic area was 24.7±1.7% of the total myocardial area.

Mass by Multislice Magnetic Resonance Imaging

Linear regressions of actual left ventricular mass and MRI mass are displayed in Figure 3. Before infarction, MRI mass correlated to actual measured mass: r=0.98, slope=1.04, and SEE=5.1 g. After myocardial infarction, correlation was again excellent: r=0.95, slope=1.06, and SEE=6.9 g. MRI heart mass before and after infarction did not change; mean mass before infarction was 111±6 g, and after infarction, it was 116±6 g. Preinfarction and postinfarction mass correlated: r=0.98, slope=1.01, and SEE=4.9 g.
**In Vivo Mass at End Diastole and End Systole**

When preinfarction mass was calculated from a set of short-axis slices recorded at the same phase of the cardiac cycle (Figure 4), MRI mass correlated with actual mass: in diastole, values were \( r=0.93 \), slope=0.93, and SEE=8.9 g; in systole, values were \( r=0.98 \), slope=1.1, and SEE=5.5 g. When postinfarction mass was calculated, MRI mass correlated again with actual mass: in diastole values were \( r=0.94 \), slope=1.0, SEE=8.7 g. At end systole after infarction, when shape distortion of the infarcted ventricle is maximal, MRI mass correlated with actual mass: \( r=0.97 \), slope=1.1, and SEE=6.6 g. End-diastolic and end-systolic mass correlated: \( r=0.98 \), slope=1.01, and SEE=3.9 g. Neither the size of the heart nor the size and location of the ischemic area affected the accuracy of these measurements.

Images of each slice at end diastole and end systole were compared (Figure 5). Differences were not significant between the extremes of the cardiac cycle.

**Interobserver and Intraobserver Variability**

When one observer repeated the measurements of a series of 20 slices after an interval of 2 months,
there was correlation: $r=0.97$, slope=1.01, and SEE=1.5 cm$^2$. When two observers independently measured a series of 24 slices, there was correlation: $r=0.95$, slope=0.94, and SEE=1.6 cm$^2$.

**Discussion**

Left ventricular mass determination by MRI is accurate despite ischemic distortion of ventricular shape and should provide precise data on heart mass in patients with ischemic heart disease. Previous clinical methods for estimating mass are not ideal for this population. For example, electrocardiographic estimates of hypertrophy are qualitative and are not satisfactory for quantitative assessment. Radionuclide scans$^{10}$ are sensitive to flow abnormalities and are, therefore, not appropriate for studying mass in ischemic heart disease. M-mode echocardiography samples only a small portion of the left ventricle and requires assumptions about shape and symmetry that may not be warranted, especially in disease states. Accurate mass data have been obtained in humans with two-dimensional echocardiography,$^8$ but even this method extrapolates data from a limited sampling of the left ventricle to measurement of global mass, and it may become inaccurate in individuals in whom patterns of infarction have produced unusual shape abnormalities. Although three-dimensional reconstruction of multiple two-dimensional echocardiograms provides accurate left ventricular mass determination,$^{20}$ current methods are tedious and time consuming. With MRI, almost the entire ventricle is visualized, so assumptions about shape are unnecessary. In radiographic computed tomography,$^{11,12}$ the entire left ventricle is sampled, and mass can be accurately measured, but such methods require intravenous contrast agents and exposure to ionizing radiation.

The main drawback of MRI is that long scanning times are sometimes required. If mass could be determined with one multislice image acquisition without repeated iterations, scanning time would be greatly reduced. In this study, we noted that mass obtained with a multislice method was as accurate as mass obtained with each slice recorded at the same phase in the cardiac cycle. Indeed, there were no significant mass changes of any slice between the extremes of the cardiac cycle. This was not expected, because several factors affecting mass determination may change during the cardiac cycle. Myocardial blood content, for example, may be greater in diastole than in systole. Using the dynamic spatial reconstructor, Iwasaki et al$^{11}$ studied phasic changes in left ventricular mass and found a 12% increase in mass during early systole. Mass then decreased and reached baseline before late systole. This transient change might affect only a single slice of a multiphase MRI acquisition, and our data show that this does not reduce the accuracy of whole heart mass determination. The study of Iwasaki et al$^{11}$ is, therefore, in agreement with our finding that mass at end diastole is similar to that at end systole; differences due to changing blood content must be small and below the limits of resolution of this system.

Motion of the heart through the short-axis imaging plane during systole may also affect mass determinations, depending on the phase of the cardiac cycle. During systole, the cardiac base moves downward toward the apex. A short-axis slice positioned at the base in diastole may not intersect myocardium at all during systole, which would yield a falsely low mass determination for the whole heart. This did not occur during this study, suggesting that downward motion of the base is small in the open-chest dog model. Our recent experience with MRI myocardial tagging,$^{22}$ a new method that permits the placement of noninvasive markers using differential magnetization, confirms that while this motion is only 2–3 mm in the open-chest dog, the normal human cardiac base moves down 16.5 mm.$^{23}$ For studies in patients, therefore, multislice imaging should be timed to avoid data acquisition during systole or the rapid-filling period of diastole. This can be accomplished on most MRI systems by inserting a delay of 450–500 msec after the QRS complex so that all slices are acquired during diastasis.

The few instances of overestimation of left ventricular mass in our data may have resulted from including the signal from flowing blood as the left ventricular wall. New pulse sequences that include presaturation of blood flowing into the image plane$^{21}$ may reduce this problem. Underestimation of mass could result from improper selection of short-axis planes so that the whole ventricle is not included in the five slices. Inaccuracy of some points could also result from partial volume effects near the apex, but with selection of short-axis slices as described, this appears not to be a major problem.
Marked increases in myocardial mass due to hypertrophy have been demonstrated in animals after experimental myocardial infarction. To what extent this phenomenon occurs in humans is unknown because previous studies, based on autopsy data, reported conflicting data. Serial MRI studies in patients with acute myocardial infarction should clarify the conditions leading to postinfarction hypertrophy and its prognostic implications. In addition, MRI should be well suited in testing interventions that reduce hypertrophy in hypertrophic cardiomyopathy, which is often localized and irregular, and also in hypertension where left ventricular shape may be irregular in some individuals.

In conclusion, MRI is an accurate method for predicting left ventricular mass even when ventricular geometry is distorted by infarction and aneurysm. Mass calculation of any slice and of the whole heart was not dependent on the phase of the cardiac cycle in this study. Determination of left ventricular mass by multislice MRI is noninvasive, so serial studies may be obtained. Also, it is easy to perform, and requires only a single acquisition with a short imaging time. Calculations are simple and can be aided by measurement software available on many MRI systems.

References

Key Words: nuclear magnetic resonance imaging • hypertrophy
Determination of left ventricular mass by magnetic resonance imaging in hearts deformed by acute infarction.

E P Shapiro, W J Rogers, R Beyar, R L Soulen, E A Zerhouni, J A Lima and J L Weiss