Assessment of Left Ventricular Mass by Cardiovascular Magnetic Resonance

Saul G. Myerson, Nicholas G. Bellenger, Dudley J. Pennell

Abstract—Left ventricular hypertrophy is associated with significant excess mortality and morbidity. The study and treatment of this condition, in particular the prognostic implications of changes in left ventricular mass, require an accurate, safe, and reproducible method of measurement. Cardiovascular magnetic resonance is a suitable tool for this purpose, and this review assesses the technique in comparison with others and examines the clinical and research implications of the improved reproducibility. (Hypertension. 2002;39:750-755.)

Key Words: myocardium ▪ hypertrophy ▪ magnetic resonance imaging

The importance of left ventricular hypertrophy (LVH) in medicine is not widely appreciated. The Framingham Study, among others, showed that increased left ventricular (LV) mass is associated with a significant excess of cardiovascular mortality and morbidity. This is independent of presence of coronary artery disease or hypertension, with a tripling of the mortality rate in subjects with and without either of these. The risks of coronary, peripheral, or cerebrovascular disease are also raised, even among normotensive subjects with LVH.

The accurate measurement of LV mass has in the past been difficult, partly because of the oblique angle at which the heart lies within the chest, its continuous movement, and the lack of a technique for imaging the whole left ventricle. Initial measurements with ECG data were surrogate markers for LV mass, with values affected by positioning of the leads, orientation of the heart, and obesity. Nevertheless, criteria were developed for identifying LVH with ECG that correlated to an extent with true LVH but were insensitive and nonspecific (specificity, 6% to 56%). Imaging techniques have now supplanted the ECG, and we review these with particular reference to cardiovascular magnetic resonance (CMR).

Echocardiography

Echocardiography (echo) was a distinct advance for LV mass measurement over the ECG, with direct visualization of the myocardium and real-time imaging, and many important studies examining the prognostic effects of LVH have used this method. However, obtaining good quality images is dependent on a skilled operator, patient position and anatomy, obesity, and angle of the transducer beam, and images of sufficient quality for LV mass measurement may not be obtained in up to one third of cases. The assumed geometric shape for both M-mode and 2D echo may lead to error, particularly as variations in ventricular geometry affect calculated LV mass. The landmark trials, such as Framingham, overcome the deficiencies in accuracy and reproducibility of echo with large numbers of subjects.

M-mode is the commonest echocardiographic method for measuring LV mass, the images being easier to obtain and the calculations straightforward. Although validated against postmortem mainly normal hearts, it suffers most from the assumption of geometric shape, and this variability is reflected in the poor accuracy of the technique, with standard errors of the estimate (SEE) of 29 to 97 g (95% confidence interval [CI], 57 to 190 g). Interstudy reproducibility is also poor, with SDs of the difference between successive measurements of 22 to 40 g (95% CI, 45 to 78 g). The importance of operator skill is underlined by the large interobserver variability of a similar degree (SEE, 28 to 41 g; 95% CI, 55 to 80 g).

2D echo has advantages over M-mode echo, as measurement is made of the ventricular length and minor axis in 2 planes. It still, however, assumes a prolate ellipsoid shape of the left ventricle and, to an extent, uniform wall thickness and is thus prone to similar inaccuracies as M-mode echo. The accuracy (SEE, 31 to 39 g) and reproducibility are moderately improved over those of M-mode, although the increased difficulty in obtaining suitable quality images for evaluation may limit the ability to determine LV mass.

3D echo removes the assumption of shape and wall thickness. It has been shown to be more accurate than 2D or M-mode echo and is comparable to CMR, particularly with the newer transesophageal 3D echo (95% CI, ±12.8 g). The technique requires skill and time; however, and a number of subjects may not have suitable acoustic windows.
There are currently relatively few units worldwide practicing the technique on a regular basis, and the transesophageal route may not be acceptable to some subjects.

**Electron-Beam Computed Tomography**

The fast imaging time of electron beam computed tomography (EBCT), when coupled with blood-pool contrast agents, has facilitated 3D cardiac imaging precise enough to measure LV mass. The technique is similar to 3D echo and CMR in that multiple contiguous image planes are summed to measure myocardial volume, employing Simpson’s rule. When multiplied by the density of myocardial tissue (1.05 g/cm³), the LV mass is obtained. The ability to acquire many slices in a single breath-hold is also an advantage. There is good reported accuracy\(^ {36,37} \) (SEE, 16 g in humans) and reproducibility,\(^ {38} \) although human validation studies are limited. The disadvantages are the exposure to ionizing radiation and need for an intravenous contrast agent to delineate the cardiac blood pool. In addition, the image slices are not true short axes but an approximation, because of the limitations of available image planes, which decrease accuracy because of partial volume effects.

**Cardiovascular Magnetic Resonance**

3D techniques such as EBCT and 3D echo are clearly better than 1D or 2D methods with assumptions about ventricular shape. CMR shares this advantage without the ionizing radiation or need for contrast agents with EBCT and without the problems of acoustic windows for echo. The free choice of imaging planes and good tissue visualization mean that virtually all images are of sufficient quality for LV mass determination.

**CMR Technique**

For the most accurate measurements, the image stack should be parallel to the true LV short axis, minimizing partial volume errors (Figure). The short axis is identified by first piloting the vertical long axis (VLA) plane from transaxial images, passing through the center of the mitral valve and apex of the LV. A horizontal long axis (HLA) plane is then obtained perpendicular to the VLA, again passing through the center of the mitral valve and apex. From the HLA, a stack of short-axis images is obtained, covering the length of the LV. ECG-gated cine CMR is acquired to measure LV mass at a single time point within the cardiac cycle (the standard is end-diastole). In addition, acquiring each image slice within a single breath-hold removes respiratory artifact. Usually 10 slices will cover the ventricle, and with a 10-second breath-hold per slice, this can be achieved in <10 minutes. With the newest scanners, cine stack can be obtained in a single breath-hold, reducing the time taken for a scan to 8 seconds.\(^ {39} \) The image stack can also provide volume information by summing the endocardial area on each slice to derive left (and right) ventricular volumes. The cine nature of the images allows end-diastolic and end-systolic volume to be measured and thus also stroke volume, as well as regional ventricular function.

**Accuracy and Reproducibility**

The accuracy of CMR measurements of LV mass has been validated using postmortem hearts, imaged ex vivo for humans\(^ {26,46} \) or in vivo for animal studies\(^ {41-46} \) (Table 1). These show good agreement between the CMR-obtained and true LV masses, with SD of the difference of \( \approx 8 \) g (95% CI, \( \approx 15 \) g) in human studies and 10 g (95% CI, \( \approx 19 \) g) in canine studies. The gold-standard validation of comparing in vivo images with subsequent postmortem weights has not been performed in humans, and this important comparison remains to be done.

The reproducibility of LV mass measurements is of importance for assessing changes over time, both for individuals and research studies. This encompasses interstudy (ie, test-retest reliability) and inter- and intraobserver variability in values. Again these are very good for CMR (Table 2),\(^ {26,27,40,47-53} \) with interstudy variability having a mean weighted SD of the difference of 7.8 g (95% CI, 15.3 g).\(^ {26,27,47,48} \) Mean weighted intra- and interobserver variabilities are 4.8 and 9.0 g, respectively.\(^ {47,53} \) By comparison, the mean weighted interstudy SD of the difference for M-mode, 2D, and 3D echo is 27.7,\(^ {21,24-28} \) 19.2,\(^ {28,30} \) and 19.2 g,\(^ {35,35} \) respectively.

**Clinical Implications**

The greater accuracy and reproducibility of 3D techniques, such as CMR, has important implications for clinical practice and research. The improved reproducibility means that in group studies, much smaller sample sizes can be used to detect the same change in LV mass. Alternatively, using the same sample size, smaller degrees of change can be identified. A comparison between CMR and echo of the sample
sizes needed to detect a statistically significant change in mean LV mass of 10 g are shown in Table 3. The numbers needed with CMR are 8% of those with M-mode and 17% of those with 2D echo, with considerable savings in cost and study duration. CMR has already been used in clinical trials to identify very small differences in LV mass between groups: 9 to 11 g/m² with 15 to 20 subjects per group \(^5^4,^5^5\) and 7 g with groups of 30 to 40 subjects each. \(^5^6\)

For individual patients, the 95% CI for serial studies using M-mode echo of \(\pm 45\) to 78 g\(^2^1,^2^4–^2^7\) means that serial LV mass measurements cannot detect a change of less than this amount with any certainty. Given that most therapeutic interventions are likely to effect a change that is smaller than this, M-mode echo would not be an ideal method for serial changes. 2D echo has improved reproducibility, which results in better confidence intervals (\(\pm 39\) g),\(^3^9\) and these are \(\pm 13\) to \(\pm 45\) g for 3D echo, depending on the route used (transesophageal versus transthoracic).\(^3^4,^3^5\) CMR has 95% CIs of \(\pm 12\) to 22 g,\(^2^6,^2^7,^4^7,^4^8\) and this or another 3D technique should be used for individual changes in LV mass.

### TABLE 1. Accuracy of CMR-Determined LV Mass in Human and Animal Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>No.</th>
<th>SDD</th>
<th>95% CI</th>
<th>Mean % Difference</th>
<th>Mean % Difference</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bottini et al(^2^6)</td>
<td>6</td>
<td>8.9 g</td>
<td>(\pm 17.5) g</td>
<td>0.7 g</td>
<td>4.0%</td>
<td>Human</td>
</tr>
<tr>
<td>Katz et al(^4^0)</td>
<td>10</td>
<td>7.4 g</td>
<td>(\pm 14.5) g</td>
<td>10.2 g</td>
<td>5.3%</td>
<td>Human</td>
</tr>
<tr>
<td>Human studies (mean values)</td>
<td>16</td>
<td>8.0 g</td>
<td>(\pm 15.7) g</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>McDonald et al(^4^1)</td>
<td>10</td>
<td>1.8 g</td>
<td>(\pm 3.5) g</td>
<td>4.4 g</td>
<td>5.2%</td>
<td>Canine</td>
</tr>
<tr>
<td>Shapiro et al(^4^2)</td>
<td>10</td>
<td>6.7 g*</td>
<td>(\pm 13.1) g</td>
<td></td>
<td></td>
<td>Canine normal</td>
</tr>
<tr>
<td>Caputo et al(^4^3)</td>
<td>8</td>
<td>8.7 g*</td>
<td>(\pm 17.1) g</td>
<td></td>
<td></td>
<td>Canine post-MI</td>
</tr>
<tr>
<td>Caputo et al(^4^3)</td>
<td>13</td>
<td>13.7 g*</td>
<td>(\pm 26.9) g</td>
<td>10.0%</td>
<td></td>
<td>Canine normal + LVH</td>
</tr>
<tr>
<td>Keller et al(^4^4)</td>
<td>10</td>
<td>3.5 g</td>
<td>(\pm 6.9) g</td>
<td>6.8 g</td>
<td>13.3%</td>
<td>Canine</td>
</tr>
<tr>
<td>Maddahi et al(^4^5)</td>
<td>8</td>
<td>4.9 g*</td>
<td>(\pm 9.6) g</td>
<td></td>
<td></td>
<td>Canine; in vivo</td>
</tr>
<tr>
<td>Florentine et al(^4^6)</td>
<td>11</td>
<td>13.1 g*</td>
<td>(\pm 25.7) g</td>
<td></td>
<td></td>
<td>Canine + feline</td>
</tr>
</tbody>
</table>

Values are compared to postmortem derived LV mass. Mean values are weighted for sample size. SDD indicates standard deviation of the difference between the 2 measurements; CI, confidence interval (1.96 \(\times\) SDD); and MI, myocardial infarction.

*SE of the estimate from regression equation.

### TABLE 2. Reproducibility of CMR-Derived LV Mass Measurements from Human Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>No.</th>
<th>Interstudy</th>
<th>Intraobserver</th>
<th>Interobserver</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bellenger et al(^4^7)</td>
<td>15</td>
<td>6.4 g (2.8%)</td>
<td>3.0 g (1.6%)</td>
<td>5.1 g (2.4%)</td>
<td>Normal subjects</td>
</tr>
<tr>
<td>Bottini et al(^2^6)</td>
<td>4</td>
<td>8.2 g</td>
<td>6.4 g (3.0%)</td>
<td>5.9 g (2.7%)</td>
<td>Heart failure</td>
</tr>
<tr>
<td>Germain et al(^4^7)</td>
<td>20</td>
<td>11.2 g (6.7%)</td>
<td>9.6 g (3.8%)</td>
<td>9.6 g (3.8%)</td>
<td>Normal subjects</td>
</tr>
<tr>
<td>Grothues et al(^4^6)</td>
<td>20</td>
<td>4.2 g (2.3%)</td>
<td>2.0 g (1.1%)</td>
<td>2.0 g (1.1%)</td>
<td>Normal subjects</td>
</tr>
<tr>
<td>Bogaert et al(^4^5)</td>
<td>12</td>
<td>4.7–6.1%</td>
<td>3.5–4.8%</td>
<td>5.5%</td>
<td>Normal subjects</td>
</tr>
<tr>
<td>Mathjeisjen et al(^4^2)</td>
<td>8</td>
<td>3.6%</td>
<td>3.6%</td>
<td>3.6%</td>
<td>MI</td>
</tr>
<tr>
<td>Yamaoka et al(^4^5)</td>
<td>10</td>
<td>5.8 g</td>
<td>17.8 g</td>
<td>17.8 g</td>
<td>Normal, LVH, and DCM</td>
</tr>
<tr>
<td>Katz et al(^4^0)</td>
<td>10</td>
<td>6.1%</td>
<td>7.2%</td>
<td>7.2%</td>
<td>Normal, LVH, and DCM</td>
</tr>
</tbody>
</table>

Values are standard deviations of the difference between successive scans (g) or % variability. Mean values are for studies with absolute values, weighted by sample size. DCM indicates dilated cardiomyopathy; MI, myocardial infarction.
TABLE 3. Comparison of Sample Sizes Needed to Detect a Statistically Significant Change in Mean LV Mass of 10 g

<table>
<thead>
<tr>
<th>Power (1-β Error)</th>
<th>CMR</th>
<th>2D Echo</th>
<th>M-Mode Echo</th>
</tr>
</thead>
<tbody>
<tr>
<td>99%</td>
<td>23</td>
<td>136</td>
<td>283</td>
</tr>
<tr>
<td>95%</td>
<td>16</td>
<td>96</td>
<td>199</td>
</tr>
<tr>
<td>90%</td>
<td>13</td>
<td>78</td>
<td>162</td>
</tr>
<tr>
<td>80%</td>
<td>10</td>
<td>58</td>
<td>121</td>
</tr>
</tbody>
</table>

These assume a 2-tailed unpaired t test with 0.05 level of significance (α-error) and refer to the sample size in each group (2 parallel treatment groups would need twice this number in total). We used the weighted values of interstudy standard deviation of the difference for M-mode echo (27.7 g),21,24–28 2D echo (19.2 g),28,30 and CMR (7.8 g).26,27,47,48

Limitations of CMR
Patient factors can sometimes limit the usefulness of the technique. Because of the enclosed nature of the CMR scanner, some people find this too claustrophobic. In practice, the incidence of this is ≈3% to 5%, though light intravenous anxiolyzation with diazepam can reduce this to 1%.53 Advances in equipment technology, with shorter and more open magnets together with reduced time in the scanner from faster imaging, will also improve conditions for these patients. The same restrictions as for any MR scanner apply for patients with cranial aneurysms clips, ocular metallic shards, and pacemakers. The need for breath-holding to remove respiratory motion artifact can present problems for some patients with severe cardiac or respiratory disease; for these patients, “navigator” sequences can be used in which free breathing is allowed and the diaphragm is continuously monitored, with imaging adjusted for the diaphragm position.54 This has the disadvantage of slightly increased imaging time, but image quality is well maintained.

Currently, the availability of CMR scanners capable of cardiac work and the skilled personnel needed to obtain and interpret the images limits the widespread clinical use of this technique, although many pharmacological studies with CMR have already been performed. This is likely to change in the near future, with nearly all new MR scanners having the required hardware and the cardiac software. Although the initial cost of the scanner is high, for research purposes the savings from the reduced number of subjects may offset this substantially. A single study takes ≈15 minutes for postprocessing with standard techniques. Although this is longer than for echo, the new generation of machines coupled with automated image processing will greatly reduce these times and will allow a fast-throughput service.

Conclusions
LVH is a potent risk factor for cardiovascular disease and is associated with significant increases in morbidity and mortality, but traditionally little has been done to specifically address this issue. This is because until recently, no reliable and reproducible technique existed to quantify LV mass. We now know that the measurement of LV mass is best accomplished with 3D techniques, and CMR has become the gold standard. 3D echo and EBCT achieve an accuracy and reproducibility close to those of CMR and are acceptable alternatives, but problems preclude their regular use. Now that good data exist in particular for the effectiveness of ACE inhibitors in reducing LV mass,59–61 and the prognostic benefits of LV mass reduction are becoming defined,62–64 coupled with a reproducible and accurate measurement technique in CMR, it is likely that more clinical and research attention will be paid to this condition. The fidelity of the CMR technique may also lead to new understanding of the precise mechanisms behind LVH,65 and why its effects on mortality are so profound, even in the absence of coronary artery disease and hypertension, although recent work implicates plaque disruption as an important issue.66

Acknowledgments
The British Heart Foundation provided funding for Dr Myerson (FS 97030). This work was also supported by the Coronary Artery Disease Research Association (CORDA) and the Wellcome Trust.

References


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Hypertension. 2002;39:750-755
doi: 10.1161/hy0302.104674

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

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