Detection of Left Ventricular Hypertrophy by M-Mode Echocardiography

Anatomic Validation, Standardization, and Comparison to Other Methods

RICHARD B. DEVEREUX

SUMMARY Because of its simplicity, widespread availability, relatively low cost, and lack of adverse effects, M-mode echocardiography has become the most widely used technique for measurement of human left ventricular mass. Necropsy comparison studies have yielded formulas for anatomically accurate estimation of left ventricular mass in patients with normally shaped ventricles using left ventricular measurements by either Penn or American Society of Echocardiography conventions, but M-mode methods are less accurate in abnormally shaped ventricles. The standard error of M-mode echocardiographic left ventricular mass measurements is approximately 40 g under difficult clinical recording conditions and 30 g or less for research studies of stable subjects. Intersstudy variability of mass estimates appeared somewhat lower, resulting in 95% confidence limits for serial change up to 58 g for individual subjects and up to 10 g for study populations of 34 patients or more. The accuracy of M-mode echocardiography for measurement of left ventricular mass is similar to that of contrast angiography but may be exceeded by newer methods with greater cost or radiation exposure, including magnetic resonance imaging, cine-computed tomography, and three-dimensional echocardiographic reconstruction. Identification of left ventricular hypertrophy needs to take into account the influence of sex and body size, the variables that most influence normal ventricular mass, with provisional criteria for recognition of hypertrophy being left ventricular mass index over 134 g/m² in men and above 110 g/m² in women. (Hypertension 9 [Suppl II]: II-19–II-26, 1987)

KEY WORDS • echocardiography • left ventricular mass • left ventricular hypertrophy

The risk of cardiovascular morbidity and mortality in patients with systemic hypertension is higher at any level of blood pressure in patients with evidence of left ventricular (LV) hypertrophy than in those without.1-4 However, this conclusion is based on studies using electrocardiographic or radiographic methods of detecting LV hypertrophy that are now known to be relatively insensitive.5-8 By the early 1970s, it was recognized that M-mode echocardiography provided direct measurements of LV chamber size and wall thickness, suggesting that it might be used to measure LV muscle mass directly.

The first echocardiographic methods introduced for measurement of LV mass were either validated indirectly by comparison with quantitative angiography,9,10 or were based on assumed geometric models of the left ventricle.11 Because M-mode echocardiography may yield inaccurate estimates of LV volumes, however, serious concern was raised about the reliability of such methods. Over the past decade extensive work has been undertaken to develop and standardize anatomically validated M-mode echocardiographic methods of measuring LV muscle mass. Determination of the usefulness of these methods depends on critical appraisal of their quantitative accuracy in measuring LV mass and the reliability of available cut-off values to separate normal from abnormal findings. In this brief review, available information will be summarized under the following headings: anatomic validation of M-mode echocardiographic methods of determining LV muscle mass, limitations of M-mode echocardiography in abnormally shaped left ventricles, quantitation of LV mass by M-mode echocardiography, comparison with other methods of measuring of LV mass, and standardization of normal limits of LV measurements.

Anatomic Validation of Left Ventricular Mass Measurement by M-Mode Echocardiography

To determine whether M-mode echocardiography could be used for accurate measurement of LV mass, we performed an initial study comparing necropsy LV weight in 34 patients to echocardiographic estimates obtained using several combinations of geometric formulas and echocardiographic measurement conventions.12 The latter included the Penn convention, which excludes the thickness of endocardial interfaces from measurements of interventricular septal (IVST) and posterior wall thickness (PWT) and includes them in the LV internal dimension (LVID; Figure 1). Highly accurate estimates of LV mass were obtained (Figure 2) by using end-diastolic Penn...
convention measurements in the following, empirically derived regression equation:

$$LV\ mass = 1.04[(IVST + LVID + PWT)^3 - LVID^3] - 13.6 \text{ g}$$

Previously published echocardiographic methods yielded less precise but still useful estimates of LV mass. These promising initial results have been confirmed in a recent study performed at Cornell, which also demonstrated a close correlation ($r = 0.92; p < 0.001$) between echocardiographic mass by the Penn method and necropsy weight.

The empirical nature of the Penn method of measuring LV mass has prompted further necropsy correlation studies to determine whether other M-mode echocardiographic measurement conventions or geometric formulas might offer improved accuracy. The results of these studies are compared in Table 1 to those obtained with the Penn method. One appealing alteration in the method would be to use the measurement convention recommended by the American Society of Echocardiography (ASE) in view of its widespread adoption for clinical and investigative use. Woythaler et al. found a reasonable relationship between echocardiographic LV mass calculated using ASE measurements in the cube function formulas ($r = 0.81, p < 0.001$) but reported that this echocardiographic method overestimated anatomic LV mass by approximately 20%. The ASE basic formula for LV mass is:

$$LV\ mass_{ASE} = 1.04[(IVSTd + LVIDd + PWT)^3 - LVIDd^3]$$

We have found similar overestimation of necropsy LV mass by the ASE-cube method and have reported a simple regression equation for correction of this error:

$$LV\ mass = 0.80 \cdot LV\ mass_{ASE} + 0.6 \text{ g}$$

An alternative geometric formula, proposed by Teichholz et al. to correct errors in echocardiographic estimation of LV volumes, has been adopted by some investigators for clinical research in hypertension. The Teichholz formula reduces LV volume estimates derived from above average M-mode echocardiographic LVID and increases volumes estimated from small internal dimensions. Application of this correction to estimates of LV cavity and total (cavity plus myocardial) volumes

$$r^2 = 0.96$$

$$s.d = 29\text{ g}$$

$$(g)$$

![Figure 2. Relationship between left ventricular mass at necropsy (LVMA; horizontal axes) and left ventricular mass determination by two M-mode echocardiographic measurements (LVME; vertical axes). A. Echocardiography consistently overestimated anatomic LVM when standard echocardiographic measurements were used. B. A close correspondence occurred between anatomic LVM and echocardiographic estimates made by the Penn method. MMT = mean myocardial thickness; other abbreviations as in Figure 1. (Reprinted from Devereux and Reichek with permission of the American Heart Association.)](http://hyper.ahajournals.org/)
was recently shown in a study from our laboratory\textsuperscript{12} to result in severe underestimation of anatomic LV mass (Table 1).

The available data establishing the anatomic accuracy of M-mode echocardiographic LV mass determination have been mostly obtained using high-resolution single-crystal instruments designed to optimize information obtained by M-mode echocardiography. The gradual replacement of such equipment by two-dimensional echocardiographs that provide lower quality M-mode echocardiograms may adversely affect the ability to obtain equally accurate quantitative data. Further research using necropsy reference standards will ascertain whether technological evolution has affected the accuracy of M-mode echocardiographic LV mass measurements.

### Limitations of M-Mode Echocardiography in Abnormally Shaped Ventricles

Since M-mode echocardiography only delineates the LV along its anteroposterior minor axis, accurate estimation of chamber and myocardial volume is possible only if the ratio between measurements along this and other axes remains within a relatively narrow normal range. Fortuitously, none of the 34 patients in our initial necropsy validation study\textsuperscript{12} exhibited severe distortion of LV geometry. Admiring patients with LV aneurysms due to coronary artery disease or other causes of altered LV geometry has undoubtedly contributed to the slightly greater error of M-mode echocardiographic LV mass estimates reported more recently by Woythaler et al.\textsuperscript{15} and by our group.\textsuperscript{13}

Direct confirmation of the effect of altered LV geometry on the accuracy of M-mode myocardial mass estimates has been provided by Reichek et al.\textsuperscript{13} Of their 21 patients, 5 had current or previously resected LV aneurysms, 7 had transmural myocardial infarctions, and 11 had right-heart dilatation and failure. M-mode echocardiography substantially overestimated anatomic LV mass (Figure 3), but a reasonable correlation ($r = 0.86$, $p < 0.001$) was preserved between echocardiographic and necropsy mass in the 18 patients with technically adequate M-mode echocardiograms.

In addition to fixed distortion of cardiac shape, functional abnormalities may cause marked alteration of LV geometry between end diastole and end systole. This may be produced both by regional LV dyssynergy and by abnormal overall heart motion, which causes the M-mode echo beam to lose its normal orientation along the left ventricle’s minor axis during part of the cardiac cycle. These abnormalities would cause LV muscle mass calculated from end-diastolic and end-systolic echo dimensions in the same patient to differ significantly. As shown in Figure 4, end-diastolic and end-systolic LV mass estimates were quite close in 37 patients with symmetric LV wall motion studied in our laboratory, whereas greater differences were observed in five patients with paradoxical septal motion or swinging of the heart within large pericardial effusions.

### Quantitation of Left Ventricular Mass by M-Mode Echocardiography

Although highly significant correlations exist between echocardiographic and necropsy measurements of LV mass, all studies demonstrate a degree of scatter to the relationship (Figure 2). This causes the sensitivity and specificity of echocardiography for detection of anatomic LV hypertrophy to fall short of the desired 100%. For instance, in the combined results of two studies of patients who predominantly had normally shaped left ventricles,\textsuperscript{12–13} measurements of LV mass by the Penn method exhibited 97% sensitivity (31 of 32) and 89% specificity (48 of 54) using 215 g as the partition value to separate normal from increased LV mass by both echocardiography and necropsy measurements.

More direct insight into the accuracy of M-mode echocardiography for quantitating LV muscle mass is provided by the standard deviation of echocardiographic measurements about the line of its regression on necropsy LV mass (i.e., the line of identity for regression-corrected anatomically validated methods). As shown in Table 1, the standard deviation of echocardiographic LV mass by Penn and ASE methods has ranged from 29 g in patients with normal LV geometry to 59 g in patients with severely abnormal LV shape. A relatively low figure — 30 g or perhaps lower — is probably applicable to hypertension research because patients with uncomplicated essential hypertension have symmetric LV geometry and studies are performed under optimal circumstances. Similarly the standard deviation of repeat measurements of LV muscle mass by M-mode echocardiography has been shown to be under 30 g.\textsuperscript{19} With this error of the method, 95% confidence limits of mean LV mass in groups of patients are acceptably narrow (Table 2): ±20 g for 10 patients and ±10 g for 34 patients. Available studies are in conflict as to whether two-dimensional echocardiographic techniques improve the accuracy with which LV mass is measured.\textsuperscript{15, 18, 20} Reduction of the standard deviation to 20 g or possibly 10 g (as may be attainable by three-dimensional echocardiographic reconstruction or fast computed tomographic methods) would narrow the 95% confidence limits to less than 10 g for study populations of 18 or more patients. Thus, the benefit of these more complex and expensive methods would be slight for large-scale clinical or epidemiologic studies. To obtain adequate accuracy in studies of small numbers of patients, however, methods more precise than M-mode echocardiography should be used if the additional expense or radiation expo-

### Table 1: Anatomic Validation of Left Ventricular Mass Determination by M-Mode Echocardiography

<table>
<thead>
<tr>
<th>Reference</th>
<th>$n$</th>
<th>Anatomic LV mass (g)</th>
<th>Echocardiographic method</th>
<th>Standard deviation (%)</th>
<th>Echocardiographic LV mass (%)</th>
<th>LV geometry</th>
</tr>
</thead>
<tbody>
<tr>
<td>Devereux and Reichek\textsuperscript{12}</td>
<td>34</td>
<td>105–505</td>
<td>Penn</td>
<td>0.96</td>
<td>29</td>
<td>1.00</td>
</tr>
<tr>
<td>Woythaler et al.\textsuperscript{15}</td>
<td>50</td>
<td>109–437</td>
<td>ASE</td>
<td>0.81</td>
<td>NA</td>
<td>1.18*</td>
</tr>
<tr>
<td>Devereux et al.\textsuperscript{13}</td>
<td>52</td>
<td>96–625</td>
<td>Penn</td>
<td>0.92</td>
<td>43</td>
<td>1.06</td>
</tr>
<tr>
<td>Devereux et al.\textsuperscript{13}</td>
<td>52</td>
<td>96–625</td>
<td>ASE</td>
<td>0.90</td>
<td>47</td>
<td>1.22*</td>
</tr>
<tr>
<td>Reichek et al.\textsuperscript{18}</td>
<td>18</td>
<td>77–454</td>
<td>Penn</td>
<td>0.86</td>
<td>60</td>
<td>0.70*</td>
</tr>
</tbody>
</table>

LV = left ventricular; ASE = American Society of Echocardiography; NA = not applicable.

*p < 0.001, echocardiographic vs necropsy LV mass.
sure can be justified. Three-dimensional echocardiographic reconstruction has particularly great promise for this purpose, as do cine-computed tomography and nuclear magnetic resonance imaging, if the impressive results obtained in meticulously controlled animal experiments can be replicated under the more arduous circumstances of human necropsy comparison studies.

Comparison with Other Methods of Detecting Left Ventricular Hypertrophy

Normal limits of LV muscle mass were originally established pathologically. LV mass is less than 175 g in normal adults of normal size and less than 220 g even in normal individuals of above average size and physical activity. All methods of detecting LV hypertrophy that are currently in clinical use have been validated directly or indirectly with the reference standard of necropsy measurements. Table 3 compares the quantitative and diagnostic accuracy of echocardiography and other available methods in studies using autopsy or angiographic determination of LV muscle mass as the reference standard.

Quantitative angiography provides radiographic measurements of LV wall thickness and chamber volume. Calculating LV mass from biplane angiographic measurements of wall thickness and chamber volume, Kennedy et al. found a close correlation with autopsy LV weight in 28 patients (Table 3) but obtained seriously inaccurate measurements in two additional patients with right ventricular hypertrophy. Because single-plane angiograms give chamber volume estimates similar to those of biplane angiography, the former technique is often used to measure LV mass although no study has been done to validate this approach. Similarly, necropsy comparison data are not yet available to determine the accuracy of digital subtraction angiography for detection of LV hypertrophy.

Chest x-rays are commonly used for evaluation of LV dilatation and hypertrophy. Since the size and shape of the heart reflects the sum of intracavitary blood in all four chambers, myocardium and pericardium, however, this method is relatively inaccurate. The cardiothoracic ratio correctly predicted the presence or absence of LV hypertrophy in 70% of patients in the series by Glover and co-workers, but Chikos et al. found it to
be within the normal range in 53% of patients with concentric LV hypertrophy and in 28% of those with eccentric LV hypertrophy. More complicated methods of analysis improve detection of LV hypertrophy, but correlations between total heart volume and LV mass were only 0.66 and 0.53, respectively, in these series.5,27

The electrocardiogram remains the most commonly used means of detecting LV hypertrophy, but conventional electrocardiographic (ECG) and vectorcardiographic methods reach a limit of about 60% sensitivity when specificity approaches 95%.5-7, 28-29 The reason for such limited performance is clear (Table 3): correlation is relatively poor (r = 0.40–0.61) between conventional ECG or vectorcardiographic criteria and LV mass regardless of whether the latter is determined angiographically28,29 or echocardiographically.5,7 This results in LV mass estimates with standard deviations in excess of 100 g, three times that of either angiographic or echocardiographic methods.

Table 2. Effect of Method Accuracy and Sample Size on 95% Confidence Limits of Left Ventricular Mass Estimates

<table>
<thead>
<tr>
<th>Technique</th>
<th>Reference</th>
<th>n</th>
<th>Accuracy of quantitation</th>
<th>Accuracy of diagnosis (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Echocardiography (Penn)</td>
<td>Devereux and Reichek12</td>
<td>34</td>
<td>Autopsy</td>
<td>r = 0.96 (29)</td>
</tr>
<tr>
<td>Angiocardiography (biplane)</td>
<td>Kennedy et al.26</td>
<td>28</td>
<td>Autopsy</td>
<td>0.97 (32)</td>
</tr>
<tr>
<td>Chest x-ray (CT ratio)</td>
<td>Glover et al.27</td>
<td>205</td>
<td>Angiography</td>
<td>0.38 (—)</td>
</tr>
<tr>
<td>Chest x-ray (heart volume)</td>
<td>Glover et al.27</td>
<td>205</td>
<td>Angiography</td>
<td>0.53 (—)</td>
</tr>
<tr>
<td>126-lead ECG</td>
<td>Holt et al.28</td>
<td>71</td>
<td>Angiography</td>
<td>0.92 (49)</td>
</tr>
<tr>
<td>ECG S60 + RV5-S point score</td>
<td>Holt et al.28</td>
<td>113</td>
<td>Angiography</td>
<td>0.85 (64)</td>
</tr>
<tr>
<td>Vectorcardiogram</td>
<td>Romhilt et al.29</td>
<td>93</td>
<td>Angiography</td>
<td>0.59 (105)</td>
</tr>
<tr>
<td>Left ventricular</td>
<td>Conn and Cole32</td>
<td>50</td>
<td>Angiography</td>
<td>0.58 (106)</td>
</tr>
</tbody>
</table>

CT = computed tomography; ECG = electrocardiogram.

Evaluation of a patient with suspected heart disease begins at bedside with the history and physical examination. Many clinicians are convinced that evaluation of the location, size, and character of the LV impulse provides considerable information about the presence of LV hypertrophy. Conn and Cole32 have supported this view in a study of 50 patients whose LV volume and mass were measured by quantitative angiography. Among patients with a holosystolic LV impulse, 88% had LV hypertrophy whereas 78% of those with an apex impulse confined to early systole had a normal LV mass. In 29 of 36 patients (81%) in whom the LV impulse was limited to one intercostal space, LV volume was normal, but LV mass was increased in 11 of 14 (79%) in whom the LV impulse could be palpated in two or more intercostal spaces.

Standardization of Normal Limits of Left Ventricular Anatomic Measurements

Detection of abnormal LV size and muscle mass depends on correct definition of normal limits. This in turn requires recognizing which of several possible factors (including age, sex, and body habitus) influence LV dimensions sufficiently to be taken into account in defining normal limits for clinical use. Furthermore, it must be determined which measurements of LV anatomy most reliably separate individuals with hypertrophy from those with normal LV mass. In this section we will review those studies in which large numbers of normal subjects have undergone echocardiography to answer these questions.5,24,28-33

The initial study of a large population of apparently normal subjects (n = 136, ranging in age from 20 to 97 years) was undertaken by Gardin et al.24 Based on a previous study in
children, they used body surface area (BSA) as their index of body size and found that LV wall thickness and muscle mass were substantially greater in older than in younger adults. Significant but smaller differences were also found between men and women in LV wall thickness and mass indexed for BSA with values 6 to 7% higher in men. The true sex difference probably was somewhat understated in this study, however, because men predominated among subjects aged 51 years or more (66%) whereas the sex distribution was equal in younger subjects. In this study, as in a subsequent reanalysis of the same echocardiograms according to the mathematical optimization of the ASE, statistical confidence limits of normal echocardiographic measurements were expressed by regression equations, its innate complexity has precluded routine clinical use.

More straightforward normal limits of LV anatomic measurements were provided subsequently by Valdez et al. They studied a random sample of Stanford University employees, comprising 106 men and 96 women ranging in age from 26 to 64 years. Significant differences were found between men and women for most primary anatomic measurements (Table 4), but these were abolished by indexing for BSA. Since LV mass is proportional to the cube of M-mode echo measurements, however, these data indicate that a sex difference in LV mass would remain after indexing by BSA. In contrast to the reports of Gardin et al. and Henry et al., neither our group nor Valdez et al. found a relationship between any LV measurement and subject age.

To improve standardization of echocardiographic LV anatomic measurements, we recently related echographic LV dimensions and mass (determined by the Penn method) to body size indices, sex, age, and blood pressure in 225 apparently normal subjects from two independent populations. All measurements of LV chamber size, wall thickness, and mass differed between men and women (Table 5). LV mass was more closely related in men and women from each population to BSA than to height, weight, or other indices of body habitus. Indexing by BSA eliminated sex differences in wall thicknesses and internal dimensions, but a significant difference in LV mass index between men and women persisted (89 ± 21 vs 69 ± 19 g/m², p < 0.001). The 97th percentile of LV mass index was virtually identical in both groups of men (136 and 132 g/m²) and women (112 and 109 g/m²; Figure 5). The reproducibility of these normal limits in two independent populations suggests that cut-off values of 134 g/m² in men and 110 g/m² in women represent suitable criteria for recognition of LV hypertrophy.

Information was also obtained from this study about additional factors contributing to the variability in LV muscle mass among normal subjects. Thus, a striking difference in lean body mass was found between men and women (58 ± 15 vs 40 ± 13 kg, p < 0.001). Use of lean body mass rather than BSA as the means of indexing LV muscle mass abolished the previously observed sex difference in LV mass. Furthermore, weak but statistically significant relationships were observed between both systolic and diastolic blood pressure and LV mass indexed for lean body mass. While it is not practical to incorporate either lean body mass or blood pressure into clinically applicable normal limits, their use might improve identification of LV hypertrophy for selected research purposes.

A recent analysis of echocardiographic measurements in a large number of normal subjects enrolled in the Framingham Heart Study is mostly, but not entirely, in accord with the results obtained by Valdez et al. and by our group. Savage et al. found that LV mass was strongly related to body size in both sexes and that normal limits differed importantly between men and women even after adjustment for body size. Similarly, LV mass was not related to age among men. Among women in the Framingham Study, however, a progressive rise in LV mass adjusted for body size was observed with increasing age. Among men and middle-aged to older women, the upper 95th percentile limits obtained from the regression equations developed by Savage and colleagues are similar to the upper normal limits we have proposed (see above), whereas the Framingham

**Table 5. Left Ventricular Anatomic Measurements in Normal Population**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Women (n=119)</th>
<th>Men (n=106)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV mass (g)</td>
<td>121 ± 40 (201)</td>
<td>176 ± 45 (366)</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>LV mass index (g/m²)</td>
<td>69 ± 19 (109)</td>
<td>89 ± 21 (134)</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>Cross-sectional area (cm²)</td>
<td>13.6 ± 3.7 (19.0)</td>
<td>17.4 ± 3.4 (24.3)</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>Cross-sectional area index (cm²/m²)</td>
<td>8.3 ± 1.5 (11.2)</td>
<td>9.1 ± 1.6 (12.3)</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>Interventricular septal thickness (cm)</td>
<td>0.9 ± 0.2 (1.2)</td>
<td>1.0 ± 0.2 (1.3)</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>Posterior wall thickness (cm)</td>
<td>0.8 ± 0.1 (1.1)</td>
<td>0.9 ± 0.2 (1.2)</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>Relative wall thickness†</td>
<td>0.34 ± 0.08 (0.49)</td>
<td>0.34 ± 0.08 (0.49)</td>
<td>NS</td>
</tr>
<tr>
<td>Left ventricular internal dimension (cm)</td>
<td>4.6 ± 0.4 (5.4)</td>
<td>5.0 ± 0.5 (5.9)</td>
<td>p &lt; 0.001</td>
</tr>
</tbody>
</table>

All measurements are means ± SD; mean plus two standard deviations is given in parentheses.

*Standard significance of differences assessed by Student's t test.

†Relative wall thickness = 2 X (posterior wall thickness)/(left ventricular internal dimension).

Adapted from Devereux et al. 26
normal limits are appreciably lower in young women. This resulted in low apparent specificity of the Framingham criteria for echocardiographic detection of LV hypertrophy when applied prospectively to an expanded sample (n = 160) of our normotensive employed population. Further study will be needed to resolve this discrepancy between results from Cornell and Framingham, which have otherwise been in close agreement. As long-term follow-up data become available in prospectively followed cohorts, it will become possible to determine whether individuals whose LV mass falls in the upper part of currently defined normal ranges actually have clinically undetected heart disease. This finding is suggested by our recent observation that men with uncomplicated mild essential hypertension whose LV mass index exceeded 125 g/m² experienced an increased rate of morbid events during the 5-year follow-up. If this finding is replicated among clinically normal subjects, it would suggest a need to revise downward the upper limit of truly normal LV mass.

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