M-Mode Echocardiography Overestimates Left Ventricular Mass in Patients with Normal Left Ventricular Shape: A Comparative Study Using Three-Dimensional Echocardiography

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Aims: We sought to evaluate whether left ventricular (LV) mass (M) determined by M-mode echocardiography is overestimated compared with LVM calculated by three-dimensional (3D) echocardiography (E) in patients with normal LV shape.

Methods and Results: A total of 112 studies in 56 patients (60 ± 13 years) with hypertension (n = 25) or aortic stenosis (n = 31) and 30 control subjects (57 ± 14 years) evaluated for cardiac sources of embolism were analyzed. LVM by M-mode and 3DE was highly correlated (r = 0.85; p < 0.001). However, there were broad limits of agreement (−255 to 58 to 110 g) demonstrating large variability between the methods. M-mode overestimated 3DE LVM by a mean of 15 ± 24% (p < 0.001) with overestimation in controls and the different patient groups. Variability was unrelated to increasing quartiles of LVM values. Using technique-specific partition values for normal LVM, the agreement between M-mode and 3DE for the detection of LV hypertrophy was 83% (Kappa = 0.59; p < 0.001).

Conclusion: Although M-mode and 3DE correlate well for the calculation of LVM, there is a systematic difference between the two techniques leading to overestimation of LVM by the 1D technique. Thus, previously published cutoff values for normal LVM derived from M-mode may not apply for 3DE. However, the use of technique-specific partition values allows stratification of patients for the presence of LV hypertrophy with reasonable agreement.

Key Words: left ventricular mass; three-dimensional echocardiography; M-mode.

Introduction

Increased left ventricular (LV) mass (M) has been identified as an important predictor of cardiovascular morbidity and mortality independent of traditional risk factors[1–3]. Thus, determination of LVM is clinically important for risk stratification and identification of patients needing increased medical attention. Despite its well-known limitations, M-mode echocardiography has been used extensively for the estimation of LVM. The method has been validated anatomically in studies with necropsy human hearts including a selected patient population with predominantly normal LV geometry[4–6]. Using three-dimensional (3D) echocardiography (E) and magnetic resonance imaging (MRI) as reference methods, M-mode has been reported to overestimate LVM in patients with more severe heart disease, such as patients with heart failure[7], heart transplant recipients[8] as well as patients with hypertensive heart disease[9–11]. However, these studies were limited by a small number of subjects and by the lack of a control group. Therefore, it is not well established whether differences between M-mode and the 3D imaging techniques are primarily related to cardiac deformation or whether it represents a systematic bias between the modalities. This is an important issue because if M-mode systematically yields larger
LVM values compared with 3D imaging techniques in patients with normal LV shape, the previously published partition values for normal LVM derived from M-mode may not apply for the 3D imaging modalities.

3D echocardiography allows accurate quantitation of LVM and has shown excellent agreement with necropsy mass [7,12] as well as with MRI in patients with normal and diseased hearts [13-15]. Thus, the aims of the study were to (1) compare M-mode and 3DE for the calculation of LVM in patients with normal LV shape; (2) determine whether M-mode LVM systematically deviates from 3DE LVM in these patients comparing results of control subjects with those of patients with LV hypertrophy; (3) evaluate the value of M-mode for the stratification of patients for the presence of LV hypertrophy compared with 3DE.

**Methods**

**Patients**

The study group included 86 subjects (mean age 60 ± 13 years, range 22–83; 44 females). Patients with previous myocardial infarction, LV aneurysm, severe dilatation of the left ventricle or asymmetric distribution of LVM were excluded from the study. Thirty patients (mean age 57 ± 14 years, range 22–73 years; nine females) with normal blood pressure and without history of cardiac disease served as normal control group. These patients were evaluated for the presence of cardiac sources of embolism after a suspected cerebral ischemic embolic event. Echocardiography revealed normal cardiac dimensions, geometry and normal systolic function. The patient group included 25 patients who underwent echocardiography for evaluation of hypertensive heart disease. All of these patients received antihypertensive treatment. Additionally, 31 patients underwent echocardiography for pure severe aortic stenosis. Of these, 26 patients received aortic valve replacement for clinical reasons and were reevaluated 1 year after valve surgery. Thus, a total of 112 comparative studies were available for final analysis. A part of the patient population has been characterized previously [16]. 3DE and M-mode were performed immediately after each other on the same day. One hundred and six studies (95%) revealed normal LV function as assessed semi-quantitatively by an experienced observer (HPK) during the echocardiographic examination. The remaining six patients had mildly reduced systolic function. Coronary artery disease was excluded in these patients by invasive angiography. All but two patients were in stable sinus rhythm and each patient gave informed consent prior to inclusion in the study in accordance with the requirements of the local Ethics Committee.

**Echocardiographic Data Acquisition**

Transthoracic and transesophageal echocardiography were performed with standard equipment (Sonos 5500, Philips Medical Ultrasound, Andover, MA). A detailed description of the 3D echocardiographic system and the technique of data acquisition have been published previously [13,17,18]. In brief, transesophageal 3DE studies were performed using an unmodified, commercially available multiplane probe (Omniplane II, 64 elements) and the implemented 3D acquisition software. All patients received topical anesthesia of the pharynx and were mildly sedated with 2.0–3.0 mg of midazolam during the study. 3D data acquisition was triggered by electrocardiographic and respiratory gating. A complete scan consisted of 60 sequential cine loops acquired at 3° intervals from 0 to 180. The cine loops were digitally stored on optical disc.

**Data Analysis**

Accuracy and reliability of the technique for assessment of LVM in patients have been reported previously in a validation study comparing mass determined by 3DE with that determined by MRI [13]. A detailed description of the algorithm and the measurement procedure has been published elsewhere [19]. Data analysis was performed off-line in the 3D data set after reformattting the raw data to obtain a voxel-based 3D data set using commercially available software (EchoView 4.2, TomTec, Unterschleißheim, Germany). Myocardial volumes obtained by 3DE analysis were multiplied with 1.05 g/ml to yield mass. All measurements were repeated once and the average value of two measurements was taken for data analysis.

**M-mode Echocardiography**

M-mode was performed with the patients positioned in the left lateral decubitus position using a standard transthoracic transducer. To limit variability, data acquisition and analysis were performed by the same investigator. From a parasternal long axis view, correct alignment of the cursor was performed under 2D guidance. Meticulous care was taken to strictly intersect the septum and posterior wall perpendicularly to the endocardium. Image acquisition was performed in end-expiratory breath hold to obtain high-quality tracings demonstrating continuous recordings of the right and left-hand side of the interventricular septum and the endocardial and epicardial surface of the posterior wall in at least three to five consecutive beats at a speed of 50 mm/s and stored on video tape. Gain settings were adjusted individually in each patient in such a way that borders represented thin rather than thick lines. If the 2D-guided M-mode
beam could not be optimally oriented due to an oblique orientation of the long-axis view, the 2D short-axis view was used. In cases where a perpendicular orientation of the M-mode cursor could not be achieved, measurements were performed in the 2D image. Measurements of the interventricular septum thickness, posterior wall thickness and LV internal diameter were performed according to the recommendations of the ASE at the beginning of the QRS complex at end-diastole. LVM was calculated according to the cube formula using the correction described by Devereux et al\textsuperscript{[5]}.

\[
LVM = 0.8[\text{ASE cube LVM}] - 0.6
\]

Additionally, in 45 patients measurements were also performed according to the PENN convention which includes endocardial boundaries of septum and posterior wall into the measurements of the LV internal diameter at the top of the R-wave. LVM was calculated according to the formula published by Devereux and Reichek\textsuperscript{[4]}.

\[
LVM = 1.04[(\text{SWT} + \text{LVID} + \text{PWT})^3 - (\text{LVID})^3] - 13.6
\]

LVM measurements from three consecutive beats for patients with sinus rhythm and five consecutive beats for patients with atrial fibrillation were averaged to give final LVM values.

**Statistical Analysis**

LVM assessed by M-mode and 3DE was analyzed using linear regression analysis. Differences between means were compared using the paired \( t \)-test. Differences between individual values were assessed according to the method described by Bland and Altman\textsuperscript{[20]}. Coefficients of variability were calculated to assess variability between the methods for increasing quartiles of LVM. The unpaired \( t \)-test was used to compare differences between the different patient groups and normal controls. Kappa statistic was used to assess the agreement between the methods to identify LV hypertrophy.

**Results**

Results of LVM assessed by 3DE and M-mode for the whole study population as well as for controls and patients are summarized in Table 1. For the whole study population, mean LVM was 193 ± 65 g with 3DE (range 68–412 g) and 219 ± 81 g (range 95–553 g) with M-mode (\( p < 0.001 \) vs. 3DE). LVM values assessed with both techniques were highly correlated (\( r = 0.85; \ p < 0.001; \) Fig. 1). The linear relationship between LVM estimates by 3DE and M-mode can be described by the equation \( LVM_{3DE} = 1.06 \times (LVM_{3DE}) + 15.1 \) g (SEE 42 g). Bland–Altman analysis revealed a systematic bias with a mean difference of 26 ± 42 g (\( p < 0.001 \) vs. 0) corresponding to a net overestimation of 15 ± 24% by M-mode (Fig. 2). Based on the variability among differences between the two techniques, the 95% confidence limits of agreement between 3DE and M-mode ranged from −58 to 110 g. Variability between the methods was unrelated to increasing quartiles of LVM as demonstrated by the coefficients of variability (81, 54, 74 and 52, for the first to fourth quartile of LVM, respectively). There was a tendency of increasing overestimation with increasing LV weight (\( r = 0.38; \ p < 0.001 \)). LVM assessed by M-mode and 3DE differed significantly between controls and patients (Table 1). However, the mean relative differences between M-mode and 3DE were not different between controls and the different patient groups. Additionally, broad limits of agreement were detected for both controls and patients (Table 1).

A significant remodeling of the left ventricle was observed for the 26 patients who underwent aortic valve surgery for aortic stenosis with LVM regression paralleled by a decrease in relative wall thickness and a decrease in the volume to mass ratio (Table 1). However, the remodeling process was incomplete 1 year after valve surgery when compared with the group of control subjects.

**Comparison of LVM Calculated by the PENN Formula with 3DE**

PENN LVM was highly correlated to 3DE LVM (\( r = 0.93; \ p < 0.001 \)). The linear relationship between LVM estimates by 3DE and M-mode can be described by the equation \( LVM_{\text{M-mode}} = LVM_{\text{PENN}} = 1.35 \times (LVM_{3DE}) - 29.3 \) g (SEE 35 g). Analysis of differences showed a similar mean difference (30 ± 42 g or 15%; \( p < 0.001 \)) and a similar width of the 95% confidence interval of 164 g (range −52 to 112 g) compared with ASE measurements.

**Agreement Between 3DE and M-mode for the Detection of LV Hypertrophy**

Mean LVM assessed by 3DE in the group of controls was 132 ± 34 g. The upper limit of normal mass was set to mean LVM plus 2 standard deviations resulting in a cutoff value for normal LVM of 200 g. Using this partition value, 76 studies (68%) revealed normal LVM whereas 36 studies (32%) demonstrated LV hypertrophy by 3DE. For M-mode, an upper limit of normal LVM for both men and women (254 g) was applied that had been previously calculated from a cohort of 160 normotensive subjects\textsuperscript{[21]}. Using this cutoff value, 83 studies (74%) revealed normal mass values whereas 29 studies (26%) demonstrated LV
hypertrophy by M-mode. Agreement between 3DE and M-mode for the presence or absence of LV hypertrophy was 83% (93/112 studies; Kappa = 0.59; p < 0.001). Nineteen studies (17%) were scored differently by M-mode with presence of hypertrophy in six patients scored normal by 3DE and absence of hypertrophy in 13 patients scored hypertrophied by 3DE (Table 2).

## Discussion

The results of this study demonstrate that LVM calculated by M-mode systematically deviates from LVM determined by 3DE with a net overestimation of 15% by the 1D technique. This systematic difference was not only present in the group of patients with hypertension and aortic stenosis but was also detected in the control group. Variability between the two methods was unrelated to increasing quartiles of LVM, which supports the hypothesis of a systematic bias between the two imaging techniques. Large limits of agreement were demonstrated indicating that M-mode and 3DE cannot be considered as interchangeable imaging modalities for the determination of LVM in these patients. When using PENN convention measurements, a similar amount of difference and variability was detected showing that there is no advantage of using this measurement convention compared with ASE measurement standards. Although both techniques markedly differed in the calculation of absolute mass values, M-mode and 3DE agreed reasonably well for the detection of LV hypertrophy when technique-specific partition values for normal LVM were used.

### Table 1. Results of LVM and wall thickness measurements.

<table>
<thead>
<tr>
<th></th>
<th>All studies (n = 112)</th>
<th>Controls (n = 30)</th>
<th>Hypertensives (n = 25)</th>
<th>Aortic stenosis preop. (n = 31)</th>
<th>Aortic stenosis postop. (n = 26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3DE-LVM (g)</td>
<td>193 ± 65</td>
<td>132 ± 34</td>
<td>216 ± 61*</td>
<td>242 ± 60*</td>
<td>183 ± 39*</td>
</tr>
<tr>
<td>MM-LVM (g)</td>
<td>219 ± 81</td>
<td>151 ± 31</td>
<td>264 ± 84*</td>
<td>266 ± 79*</td>
<td>198 ± 51*</td>
</tr>
<tr>
<td>Diff-LVM (g)</td>
<td>26 ± 42</td>
<td>19 ± 27</td>
<td>48 ± 37*</td>
<td>24 ± 53</td>
<td>16 ± 43</td>
</tr>
<tr>
<td>%Diff-LVM</td>
<td>15 ± 24</td>
<td>19 ± 31</td>
<td>22 ± 14</td>
<td>10 ± 22</td>
<td>10 ± 24</td>
</tr>
<tr>
<td>Limits of agreement (g)</td>
<td>–58 to +110</td>
<td>–35 to +73</td>
<td>–26 to +122</td>
<td>–82 to +130</td>
<td>–70 to +102</td>
</tr>
<tr>
<td>SWT (cm)</td>
<td>1.3 ± 0.3</td>
<td>1.0 ± 0.1</td>
<td>1.5 ± 0.3*</td>
<td>1.5 ± 0.3*</td>
<td>1.3 ± 0.2*</td>
</tr>
<tr>
<td>LVID (cm)</td>
<td>4.7 ± 0.6</td>
<td>4.8 ± 0.4</td>
<td>4.8 ± 0.6</td>
<td>4.6 ± 0.6*</td>
<td>4.7 ± 0.7</td>
</tr>
<tr>
<td>PWT (cm)</td>
<td>1.1 ± 0.3</td>
<td>0.8 ± 1.3</td>
<td>1.2 ± 0.2*</td>
<td>1.3 ± 0.2*</td>
<td>1.1 ± 0.2*</td>
</tr>
<tr>
<td>LVM/EDV (g/ml)</td>
<td>2.3 ± 0.9</td>
<td>1.2 ± 0.2</td>
<td>2.1 ± 0.8*</td>
<td>2.7 ± 0.5*</td>
<td>2.3 ± 0.5*</td>
</tr>
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</table>
| RWT                  | 0.48 ± 0.14           | 0.33 ± 0.06      | 0.51 ± 0.11*           | 0.60 ± 0.15*                  | 0.48 ± 0.1*                   

*p < 0.05 versus controls; *p < 0.001 versus controls; †p < 0.05 versus aortic stenosis preop.

3DE, three-dimensional echocardiography; LVM, left ventricular mass; MM, M-mode echocardiography; Diff-LVM, difference in LVM between MM and 3DE; %Diff-LVM, percentage difference in LVM between MM and 3DE; SWT, septal wall thickness; LVID, left ventricular internal diameter; PWT, posterior wall thickness; RWT, relative wall thickness; preop./postop., pre and postaortic valve surgery.

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**Figure 1.** Linear regression analysis for LVM calculated by M-mode using ASE measurement standards (y-axis) and 3DE (x-axis).

**Figure 2.** Bland–Altman analysis of individual differences between M-mode and 3DE plotted against their mean. A significant bias with overestimation of mean LVM (dotted line) and broad limits of agreement (bold solid lines) can be appreciated.
Table 2. Agreement between M-mode and 3DE for detection of LV hypertrophy.

<table>
<thead>
<tr>
<th></th>
<th>M-mode</th>
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<tbody>
<tr>
<td></td>
<td>≤254g</td>
<td>&gt;254g</td>
<td></td>
</tr>
<tr>
<td>3DE</td>
<td>70</td>
<td>6</td>
<td>76</td>
</tr>
<tr>
<td></td>
<td>13</td>
<td>23</td>
<td>36</td>
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<tr>
<td></td>
<td>83</td>
<td>29</td>
<td>112</td>
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*p = 0.167 by McNemar’s test.

Potential Mechanisms for Increased Variability and Overestimation

False geometric assumptions about the shape of the left ventricle and image plane positioning errors are believed to be the most important factors for the variability between M-mode and 3D imaging techniques for LVM calculation, especially in patients with abnormal LV geometry. In the present study, patients with distortion of LV shape such as previous infarction, aneurysms, severe dilatation or asymmetric hypertrophy were excluded and nearly all studies (95%) revealed normal systolic LV function. Therefore, these ventricles were supposed to fulfill the geometrical assumptions of the 1D algorithm. The large variability between the techniques observed for both controls and patients with LV hypertrophy, may partly reflect differences between the assumed LV geometry of the model and the individual LV shape of the patients as well as errors associated with image plane positioning. A potential mechanism for the overestimation observed by M-mode may be explained by the geometrical assumption underlying the M-mode formula, which assumes an even distribution of mass based on an even distribution of wall thickness throughout the left ventricle. However, it has been shown by anatomic measurements that there is a gradual decline in wall thickness from base to apex of the left ventricle. Using 3DE we have previously shown that wall thickness decreased from base to apex not only in subjects with normal hearts but also in patients with hypertensive LV hypertrophy and hypertrophic cardiomypathy. We explicitly exclude the possibility of significant underestimation of LVM by 3DE since we have previously validated our method using MRI as reference demonstrating no bias between the two techniques. Additionally, LVM values in the control group closely agreed with recently published values in normal subjects calculated by MRI. Overestimation observed by M-mode may be explained by the geometrical assumption underlying the M-mode formula, which assumes an even distribution of mass based on an even distribution of wall thickness throughout the left ventricle. However, it has been shown by anatomic measurements that there is a gradual decline in wall thickness from base to apex of the left ventricle. Using 3DE we have previously shown that wall thickness decreased from base to apex not only in subjects with normal hearts but also in patients with hypertensive LV hypertrophy and hypertrophic cardiomypathy. We explicitly exclude the possibility of significant underestimation of LVM by 3DE since we have previously validated our method using MRI as reference demonstrating no bias between the two techniques. Additionally, LVM values in the control group closely agreed with recently published values in normal subjects calculated by MRI. 

Detection of LV Hypertrophy

Risk stratification of patients with hypertensive heart disease is of clinical importance to identify subjects with LV hypertrophy needing increased medical attention. Despite the observed differences between 3DE and M-mode for calculation of absolute LVM values, the latter technique has been reported to allow accurate stratification of patients for the presence of LV hypertrophy. Detection of LV hypertrophy is dependent on the definition of an appropriate cutoff value separating hypertrophied ventricles from normal hearts, which differs between the methods investigated. For 3DE, the cutoff value of 200 g calculated from the group of predominantly male control subjects closely agreed with recently published data in normal male subjects from the Framingham population (201.4 g) and with other previously published data of normal subjects calculated by MRI. For M-mode we used a previously published cutoff value for normal LVM for both men and women derived from a cohort of 160 normotensive subjects. Using this partition value agreement between M-mode and 3DE for the detection of LV hypertrophy was 83%. If partition values were calculated separately for men (n = 21) and women (n = 9) using 3DE and compared with M-mode specific partition values for men (259 g) and women (166 g) derived from the Framingham cohort agreement was found in 87% (Kappa = 0.70) for men and 78% (Kappa = 0.52) for women. These results demonstrate that although M-mode and 3DE show increased variability for the calculation of absolute LVM values, the methods agree reasonably well for stratification of patients for the presence of LV hypertrophy when using technique-specific partition values.

Limitations

We used the transesophageal approach for 3D data acquisition and reconstruction because of improved image quality. However, due to the semi-invasive nature and procedure-related discomfort, the method is not suited for clinical routine and will only exceptionally be indicated for calculation of LVM. Moreover, acquisition, processing and analysis of 3D data is time-consuming compared with M-mode, although rapid quantification of 3D data sets has
recently been reported. The introduction of high-resolution, real-time transthoracic 3DE may potentially overcome the limitations of transesophageal 3DE and become a valuable alternative for rapid and accurate quantification of the left ventricle in the future.

Although all control subjects showed normal cardiac dimensions and function by echocardiography these patients may not represent a real control group being evaluated for possible embolic sources of emboli after a suspected cerebrovascular event. Moreover, the predominance of male subjects in the control group precluded reliable assessment of sex-related partition values especially for the group of females. There was no independent reference standard for LVM calculation such as MRI, which is considered as gold standard for LVM determination. However, based on the good image quality of the transesophageal 3DE data sets and our previous validation study we do not expect significant differences between the two techniques. Yet, confirmation of the findings of this study using MRI would be desirable.

Conclusions

Although M-mode and 3DE correlate well for the calculation of LVM, there is a systematic difference between the two techniques leading to overestimation of LVM by the 1D technique. Thus, the previously published cutoff values for upper limit of normal LVM derived from M-mode may not apply for 3DE. However, the use of technique-specific partition values for M-mode and 3DE allows stratification of patients for the presence of LV hypertrophy with reasonable agreement.

References

[23] Frielingsdorf J, Franke A, Kühl HP et al. Evaluation of regional systolic function in hypertrophic cardiomyopathy and


