Secondary Harmonic Imaging Overestimates Left Ventricular Mass Compared to Fundamental Echocardiography

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**Aims:** The significance of left ventricular hypertrophy in hypertension is well documented, being an independent risk factor for cardiovascular morbidity and mortality. Normal values for left ventricular mass and partition values for left ventricular hypertrophy come from measurements obtained by fundamental echocardiography. Secondary harmonic imaging improves definition of cardiac borders. We hypothesise that this overestimates left ventricular mass compared to fundamental imaging.

**Methods and Results:** Thirty patients had four para-sternal long-axis M-modes performed, two using 1.7 mHz output frequency, receiving at two octaves higher and two using fixed frequency of 2.5 mHz (fundamental imaging). Absolute left ventricular mass and left ventricular mass index were calculated for each modality. Intra-observer variability was <7%. Range on fundamental imaging was 54–264 g/m² compared to 80–293 g/m² on secondary harmonic imaging. Mean left ventricular mass index for the group was 118 g/m² (fundamental imaging) vs 147 g/m², \( P < 0.001 \). Twenty-nine of 30 patients had higher left ventricular mass index on secondary harmonic imaging compared to fundamental imaging. Left ventricular mass index was an average of 26% higher on secondary harmonic imaging, range (−7 to 65%) corresponding to average absolute left ventricular mass difference of 55 g. Eleven of 30 patients had left ventricular hypertrophy on fundamental imaging and 17/30 on secondary harmonic imaging.

**Conclusion:** Secondary harmonic imaging overestimates left ventricular mass index compared to fundamental imaging. Normal left ventricular mass index range is based on equations using fundamental imaging measurements. Management decisions and prognostic implications made on the basis of raised left ventricular mass index using secondary harmonic imaging should be done so with caution.


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**Key Words:** left ventricular mass; secondary harmonic imaging; left ventricular hypertrophy; echocardiography.

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**Introduction**

The importance of left ventricular hypertrophy as a manifestation of hypertensive heart disease is well recognized, and is a potent, independent risk factor for cardiovascular morbidity and mortality\(^{[1,2]}\). ECG-defined left ventricular hypertrophy confers a four-fold increase in mortality\(^{[1,3]}\). However, echocardiography is a superior method of assessing the presence of left ventricular hypertrophy\(^{[4,5]}\) and echo-defined left ventricular hypertrophy is also a powerful predictor of morbidity and mortality\(^{[2,6]}\).

Furthermore, there is evidence of an independent relationship between absolute left ventricular mass and subsequent adverse events. In the Framingham study, every 50 g/m² increase in left ventricular mass conferred an increased risk of sudden death by a factor of 1.7\(^{[2]}\). More recently, the MAVI study reported a 40% increase in events with every 39 g increase in left ventricular mass in a hypertensive population\(^{[7]}\).

Echocardiographic left ventricular mass assessment aids risk stratification in the hypertensive population and those found to have left ventricular hypertrophy in the absence of hypertension need to be investigated for potential hypertrophic cardiomyopathy.

Echocardiographic measurement of left ventricular mass has been used for more than 20 years, based on a formula first described by Devereux in 1977 and...
revised in 1986\cite{8,9}. This formula allows calculation of left ventricular mass from standard M-mode measurements and is based on comparison to necropsy findings. Correction for body surface area provides left ventricular mass index and numerous partition values for left ventricular hypertrophy have been defined.

However, the formula and partition values are based on measurements from studies using fundamental imaging, which uses a fixed output and receiving frequency, usually in the region of 2.5 mHz. Low frequency wavelengths allow greater tissue penetration, but higher frequencies permit sharper image resolution and, therefore, fundamental imaging is a compromise between the two. The advent of secondary harmonic imaging allows the utilization of the harmonic properties of ultrasound where low frequency ultrasound is emitted to allow good penetration and the signal received at two octaves higher. This improves imaging and is replacing fundamental imaging in clinical practice. We hypothesise that secondary harmonic imaging overestimates left ventricular mass due to improved definition of pericardial and endocardial borders and report an echocardiographic study comparing the two modalities.

**Methods**

**Patients**

Thirty patients referred for transthoracic echocardiography were recruited for this study: 21 males, mean age 52 (range 29–80 years). Indications for echocardiography were for assessment of left ventricular function (16), left ventricular mass (nine) and potential valve disease (five).

**Echocardiography**

Two-dimensional M-mode studies were performed by a single operator (ADMcG) in accordance with the American Society of Echocardiography guidelines\cite{10}. Four parasternal long-axis M-mode recordings were made on a Vingmed System-V Ultrasound Machine (General Electronics, Milwaukee, WI, U.S.A.), two using a fixed frequency of 2.5 mHz (fundamental imaging) and two using an output frequency of 1.7 mHz, receiving at two octaves higher (secondary harmonic imaging). Off-line analysis was performed by an observer blinded to imaging modality (NERG). Left ventricular mass was calculated using the Devereux equation\cite{9} following average of two measurements for each modality:

\[
\text{LV mass} = 0.8 \times (1.04 \times [(\text{IVS} + \text{LVID} + \text{PW})^3 - (\text{LVID})^3]) + 0.6 \text{ g}
\]

Left ventricular mass was corrected for body surface area and left ventricular hypertrophy was defined as

\[
\frac{\text{LV mass}}{\text{BSA}} > 138 \text{ g/m}^2
\]

### Table 1

<table>
<thead>
<tr>
<th>Imaging</th>
<th>LV mass (g)</th>
<th>LVMI (g/m²)</th>
<th>FS (%)</th>
<th>IVSd (cm)</th>
<th>LVIDd (cm)</th>
<th>PWd (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean (SD)</strong></td>
<td>229 (89)</td>
<td>284 (107)</td>
<td>147 (53)</td>
<td>31.8 (1.6)</td>
<td>43.6 (1.29)</td>
<td>5.28 (0.12)</td>
</tr>
<tr>
<td><strong>Minimum</strong></td>
<td>96</td>
<td>135</td>
<td>54</td>
<td>10.6</td>
<td>16.8</td>
<td>4.17</td>
</tr>
<tr>
<td><strong>Maximum</strong></td>
<td>505</td>
<td>562</td>
<td>264</td>
<td>50.0</td>
<td>52.6</td>
<td>6.64</td>
</tr>
</tbody>
</table>

Data for fractional shortening (FS), measurements in diastole for interventricular septal thickness (IVSd), left ventricular internal diameter (LVIDd) and posterior wall thickness (PWd) are also shown for both modalities.
left ventricular mass index >131 g/m² for men and 100 g/m² for women\(^{[11]}\).

**Statistical Analysis**

Values for group left ventricular mass index are expressed as mean ± SD. Correlation was assessed by Pearson's correlation and group means compared using two-tailed Student's \(t\)-test. A \(P\) value of <0.05 was considered significant.

**Results**

Intra-observer variability was <7% for measurement of left ventricular mass and left ventricular mass index in both modalities. Correlation of left ventricular mass between repeated measurements was excellent \((r = 0.98\) and 0.91, respectively\) for both fundamental imaging and secondary harmonic imaging, as was correlation of left ventricular mass index \((r = 0.98\) and 0.91) with mean absolute differences (SD) of 7 g/m² (seven) and 11 g/m² (20).

There was a strong correlation between absolute left ventricular mass and left ventricular mass index using fundamental imaging and secondary harmonic imaging \((r = 0.91\) and 0.9\). However, 29/30 patients had higher absolute left ventricular mass and left ventricular mass index on secondary harmonic imaging compared with fundamental imaging. Means (SD) for group left ventricular mass were on average 55 g (45) higher in the secondary harmonic imaging studies \((P < 0.001)\), with an average increase in left ventricular mass index of 29 g/m² (23), \(P < 0.001\). This corresponds to an average 26% (17) increase in absolute left ventricular mass and 26% (18) in left ventricular mass index (range: −7 to 65%). Table 1 shows values for left ventricular mass and left ventricular mass index for both modalities. Data for diastolic values of septal and posterior wall thickness and left ventricular internal diameter are also shown, demonstrating increased measured wall thickness and reduced cavity diameter using secondary harmonic imaging. Similar differences are seen with systolic measurements (data not shown). The increase in left ventricular mass index on secondary harmonic imaging was seen across a wide range of left ventricular mass (Fig. 1).

On fundamental imaging, 11/30 patients had left ventricular hypertrophy. However, using the same partition values, an additional six patients (17/30) had left ventricular mass index in the left ventricular hypertrophy range.

**Discussion**

This is the first study demonstrating the effect of echocardiographic imaging modality on the measurement of left ventricular mass. Values for left ventricular mass and left ventricular mass index calculated from images acquired by secondary harmonic imaging are significantly higher than corresponding values based on fundamental imaging. This was seen across a wide range of absolute values in both men and women. Similar results were obtained using data acquired using the PENN convention (data not shown). Furthermore, more patients were deemed to have left ventricular hypertrophy using secondary harmonic imaging.

Although the original equation for calculation of left ventricular mass has been well validated, it is important to remember that it was created to give
values similar to those found at necropsy using measurements available from M-mode echocardiography. It is therefore a complex equation utilizing a ‘best-fit’ principle based on measurement of wall thickness and left ventricular internal diameter. Secondary harmonic imaging gives higher values for septal and posterior wall thickness and lower values for cavity diameter. Therefore, using these values in the Devereux equation, calculated left ventricular mass is increased.

However, this does not mean secondary harmonic imaging gives a more accurate assessment of left ventricular mass. Although definition of the endocardial and epicardial borders is superior with secondary harmonic imaging, wall thickness may be overestimated due to inclusion of dense echoes of the pericardium and left side of septum, which are more likely to be excluded on fundamental imaging. Whatever the cause of the disparity between measurements obtained with the different modalities, the formula for left ventricular mass calculation was derived from measurements obtained with fundamental echocardiography and therefore, it may be inappropriate to use the same formula when using secondary harmonic imaging.

The findings from this study need to be confirmed in a larger cohort of patients and with other ultrasound machines. However, given that secondary harmonic imaging is now used routinely in echocardiographic practice, a new formula for calculation of left ventricular mass from measurements obtained in this modality needs to be created, either from necropsy data or by comparison to MRI. Until that time, one should remember that normal ranges and partition values for left ventricular hypertrophy are based on left ventricular mass calculated from fundamental imaging and decisions regarding the management of patients based on raised left ventricular mass index calculated by secondary harmonic imaging should be made with caution.

References