Standardization of M-Mode Echocardiographic Left Ventricular Anatomic Measurements

RICHARD B. DEVEREUX, MD, FACC, ELIZABETH M. LUTAS, MD, PAUL N. CASALE, MD, PAUL KLIGFIELD, MD, FACC, RICHARD R. EISENBERG, MD, ISAAC W. HAMMOND, PhD, DAVID H. MILLER, MD, GREGG REIS, MD, MICHAEL H. ALDERMAN, MD, JOHN H. LARAGH, MD, FACC

New York, New York

To improve standardization of echocardiographic left ventricular anatomic measurements, echographic left ventricular dimensions and mass were related to body size indexes, sex, age and blood pressure. Independent normal populations comprised 92 hospital-based subjects (64 women, 28 men) and 133 subjects from a population sample (55 women, 78 men). All measurements of chamber size, wall thickness and mass differed between men and women in both series ($p < 0.01$ to $p < 0.001$). Left ventricular mass was related most closely to body surface area among measurements of body size ($r = 0.37$, $p < 0.01$ to $r = 0.57$, $p < 0.001$) in all four groups. Indexation by body surface area eliminated sex differences in wall thicknesses and internal dimension, but a significant sex difference in left ventricular mass index persisted (89 ± 21 g/m² in men versus 69 ± 19 g/m² in women in the entire series, $p < 0.0001$). The 97th percentile of left ventricular mass index was identical in both groups of men (136 and 132 g/m²) and women (112 and 109 g/m²). A highly significant difference in lean body mass, estimated from 24 hour urine creatine excretion, was observed between men and women (58 ± 15 versus 40 ± 13 kg, $p < 0.001$) and no sex difference existed in left ventricular mass indexed by lean body mass (3.4 ± 1.3 versus 3.5 ± 1.5 g/kg). Weak correlations were observed between left ventricular mass/lean body mass and systolic or diastolic blood pressure ($r = 0.25$, $p < 0.05$ and $r = 0.28$, $p < 0.01$, respectively) but not age (18 to 72 years).

In conclusion: 1) left ventricular dimensions are significantly related to body surface area, 2) left ventricular mass index is 20% less in women than men but indexation by estimated lean body mass eliminates this difference, and 3) blood pressure variation in the normal range affects left ventricular mass weakly whereas age has no effect. Therefore, sex and body surface area should be used to determine clinical normal limits of anatomic left ventricular measurements; further refinement of criteria may be achieved by use of lean body mass measurements.

Despite general acceptance of the value of detecting abnormal left ventricular size and muscle mass (1–17), uncertainty persists regarding the optimal variables to characterize normal left ventricular dimensions. Echocardiography, which permits relatively complete noninvasive visualization of left ventricular anatomy, is an attractive method for detecting normality or abnormality of the left ventricle in the clinical setting. To accomplish this, one must first establish which of various echocardiographic measurements is most useful: left ventricular mass (10,11,13,18–20), posterior left ventricular wall thickness (21), interventricular septal thickness (22,23), relative wall thickness (13,24) and cross-sectional area of the myocardium (19). It is then necessary to incorporate into the definition of normal the characteristics of individual subjects that correlate strongly with left ventricular anatomy.

This study was undertaken to determine which individual characteristics, including body habitus, sex, age and blood pressure variability within the normal range, influence left ventricular dimensions sufficiently to be taken into account in defining normal limits for clinical use. Independent normal groups of subjects were studied to establish the reproducibility of the resulting normal limits of echocardiographic measurements. By this approach we have determined

©1984 by the American College of Cardiology

0735-1097/84/33.00
that separation by sex and indexation for body surface area are valuable in reducing variance among normal subjects and have developed reproducible normal limits of left ventricular anatomic measurements. Furthermore, we have demonstrated that sex differences in left ventricular mass are closely related to differences between men and women in lean body mass.

Methods

Study subjects. Normal individuals were studied from two independent groups: 1) a sample of employed adults detected through a work site screening program, and 2) a hospital-based series of subjects in whom heart disease was excluded by thorough evaluation. Each subject in both groups was studied by uniform methods including review of full clinical data and evaluation of left ventricular hypertrophy by quantitative echocardiography. The study was designed to assess determinants of normal left ventricular anatomy, define appropriate normal limits in the normal subject sample and test the applicability of the findings to the hospital-based series of normal subjects. Approval for this research protocol was given by the Committee on Human Rights in Research of Cornell University Medical College in June 1979.

Study sample. Through a previously described program sponsored by several unions and large employers, a total of nearly 100,000 adult employed New York residents are regularly screened for hypertension at work site clinics (25,26). From the registry of the initial 4,000 subjects enrolled in this program, a sample of 200 normotensive individuals with no clinically evident heart disease, stratified according to age, sex, race and renin sodium profile status, was randomly selected. Of these 200 subjects, 7 had developed borderline or sustained essential hypertension and 27 had dropped out of the study by 1981; the 166 remaining subjects underwent echocardiographic examination during 1981 to 1982. The 133 subjects (80%) who had technically optimal echocardiograms constitute the normotensive study sample. This group consists of 78 men and 55 women ranging in age from 18 to 69 years (mean 44 ± 12). Mean blood pressure was 120 ± 13/76 ± 8 mm Hg, body height ranged from 59 to 80 inches (150 to 203 cm) and weight ranged from 79 to 275 pounds (36 to 124 kg). Body surface area ranged from 1.30 to 2.49 m² (mean 1.83 ± 0.18).

Clinical series. A total of 607 subjects were randomly selected from the files of the echocardiography laboratory of The New York Hospital–Cornell Medical Center for a study of anatomic-electrocardiographic relations (27,28). Each subject had a technically optimal echocardiogram, an electrocardiogram in nonpaced rhythm and an available complete clinical record.

The subgroup of normal individuals in the clinical series, that is, those having no evidence of any diagnosable form of heart disease after complete clinical evaluation, was used in this report. These 92 subjects included 28 men and 64 women, ranging in age from 18 to 72 years (mean 33 ± 14). Body surface area ranged from 1.50 to 2.21 m² (mean 1.80). Systolic blood pressure ranged from 96 to 138 mm Hg (mean 119 ± 12) and diastolic blood pressure ranged from 58 to 88 mm Hg (mean 73 ± 8).

Echocardiographic methods. M-mode echocardiograms were performed in the partial left decubitus position using 13 mm 2.25 MHz transducers and either a Picker Echoview 80C or Smith-Kline Ekoline 20A echograph with Honeywell 1856A strip chart recorder on light sensitive paper at 50 mm/s. Simultaneous visualization throughout the cardiac cycle of interventricular septal thickness (IVS), left ventricular internal dimension (LVID) and posterior wall thickness (PWT) was sought at or just below the tips of the mitral valve leaflets. All echocardiograms were coded and read blindly by two independent investigators who had no knowledge of the clinical status of the subjects.

At end-diastole, two sets of points were identified. The first was selected according to the recommendation of the American Society of Echocardiography for measurement of interventricular septal thickness, left ventricular internal dimension and posterior wall thickness (29). The second set of end-diastolic points was selected at the peak of the R wave of the simultaneous electrocardiogram using the alternative Penn convention, in which the thickness of endocardial interfaces is excluded from measurements of septal and posterior wall thickness and included in measurements of left ventricular internal dimension (18).

Three primary measurements and three derived variables were assessed as indexes of left ventricular anatomy. End-diastolic posterior wall thickness, left ventricular internal dimension and interventricular septal thickness were the primary echographic measurements assessed. Left ventricular mass (LVM) was calculated using Penn convention measurements in the following equation (18):

\[ \text{LVM} = 1.04 \left[ (\text{LVID}_d + \text{PWT}_d + \text{IVS}_d)^3 - (\text{LVID}_d)^3 \right] - 14 \text{ g} \]

Relative wall thickness (RWT = 2PWT/LVID) at end-diastole was calculated as a second index of concentric left ventricular hypertrophy (13). A third widely used index of left ventricular hypertrophy, cross-sectional area, was calculated as:

\[ \pi \left( \frac{\text{IVS}_d + \text{LVID}_d + \text{PWT}_d}{2} \right)^2 - \pi \left( \frac{\text{LVID}_d}{2} \right)^2 \]

Indexes of body habitus. Because differences in body size have been shown repeatedly to be a major cause of variability in left ventricular measurements (30–36), several indexes of body habitus were used that could be calculated from clinical measurements. These included height, weight, body surface area, body surface area calculated from ideal rather than observed body weight (37), the ratio of
weight/height, ponderal index (38) and Quetelet's index (38). Each of these indexes was assessed with two questions in mind: which index of body habitus exhibited the closest correlation with measurements of left ventricular size, and which index of body habitus could be used to normalize left ventricular measurements in such a way as to minimize the coefficient of variability among normal subjects, expressed as:

\[
\text{Standard deviation of measurement \times 100.}
\]

In addition, because physical work capacity has been found to be related to both heart weight (39) and lean body mass (40), we estimated lean body mass from 24 hour urinary creatine excretion by the method of Forbes and Bruining (41) to examine the relation between this variable and left ventricular mass.

**Statistical methods.** All data from both series were entered into computers and were analyzed with the assistance of computer program packages (42). Simple statistical analyses were performed, including calculation of mean values, standard deviations and least squares linear correlations (43). Additional statistical analyses included analyses of variance and stepwise multiple regressions. The statistical significance of results was determined by reference to standard tables (44); \( \alpha \) was set at 0.05.

**Hypotheses tested statistically.** The first hypothesis tested was that ideal body surface area (calculated from observed height and ideal body weight (37)) would prove superior to observed body surface area or other indexes of body habitus for standardization of left ventricular measurements. This hypothesis was tested by: 1) determining which index of body size exhibited the closest correlation with indexes of left ventricular size, and 2) determining which index of body size minimized the variability of left ventricular measurements among normal subjects.

The second hypothesis tested statistically was that age and sex would exert significant effects on left ventricular measurements in apparently normal subjects. This hypothesis was tested in two ways. First, normal subjects in both series were separated by sex, and measurements in the resulting groups were compared by unpaired \( t \) tests. Second, stepwise linear regression analyses were performed in each group using left ventricular measurements indexed for body surface area as the dependent variable and age, sex and systolic blood pressure as the independent variables. Because the first analysis revealed readily apparent sex differences in each group, sex was entered as the first variable in this process.

The third hypothesis tested statistically was that sex differences in left ventricular mass would be eliminated by indexation by lean body mass. This was tested by comparing the ratio of left ventricular mass/lean body mass between men and women in the population series using an unpaired \( t \) test. Because this ratio did not differ between sexes, it was compared with age and blood pressure in the entire normal series to evaluate further the relation of these variables to left ventricular mass.

**Results**

All analyses were performed first in the clinical series, which is accordingly termed the "learning series," and were repeated in the population series ("test series") to determine their general applicability.

**Relation of left ventricular dimensions to body habitus in normal subjects (Table 1).** Left ventricular mass was most closely correlated with observed body surface area among indexes of body habitus both in men (\( r = 0.39, p < 0.005 \)) and women (\( r = 0.47, p < 0.005 \)) in the population series as well as the clinical series (\( r = 0.49, p < 0.01 \) and \( r = 0.39, p < 0.01 \), respectively) (Fig. 1 and 2).

*Table 1. Relation of Left Ventricular Mass to Indexes of Body Habitus*

<table>
<thead>
<tr>
<th>Index</th>
<th>Clinical Series</th>
<th>Population Series</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men</td>
<td>Women</td>
</tr>
<tr>
<td>BSA</td>
<td>( r = 0.49, p &lt; 0.01 )</td>
<td>( r = 0.39, p &lt; 0.01 )</td>
</tr>
<tr>
<td>Height (HT)</td>
<td>( r = 0.41, p &lt; 0.05 )</td>
<td>( r = 0.28, p &lt; 0.05 )</td>
</tr>
<tr>
<td>Weight (WT)</td>
<td>( r = 0.41, p &lt; 0.05 )</td>
<td>( r = 0.38, p &lt; 0.01 )</td>
</tr>
<tr>
<td>Ponderal index ( (3\sqrt{WT/HT}) )</td>
<td>( r = 0.07, p = \text{NS} )</td>
<td>( r = 0.19, p = \text{NS} )</td>
</tr>
<tr>
<td>Quetelet index ( (WT/HT^2) )</td>
<td>( r = 0.20, p = \text{NS} )</td>
<td>( r = 0.28, p &lt; 0.05 )</td>
</tr>
<tr>
<td>Ideal BSA</td>
<td>( r = 0.39, p &lt; 0.005 )</td>
<td>( r = 0.47, p &lt; 0.005 )</td>
</tr>
<tr>
<td>Height</td>
<td>( r = 0.30, p &lt; 0.05 )</td>
<td>( r = 0.30, p = \text{NS} )</td>
</tr>
<tr>
<td>Weight</td>
<td>( r = 0.27, p &lt; 0.05 )</td>
<td>( r = 0.31, p = \text{NS} )</td>
</tr>
<tr>
<td>Ponderal index ( (3\sqrt{WT/HT}) )</td>
<td>( r = 0.38, p &lt; 0.005 )</td>
<td>( r = 0.43, p &lt; 0.05 )</td>
</tr>
<tr>
<td>Quetelet index ( (WT/HT^2) )</td>
<td>( r = 0.15, p = \text{NS} )</td>
<td>( r = 0.24, p = \text{NS} )</td>
</tr>
</tbody>
</table>

BSA = body surface area.

The second hypothesis tested statistically was that age and sex would exert significant effects on left ventricular measurements in apparently normal subjects. This hypothesis was tested in two ways. First, normal subjects in both series were separated by sex, and measurements in the resulting groups were compared by unpaired \( t \) tests. Second, stepwise linear regression analyses were performed in each group using left ventricular measurements indexed for body surface area as the dependent variable and age, sex and systolic blood pressure as the independent variables. Because the first analysis revealed readily apparent sex differences in each group, sex was entered as the first variable in this process.

The third hypothesis tested statistically was that sex differences in left ventricular mass would be eliminated by indexation by lean body mass. This was tested by comparing the ratio of left ventricular mass/lean body mass between men and women in the population series using an unpaired \( t \) test. Because this ratio did not differ between sexes, it was compared with age and blood pressure in the entire normal series to evaluate further the relation of these variables to left ventricular mass.

**Results**

All analyses were performed first in the clinical series, which is accordingly termed the "learning series," and were repeated in the population series ("test series") to determine their general applicability.

**Relation of left ventricular dimensions to body habitus in normal subjects (Table 1).** Left ventricular mass was most closely correlated with observed body surface area among indexes of body habitus both in men (\( r = 0.39, p < 0.005 \)) and women (\( r = 0.47, p < 0.005 \)) in the population series as well as the clinical series (\( r = 0.49, p < 0.01 \) and \( r = 0.39, p < 0.01 \), respectively) (Fig. 1 and 2).

*Table 1. Relation of Left Ventricular Mass to Indexes of Body Habitus*

<table>
<thead>
<tr>
<th>Index</th>
<th>Clinical Series</th>
<th>Population Series</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men</td>
<td>Women</td>
</tr>
<tr>
<td>BSA</td>
<td>( r = 0.49, p &lt; 0.01 )</td>
<td>( r = 0.39, p &lt; 0.01 )</td>
</tr>
<tr>
<td>Height (HT)</td>
<td>( r = 0.41, p &lt; 0.05 )</td>
<td>( r = 0.28, p &lt; 0.05 )</td>
</tr>
<tr>
<td>Weight (WT)</td>
<td>( r = 0.41, p &lt; 0.05 )</td>
<td>( r = 0.38, p &lt; 0.01 )</td>
</tr>
<tr>
<td>Ponderal index ( (3\sqrt{WT/HT}) )</td>
<td>( r = 0.07, p = \text{NS} )</td>
<td>( r = 0.19, p = \text{NS} )</td>
</tr>
<tr>
<td>Quetelet index ( (WT/HT^2) )</td>
<td>( r = 0.20, p = \text{NS} )</td>
<td>( r = 0.28, p &lt; 0.05 )</td>
</tr>
<tr>
<td>Ideal BSA</td>
<td>( r = 0.39, p &lt; 0.005 )</td>
<td>( r = 0.47, p &lt; 0.005 )</td>
</tr>
<tr>
<td>Height</td>
<td>( r = 0.30, p &lt; 0.05 )</td>
<td>( r = 0.30, p = \text{NS} )</td>
</tr>
<tr>
<td>Weight</td>
<td>( r = 0.27, p &lt; 0.05 )</td>
<td>( r = 0.31, p = \text{NS} )</td>
</tr>
<tr>
<td>Ponderal index ( (3\sqrt{WT/HT}) )</td>
<td>( r = 0.38, p &lt; 0.005 )</td>
<td>( r = 0.43, p &lt; 0.05 )</td>
</tr>
<tr>
<td>Quetelet index ( (WT/HT^2) )</td>
<td>( r = 0.15, p = \text{NS} )</td>
<td>( r = 0.24, p = \text{NS} )</td>
</tr>
</tbody>
</table>

BSA = body surface area.
Height and weight, the primary measurements utilized in calculating body surface area, showed weaker individual relations to left ventricular mass in all groups. The relations between left ventricular mass and ideal body weight or ideal body surface area were accordingly less close than that between left ventricular mass and observed body surface area. In contrast to these results, ponderal index

\[
\frac{3V}{WT} = \frac{WT}{HT}
\]

(where WT = weight and HT = height) did not correlate significantly with left ventricular mass in either men or women in either series, and the Quetelet index

\[
\frac{WT}{HT^2}
\]

does not show a relation to left ventricular mass in either group of men. The Quetelet index correlated modestly with left ventricular mass in the hospital-based series of normal women (r = 0.28, p < 0.05) but not in the women in the population sample.

Table 2 summarizes the results of indexing left ventricular mass by dividing it by each index of body habitus in men and women in the clinical series. The variability of left ventricular mass as expressed by the coefficient of variance is minimized for both men and women when left ventricular mass is indexed by body surface area, compared with the unindexed measurement of left ventricular mass or indexed by the other measures of body habitus. Cross-sectional area, the other variable measuring the amount of left ventricular muscle, also minimizes variability in both men and women (coefficient of variance = 0.24 for both men and women). Indexation of cross-sectional area by body surface area has little effect on the coefficient of variance (0.22 for men and 0.23 for women). Similar results were obtained in the population series.

Relation of left ventricular mass to lean body mass. Estimated lean body mass differed significantly between men and women (58 ± 15 versus 40 ± 13 kg, respectively; p < 0.001). The proportionate increase in lean body mass in men compared with women (approximately 40%) is similar to that in previous reports (40,41,45). Indexation of left ventricular mass by lean body mass resulted in the elimination of sex differences (3.4 ± 1.3 g/kg in men and 3.5 ± 1.5 g/kg in women, p = NS).

Effect of sex, age and blood pressure on the normal left ventricle (Table 3). In the clinical series, left ventricular mass differed significantly (p < 0.001) between men (159 ± 51 g) and women (115 ± 38 g). After indexation by body surface area, a smaller but still highly significant difference (p < 0.001) was found in left ventricular mass index between these men (84 ± 24 g/m²) and women (68 ± 21 g/m²). Among the normal subjects in the population series, left ventricular mass differed significantly (p < 0.0001) between men (181 ± 44 g) and women (128 ± 42 g). Left ventricular mass index demonstrated a smaller but still highly significant difference between men and women (93 ± 22 versus 76 ± 18 g/m², p < 0.001), as did cross-sectional area (18.0 ± 3.3 versus 13.9 ± 2.6 cm², p < 0.001). Therefore, subsequent analyses were performed separately by sex using left ventricular mass indexed by body surface area.

Additional linear regression analysis revealed no significant correlation between age and left ventricular mass index in either normal men (r = −0.16, p = NS) or women (r = 0.11, p = NS) in the clinical series or in the population series (r = −0.04 and r = 0.28, respectively). In addition, no correlation existed between this measurement and systolic blood pressure for men (r = −0.05, p = NS) or women (r = 0.10, p = NS) in the clinical series or in the normal men from the population series (r = −0.005, p < 0.95). Only in the normal women from the population series was there a weak relation between systolic blood pressure and left ventricular mass index (r = 0.42, p < 0.02). Indexation of left ventricular mass by lean body mass, which
eliminated sex differences and made it possible to analyze together data from men and women in the population series, revealed that weak relations existed between this ratio and systolic blood pressure ($r = 0.25$, $p < 0.05$) and diastolic blood pressure ($r = 0.28$, $p < 0.01$), but no significant relation was observed between this ratio and age ($r = 0.14$, $p = \text{NS}$).

The other indexes of left ventricular anatomy are also shown in Table 3 for both the clinical and population series. Mean posterior wall thickness showed a modestly significant difference ($p < 0.01$) between men and women in both the clinical series ($8.4 \pm 1.9$ versus $7.4 \pm 1.4$ mm) and the population series ($8.9 \pm 1.4$ versus $8.0 \pm 1.5$ mm) (both $p < 0.02$). There was no correlation of posterior wall thickness with age or systolic blood pressure within the normal range in either men or women. A similar pattern of sex differences was also observed for interventricular septal thickness and left ventricular internal dimension. In contrast to the sex differences observed for other measurements, relative wall thickness did not differ between normal men and women. Similar to other measurements, relative wall thickness was not related either to age of subjects or systolic blood pressure. Cross-sectional area also differed significantly ($p < 0.0001$) between men and women, with no correlation with age or blood pressure.

**Clinically applicable normal limits.** To determine whether the normal limits of left ventricular anatomic measurements we have defined in relation to sex and body size are of general validity in adults, we tested the applicability of these measurements to determination of normality in totally independent populations. Upper limits of normal for each measurement from the population series were applied prospectively to the clinical series. For this purpose, the mean values ± 2 standard deviations (approximately the 97th percentile of normal) were used (Table 3, Fig. 3). The upper limit of normal for left ventricular mass index in the clinical and population series is identical in each sex. This finding confirms that these limits of normal utilizing an anatomically validated measurement of left ventricular mass (18) meet the test of prospective application to independent populations.

A relatively close correspondence between the upper limits of normal defined separately for each sex is seen in the clinical and population series for other indexes of normal left ventricular anatomy. These include left ventricular cross-sectional area, posterior wall thickness, interventricular septal thickness and left ventricular internal dimension. Because 24 hour urinary creatine excretion data are not available in the clinical series, our findings with respect to lean body mass could not be tested in this second group of subjects.

**Discussion**

Left ventricular mass indexed by body surface area as a measurement of left ventricular anatomy. The results of the present study indicate that sex and body size, best measured clinically by body surface area, exert important influences on normal left ventricular anatomy, whereas the effects of age and blood pressure variability within the normal range are not strong enough to be incorporated into clinically useful definitions of normal measurements. By
Table 2. Sex Differences in Indexes of Left Ventricular Anatomy

<table>
<thead>
<tr>
<th></th>
<th>Mean (± SD)</th>
<th>Coefficient of Variance</th>
<th>Mean (± SD)</th>
<th>Coefficient of Variance</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVM</td>
<td>159 ± 50.6 g (0.32)</td>
<td>p &lt; 0.0001</td>
<td>115 ± 37.5 g (0.33)</td>
<td></td>
</tr>
<tr>
<td>LVM</td>
<td>84 ± 24 g/m² (0.29)</td>
<td>p &lt; 0.001</td>
<td>68 ± 20.5 g/m² (0.30)</td>
<td></td>
</tr>
<tr>
<td>BSA</td>
<td>90 ± 27.2 g/m (0.30)</td>
<td>p &lt; 0.0001</td>
<td>70 ± 22.4 g/m (0.31)</td>
<td></td>
</tr>
<tr>
<td>HT</td>
<td>2.2 ± 0.6 g/kg (0.28)</td>
<td>p &lt; 0.001</td>
<td>1.8 ± 0.6 g/kg (0.32)</td>
<td></td>
</tr>
<tr>
<td>LVM</td>
<td>69 ± 22.1 g/kg² per m (0.32)</td>
<td>p &lt; 0.0001</td>
<td>48 ± 15.5 g/kg² per m (0.32)</td>
<td></td>
</tr>
<tr>
<td>PI</td>
<td>7.0 ± 2.2 g/kg per m² (0.32)</td>
<td>p &lt; 0.0001</td>
<td>4.9 ± 1.7 g/kg per m² (0.35)</td>
<td></td>
</tr>
<tr>
<td>CSA</td>
<td>16.4 ± 3.6 cm² (0.24)</td>
<td>p &lt; 0.0001</td>
<td>13.3 ± 2.8 cm² (0.24)</td>
<td></td>
</tr>
<tr>
<td>CSA</td>
<td>8.8 ± 1.7 cm²/m² (0.22)</td>
<td>p &lt; 0.0001</td>
<td>7.8 ± 1.6 cm²/m² (0.23)</td>
<td></td>
</tr>
<tr>
<td>BSA</td>
<td>28 men; 64 women. BSA = body surface area; CSA = cross-sectional area; HT = height (in meters); LVM = left ventricular mass; PI = ponderal index (3VWT/HT); QI = Quetelet index (WT/HT²); SD = standard deviation; WT = weight (in kilograms).</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

use of these normal data, we have defined echocardiographic criteria of left ventricular hypertrophy which are useful in evaluation of diverse forms of heart disease. The best clinical measurement of left ventricular anatomy was left ventricular mass indexed by body surface area. This yielded a reproducible normal range in two independent series for both men and women. The basis for the observed sex difference in left ventricular mass index appears to be a striking difference in lean body mass of approximately 40%. Further, indexation of left ventricular mass by lean body mass completely eliminated the previously observed sex differences. The ratio of left ventricular mass to lean body mass was too weakly related to systolic and diastolic blood pressure within the normal range (r² = 0.08) to be incorporated into clinically useful normal limits. The relation of left ventricular mass indexed by lean body mass to age was not significant (r² = 0.02).

Factors influencing ventricular dimensions. Our findings are in accord with those of several previous studies, but in disagreement with others. A relation between body size and left ventricular mass has been found consistently whether studies have been performed by echocardiography (34,35), angiography (36) or necropsy (30,46). Sex differences have also been reported by most investigators. Thus, left ventricular mass index has been 13 and 21%, respectively, lower in women than in men in echocardiographic (35) and angiographic (36) studies. The study by Valdez et al. (33) of a normal population indicated that men and women differ regarding primary echocardiographic measurements such as wall thicknesses and chamber internal dimension,

Table 3. Measurements of Normal Left Ventricular Anatomy*

<table>
<thead>
<tr>
<th></th>
<th>Clinical (n = 28)</th>
<th>Population (n = 78)</th>
<th>Clinical (n = 64)</th>
<th>Population (n = 55)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV mass</td>
<td>159 ± 51 (261)</td>
<td>181 ± 44 (269)</td>
<td>115 ± 38 (191)</td>
<td>128 ± 42 (210)</td>
</tr>
<tr>
<td>LV mass index</td>
<td>84 ± 24 (132)</td>
<td>93 ± 22 (136)</td>
<td>68 ± 21 (109)</td>
<td>76 ± 18 (112)</td>
</tr>
<tr>
<td>Cross-sectional area (cm²)</td>
<td>16.4 ± 3.6 (23.5)</td>
<td>18.0 ± 3.3 (24.6)</td>
<td>13.3 ± 2.8 (19.1)</td>
<td>13.9 ± 2.6 (19.0)</td>
</tr>
<tr>
<td>Cross-sectional area index (cm²/m²)</td>
<td>8.8 ± 1.7 (12.2)</td>
<td>9.5 ± 1.5 (12.4)</td>
<td>7.8 ± 1.6 (11.0)</td>
<td>8.8 ± 1.4 (11.3)</td>
</tr>
<tr>
<td>Interventricular septal thickness (mm)</td>
<td>9.5 ± 1.7 (12.8)</td>
<td>9.8 ± 1.7 (13.1)</td>
<td>8.1 ± 1.5 (11.0)</td>
<td>9.0 ± 1.8 (12.4)</td>
</tr>
<tr>
<td>Posterior wall thickness (mm)</td>
<td>8.4 ± 1.9 (11.1)</td>
<td>8.9 ± 1.4 (11.7)</td>
<td>7.4 ± 1.4 (10.1)</td>
<td>8.0 ± 1.5 (10.9)</td>
</tr>
<tr>
<td>Relative wall thickness†</td>
<td>0.34 ± 0.09 (0.51)</td>
<td>0.34 ± 0.07 (0.48)</td>
<td>0.32 ± 0.08 (0.47)</td>
<td>0.35 ± 0.08 (0.51)</td>
</tr>
<tr>
<td>Left ventricular internal dimension (cm)</td>
<td>4.9 ± 0.5 (5.9)</td>
<td>5.0 ± 0.5 (6.0)</td>
<td>4.7 ± 0.4 (5.4)</td>
<td>4.5 ± 0.4 (5.3)</td>
</tr>
</tbody>
</table>

*All measurements are given as mean ± standard deviation; mean ± 2 standard deviations is given in parentheses. †Relative wall thickness = 2 PWT/LVID. LV = left ventricular; LVID = left ventricular internal dimension; PWT = posterior wall thickness.
for the parallel between the mass of cardiac and skeletal muscle (from which lean body mass is estimated) have not been determined. However, contributory roles may well be played by sex differences in habitual physical activity levels as well as in levels of steroid or other hormones.

Role of blood pressure. Less data exist regarding the effects of blood pressure variability within the normal range and of age on left ventricular anatomy. St. John Sutton et al. (47) observed a tendency for group mean measurements of left ventricular anatomy to increase with age in a large population of presumably normal subjects studied by echocardiography. This trend was closely related to the upward trend in blood pressure observed over the same age range. However, the mean increments with advancing age were slight and no data were presented on the relation between age and left ventricular anatomy in individual patients. Other investigations have found no independent relation between blood pressure in the truly normal range and left ventricular mass. The fact that we observed only weak relations between measurements of blood pressure and left ventricular mass even after indexation by lean body mass is most compatible with a weak relation between these variables, which might be variably evident in different studies.

Role of age. The effects of age on left ventricular anatomy are more controversial. Two echocardiographic studies of normal aging individuals indicated that both posterior wall thickness (48) and left ventricular mass (49) increased dramatically with advancing age. A less striking but still significant relation of left ventricular mass to age was also observed by Gardin et al. (34). However, in the latter study, two-thirds of the elderly individuals but only half of younger subjects were male, suggesting that part or all of the apparent effect of age on left ventricular mass index may have actually been caused by the sex difference that we and others have observed. The lack of a significant relation between age and left ventricular mass index in the present study, even after indexation of left ventricular mass by lean body mass in our population series, is also compatible with the results of numerous necropsy studies (30) in which there has been no need to stratify individuals by age in order to define normal ranges.

Variation of left ventricular dimensions: methodologic and biologic factors. An important consideration in measurements of left ventricular mass is the methodology employed. In the present study, we have shown that echocardiographic measurements by the Penn method (18,50) yield similar measurements during life in normal subjects from separate populations. Although the sex and body size influences we have demonstrated are applicable to any method of left ventricular mass measurement, the upper limits of normal we have defined cannot be directly applied to values derived by other echocardiographic methods. We previously demonstrated by comparing echocardiographic measurements to necropsy left ventricular mass in two separate studies (18,50) that some echocardiographic methods of left ventricular wall thickness measurement result in serious

![Figure 3. Left ventricular mass index in women (F) and men (M) in the population series (open circles) and clinical series (closed circles) of normal subjects. Horizontal lines are drawn ± 2 standard deviations above the mean value, representing approximately the 97th percentile of normal left ventricular mass index: 110 g/m² in women and 134 g/m² in men.](image-url)
overestimation of left ventricular mass when they are combined with standard geometric formulas. The impact of using such methods of wall thickness measurement is illustrated by the recent report of Woythaler et al. (51) in which the upper limit of normal echocardiographic left ventricular mass was found to be 265 g as opposed to 215 g in our laboratory. In contrast, a formula used to correct errors in left ventricular volume estimates results in echocardiographic underestimation of anatomic left ventricular mass in nearly all instances (50,52). Use of two-dimensional echocardiography (35,53) has been shown to reduce the range of variability in left ventricular mass index slightly, but does not alter the mean estimate when an anatomically validated method is used (53,54).

Although the present study has elucidated the importance of body size, sex and, to a lesser extent, blood pressure in the normal range as determinants of left ventricular dimensions, a substantial portion of their variation among normal individuals remains unexplained. Errors in echocardiographic measurement of left ventricular dimensions undoubtedly contribute to this variation. However, in view of the excellent correlations (r = 0.96 and 0.92, both p < 0.001) between echocardiographic and necropsy left ventricular mass in previous studies of 86 patients with normal left ventricular geometry (18,50), it seems likely that most of the interindividual differences we observed represent true biological variability.

Several factors beyond those assessed in this study may influence left ventricular anatomy. First, blood pressure elevations measured by an automatic portable recorder during the stress of occupational work appeared to play a role in the development of left ventricular hypertrophy in a recent study of normotensive and mildly hypertensive subjects (55). Blood pressure measurements at rest, used in this and most other studies, may not provide an adequate measurement of hemodynamic load. Second, variation in level of habitual physical activity may influence left ventricular dimensions to a greater degree than accounted for by changes in lean body mass. Finally, it is attractive to speculate that genetic factors might influence interindividual variability in left ventricular size by mechanisms other than their influence on blood pressure.

Clinical implications. The most important result of this study is the finding that indexation of left ventricular mass by body surface area narrows the range of variability among normal subjects and results in clinically useful criteria of left ventricular hypertrophy. These criteria, which correspond roughly to the 97th percentile in our normal subjects, are a left ventricular mass index greater than 134 g/m² in men and greater than 110 g/m² in women. In a previous study (56), we demonstrated that from 59 to 100% of patients with moderate to severe degrees of pressure overload, volume overload or cardiomyopathy demonstrate left ventricular hypertrophy by use of these highly specific criteria, as did 44% of patients with mild to moderate hypertension in another study from our laboratory (20). Alternatively, a combined upper normal limit of 120 g/m² may be used for both sexes, similar to that in previous studies (11,20,57), although this results in modest decrements in both sensitivity and specificity.

We thank Jere Mitchell, MD and Daniel D. Savage, MD for helpful suggestions during preparation of this manuscript, Mariane C. Spitzer, Bonnie R. Spencer and Irene Sachs, BS for expert performance of the echocardiograms, Joan Crowley, RN for coordination of the general population study and Virginia Burns for assistance in preparation of the manuscript.

References
5. Linzbach AJ. Heart failure from the point of view of quantitative anatomy. Am J Cardiol 1960;5:370-82.


32. Smith HL. The relationship of the weight of the heart to the weight of the body and of the weight of the heart to age. Am Heart J 1928;4:79–93.


