Effect of Age, Sex, and Body Surface Area on Echocardiographic Left Ventricular Wall Mass in Normal Subjects

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SUMMARY M-mode echocardiography was used to estimate left ventricular wall mass in 136 older normal subjects (Group I: 78 men and 58 women, ages 20 to 97 years) and 105 younger normal subjects (Group II: 52 male and 53 female subjects, ages 1 day to 23 years). Echocardiographic left ventricular mass (in grams) was estimated from the following formula: left ventricular mass \( = 1.05 \left[ \text{left ventricular internal diastolic dimension + ventricular septal thickness (diastole) + posterior wall thickness (diastole)} \right]^{3} - \left[ \text{left ventricular internal diastolic dimension} \right]^{3} \). In both groups, female subjects had a slightly smaller left ventricular mass than male subjects (mean difference 7.2\% in Group I, \( p<0.05 \), and 3.6\% in Group II, \( p=0.05 \)) for any given age and body surface area. Left ventricular mass varied linearly with body surface area and increased as a function of age. In group I subjects, echocardiographic left ventricular mass (in grams) could be estimated by the general formula: left ventricular mass \( = 124 \times \text{body surface area} + A \pm C \), where \( A \) is the age-dependent intercept; \( \pm C \) encompasses a 95\% prediction interval for normal values, which is assumed to be nearly constant (\( \pm 58 \) g); and body surface area is expressed in square meters. In the Group II (younger) subjects, with age not considered, left ventricular mass (in grams) could be estimated from the following formula: left ventricular mass \( = 115 \times \text{body surface area} - 11 \pm C \), where \( \pm C = \pm 32\% \) and this 95\% prediction interval varies as a percentage of the mean. We conclude that both age and body surface area must be taken into account when evaluating echocardiographic measurements of left ventricular mass. (Hypertension 9 [Suppl II]: 11-36–11-39, 1987)

Key Words • left ventricular mass • echocardiography • body surface area • aging • sex

NONINVASIVE estimation of left ventricular (LV) wall mass by echocardiography has become an important tool in the assessment of prognosis and response to therapy in patients with systemic hypertension.1-10 In order to use echocardiographic LV wall mass measurements as a quantitative tool in patients with potential cardiac involvement, it is important to have reference data for LV mass obtained in normal subjects. Roberts and Perloff11 have noted that hearts of older individuals have smaller ventricular chambers and thicker walls than those of younger individuals studied at necropsy. Various investigators have also noted the influence of body surface area (BSA) on the dimensions and thickness of cardiac structures.12-17 In order to investigate the effects of age, body size, and gender on normal LV wall mass as well as on LV dimensions and wall thickness, we performed a series of M-mode echocardiographic studies in groups of younger and older normal subjects.13-15

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Methods

Subject Population

Our study population consisted of two subject groups. The first group included 136 subjects, 78 men and 58 women, without evidence of heart disease, who ranged in age from 20 to 97 years. None of the subjects had a history suggesting heart disease or hypertension, an abnormal electrocardiogram, or an abnormal chest x-ray. In addition, none of the subjects was a trained athlete, gave a history of excessive alcohol intake, or had a body weight more than 25\% above the upper limit for desirable weight set forth by the Metropolitan Life Insurance Company.18 The second group of subjects consisted of 105 younger normal individuals between the ages of 1 day and 23 years. None of these younger individuals had evidence of cardiovascular disease on the basis of a history or physical examination. Twelve-lead electrocardiograms were available in 87 of the younger normal individuals and were normal in each case. All subjects gave informed consent and were studied in accordance with institutional guidelines.

Echocardiography

M-mode echocardiograms were performed in the left lateral decubitus position using either a 2.25-MHz, 3.5-MHz or 5.0-MHz transducer. Each study was read independently by at least two investigators. Three consecutive measurements were made for each echocardiographic parameter and the average taken as
the value for the parameter. In approximately 5% of studies, interobserver variation was greater than 10% in dimensional measurements or 2 mm or more in wall thickness measurements. In these instances, the echocardiograms were reviewed and data included for analysis as agreed by consensus of the readers.

The LV internal dimensions at end diastole and end systole were measured immediately below the tips of the mitral valve leaflets. These measurements corresponded, respectively, to the maximum and minimum internal dimensions between the ventricular septum and endocardium of the posterior LV free wall (Figure 1). Thickness of the ventricular septum and posterobasal LV free wall was measured in late diastole, just prior to thinning of the wall.\(^{11,13}\) Measurements were made with the ultrasound beam passing through the left ventricle at or slightly below the tips of the mitral leaflets. A switched-gain circuit was used to simplify identification of the epicardium of the posterobasal free wall.\(^{11}\) In no patient was the ratio of septal thickness to posterior wall thickness greater than 1.2:1.

The LV mass was calculated as previously described\(^{20-22}\) using the following equation:

\[
LV\text{ mass} = 1.05 \left[ (LVIDd + VSTd + PWTd)^3 - (LVIDd)^3 \right]
\]

where LVID represents the LV dimension, VST = ventricular septal thickness, PWT = posterior LV wall thickness, and d = diastole.

The BSA was estimated from height and weight by the Bois and DuBois\(^{24}\) modification of the formula of DuBois and DuBois.

**Results**

**Effect of Body Surface Area**

Echocardiographic estimates of LV wall mass were analyzed for the influence of age, sex, and BSA. In the younger normal subjects, we found that the relationship of estimated LV mass to BSA could be described by the regression model:

\[
LV\text{ mass} = 115(BSA) - 11
\]

where BSA was expressed in square meters and LV mass was expressed in grams.\(^{13}\)

Although ventricular septal thickness and LV free wall thickness varied linearly with the square root of BSA, and LV internal dimensions (systolic and diastolic) varied in linear relation to the cube root of BSA, estimated LV mass varied linearly with BSA. Figure 2 demonstrates a plot of our data for estimated LV mass (in grams) versus a linear function of BSA (in square meters).

To develop a predictive equation that would contain a new normal value with 95% confidence, we expanded the above equation to include a prediction interval term. The expanded equation could be expressed as follows:

\[
LV\text{ mass} = B(BSA) - A \pm C
\]

where 2C (or ± C) is the width of the 95% prediction interval (i.e., the interval into which, with 95% confidence, a new normal observation would fall).\(^{13-15}\) In our younger normal individuals, the 95% prediction interval for LV mass varied proportionally with the mean (i.e., became wider as BSA increased) and could be expressed as ± 32% of the mean (see Figure 2).\(^{13}\)

In order to simplify the prediction equation in the older adult population (Group I), we assumed that the 95% prediction interval for LV mass had a constant width. Over the range of BSAs encountered in this older adult population, the constant assumption introduced less than a 5% difference in the prediction intervals compared with the proportionality assumption.\(^{14}\)

**Effect of Sex**

Table 1 summarizes the sex, heart rate, blood pressure, and BSA data for our older normal (Group I) population. To determine whether sex (independent of age and BSA) had an effect on LV mass, we analyzed the data for LV mass separately for men and women after correcting the data for age and BSA in our Group I subjects. There was a statistically significant difference between men and women for estimated LV mass (p < 0.05), with women having an average LV mass 7.2% smaller than that in men for any given age and BSA.\(^{14}\) In our younger normal subjects (Group II), the average LV mass in women was 3.6% smaller than that in men for any given BSA (p = 0.05).\(^{13}\)

Because the sex differences in both the older and younger groups were relatively small, we combined the data for men and women in order to simplify our calculation of regression equations and prediction intervals.

**Effect of Age**

As noted above, we analyzed our data for estimated LV mass in the Group I subjects according to the general regression equation:

\[
LV\text{ mass} = B(BSA) + A \pm C.
\]

When the older adult subjects were grouped into six age groups (as noted in Table 1), the slope of the regression relationship for estimated LV mass versus age was found to be independent of age (p > 0.05), whereas the intercept showed significant variation with age (p < 0.01). Therefore, we assumed that the intercept (A), but not the slope (B), was influenced by age, and that the width of the 95% prediction interval (± C) was constant and not appreciably influenced by age or BSA. Table 2 summarizes the value for B (124) and C (± 58 g) in our equation, as well as the values of A derived for each age group.

Figure 3 depicts the age-related changes in estimated LV mass for our older adult subjects (Group I). For this figure, the regression equation for LV mass has been analyzed for BSA.
values of 1.4, 1.8 and 2.2 m². The mean value for each age group is plotted at the mean age in each group. The figure depicts the mean and the 95% prediction interval for each age group at each of the three BSAs. Note that for a BSA of 1.8 m² there was a 15% increase in mean LV mass from 214 g in the youngest to 246 g in the oldest age group.

Discussion

Echocardiographic studies of an older and younger population without clinically apparent heart disease demonstrated that estimated LV mass showed a small but progressive increase with increasing age. This increase in LV mass was related to an increase in wall thickness (mean increase, 19%) from the 30- and-under to the over-70 age groups that was relatively greater than the decrease in LV diastolic dimension (mean decrease, 6%) over the same age range. These findings are consistent with the previously reported necropsy findings of Roberts and Perloff. A recent study by Devereux and co-workers of 225 normal subjects, age range 18 to 72 years, suggested that age had no significant effect on measurements of LV mass. However, two other echocardiographic studies of normal individuals have concluded that both posterior LV wall thickness and LV mass increase significantly with advancing age.

In our studies estimated LV mass varied linearly with BSA but was 7.2% less in adult normal females (p<0.05) and 3.6% less in younger normal females (p = 0.05) than in males of the same age and BSA. These findings suggest a small but significant relationship between sex and echocardiographic measurements of LV mass that is not eliminated by correction for BSA. In the study by Devereux et al., LV dimensions and mass were found to be closely related to BSA. Although indexing by BSA eliminated sex differences in LV wall thickness and internal dimension, a significant sex difference remained in LV mass index (89 ± 21 g/m² in men vs 69 ± 19 g/m² in women, p < 0.0001). When LV mass was indexed by lean body mass, however, no sex difference persisted. The smaller sex difference (7.2%) found in our adult normal population as compared to that reported by Devereux et al. (20%) may be related to the smaller number of women in our older age group and perhaps also to biologic variability in the relationship between BSA and...
lean body mass in the subjects in the two studies. Of interest, Valdez and co-workers, in their study of a normal population, found differences between men and women in LV echocardiographic measurements such as wall thickness and internal dimension, but they noted that these differences were eliminated by indexing for BSA.

These initial echocardiographic studies provide baseline normal data for use in quantitative evaluation of populations with suspected increased LV mass (e.g., hypertensive subjects) and for evaluation of serial changes in LV mass in response to pharmacologic and other therapeutic interventions. Studies of larger populations of subjects without clinical evidence of cardiac disease should provide additional information regarding the applicability of our regression equations to large normal and abnormal populations. In addition, provocative tests such as exercise electrocardiography or stress echocardiography might be helpful in further screening of subjects without overt cardiovascular disease in order to eliminate so-called normal subjects with asymptomatic cardiovascular disease.

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