METHODS

Limits of Normal Left Ventricular Dimensions in Growth and Development: Analysis of Dimensions and Variance in the Two-Dimensional Echocardiograms of 268 Normal Healthy Subjects

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The majority of studies generating normal echocardiographic reference values for left ventricular dimensions have been based on blindly performed M-mode measurements, and there are no previous reports based on two-dimensional echocardiography that provide a comprehensive analysis of the two-dimensional measurements from infancy to old age. This report presents the results of analyzing the left ventricular internal dimensions from cross-sectional echocardiographic studies on 268 normal healthy subjects (none were hospitalized for any reason) whose ages ranged from 6 days to 76 years. The mean data are reported as functions of body surface area and, in addition, the variance is modeled as a function of body surface area to provide an accurate and clinically useful determination of normal limits and to model changes in the cardiac dimensions and in their variance representing normal growth and development.

The data fit well to the exponential growth model (r values 0.85 to 0.95). Variance about the central values also depended significantly on body size; that relation is represented effectively by a quadratic function of body surface area (r values 0.82 to 0.98). The model parameters allow calculation of normal limits at any desired level of confidence. Areas determined by hand planimetry have significantly greater variance compared with variance of linear dimensions, and also compared with variance of cross-sectional area using ellipses generated from the anteroposterior and mediolateral dimensions. This implies that either biologic variations in the amount of infolding or errors in freehand planimetry constitute a significant source of variance; this may be remedied by filtering out high frequency oscillations of contour. There is no significant difference in midnormal values and confidence limits for corresponding dimensions measured from orthogonal views. Furthermore, the anteroposterior and mediolateral dimensions of the left ventricle superimpose at each body size, consistent with circular cross section for normal subjects throughout growth and development. The data presented should comprise a useful set of reference standards for interpretation of cross-sectional echocardiograms.

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Cross-sectional echocardiography is routinely performed for noninvasive evaluation of patients with known or suspected heart disease. It defines anatomic relations and provides numerous measurements of intracardiac dimensions. As with all clinical measurements, it is important to have accurate definition of normal limits to guide interpretation. The majority of previous studies (1-7) generating normal echocardiographic reference values for left ventricular dimensions have been based on blindly performed M-mode measurements. Unfortunately, these measurements are limited to a single dimension recorded without precise knowledge of the relation to the true major and minor axes of the left ventricle. Cross-sectional echocardiography, in contrast, provides measurements in any direction in an imaging plane, and also provides area measurements. Furthermore, it permits more precise definition of the plane from which each measurement is derived, so that the image planes that coincide with the axes of the left ventricle may be selected with accuracy.

Left ventricular measurements by cross-sectional echocardiography have been reported by our group (8) and by others (9) for adults, but there are no reports that give a...
comprehensive analysis of left ventricular measurements from infancy to full maturity. We report here the results of analyzing the left ventricular internal dimensions from cross-sectional echocardiographic studies on 268 normal healthy subjects whose ages ranged from 6 days to 76 years. The mean data are reported as functions of body surface area and, in addition, the variance is modeled as a function of body surface area to provide an accurate and clinically useful determination of normal limits.

Methods

Study subjects. Two groups of normal subjects were studied: children (Group 1) and adults (Group 2). Group 1 consisted of children presenting for well child care. These were not cardiology referrals, and no child was hospitalized for any cause. Criteria for inclusion were 1) no suspicion of cardiac or systemic disease by assessment of the attending pediatrician, 2) normal blood pressure, 3) normal sinus rhythm, and 4) no evidence of structural heart disease by echocardiography. Group 2 was generated from adult hospital employees who had no evidence of cardiac or systemic disease by history, physical examination, electrocardiogram (ECG) or chest roentgenography.

There were 196 children studied in Group 1: 99 male, 97 female. Their age ranged from 6 days to 18 years (mean 4.5 years), weight from 2.3 to 86 kg (mean 19) and height from 37 to 188 cm (mean 98). The number of normal adults studied in Group 2 was 72 (38 male, 34 female). Their age ranged from 18 to 76 years (mean 38), weight from 40 to 80 kg (mean 70) and height from 155 to 180 cm (mean 169).

Echocardiography. After informed consent was obtained (from a parent or guardian for minors), two-dimensional sectional imaging was performed with an ATL 300 series mechanical sector scanner and recorded with a Panasonic video recorder on 0.5 in. (1.27 cm) videotape. The data were acquired with either a 3.5 or a 5 MHz transducer, depending on the depth of penetration needed. Echocardiographic views included 1) parasternal long-axis, 2) parasternal short-axis at the level of the mitral valve, 3) parasternal short-axis at the midpapillary muscle level, and 4) apical four chamber, standardized as previously described (10). Two-dimensional scout imaging was used to establish the perpendicular direction of short-axis views.

Measurements. All studies were reviewed in their entirety to identify the video frame segments, including systole and diastole for each view, which exhibited optimal orientation and structural definition. These segments were then copied to video disk for measurements using calibrated electronic calipers (Microsonics Easy View II image analysis system). In views that included the mitral valve, end-systole was defined as the frame immediately before mitral valve opening, and end-diastole as the frame immediately before mitral valve closure. Because the short-axis view at the midpapillary muscle level does not record the mitral valve motion, for that view the end-systolic frame was selected as that with minimal chamber area, and the end-diastolic frame as that with maximal left ventricular area.

The linear measurements were made with use of the inner edge to inner edge convention, in the anteroposterior, mediolateral and inferosuperior directions, as appropriate to the view. Area measurements used the innermost brightest edge reflection as contour. The lines of measurement for the linear dimensions are illustrated in Figure 1. For the parasternal long-axis view, the anteroposterior dimension was taken as the length of a line drawn perpendicular to the left ventricular long axis and extending from the left septal surface to the posterior wall endocardium, passing through the tips of the mitral leaflets. The short-axis mediolateral dimension, at the mitral valve level, was taken as the length of a line drawn through the center of the chamber, parallel to the line connecting the mitral commissures. The anteroposterior line of measurement at this level was drawn orthogonal to and bisecting the
mediolateral dimension. For the short-axis view, at the mid-
papillary muscle level, the mediolateral measurement line was
drawn through the center of the cavity parallel to the line
connecting the tips of the papillary muscles. The anteroposte-
rior line of measurement was drawn perpendicular to and
bisecting the horizontal dimension and it passed vertically
between the two papillary muscles. The apical four chamber
lengths were measured from the apex to the center of the
mitral orifice, midway between the hinge points of the valve
leaflet. In the same four chamber view, the mediolateral
dimension was measured at the midventricular level, along a
line bisecting its length. This corresponds roughly to the
mediolateral dimension at the midpapillary muscle level.

Data analysis. The measurements were entered into a
VAX 11-780 computer in tabular form using the RS1 data
management system (11) to generate graphic displays as
functions of weight, age or body surface area. On the basis of
these examinations, and analysis of residuals after nonlinear
least-squares regressions, the additive errors exponential
growth model was selected:

\[ Y = a X^b + \epsilon, \]

where \( Y \) is the observed measurement, \( X \) is body surface
area computed by the modified DuBois method (11-13), \( a \)
and \( b \) are parameters of the model to be determined by curve
fitting and \( \epsilon \) is distributed as the normal frequency distri-
bution, with a mean of 0 and variance \( \sigma^2 \). The curves were
initially fit by a least-squares nonlinear regression using the
Marquardt algorithm, and then refit weighted inversely to the
observed variance (a minor correction in parameters). Vari-
ance was computed over a sliding window of 50 data points
assigned successively to the mean value of \( X \) for each of the
overlapping windowed ranges. The variance was modeled by
polynomials on \( X = \) body surface area, zero to third order.
The weights (reflecting data confidence) were determined by
interpolation from the third-order polynomial fit. Adequacy of
the univariate exponential growth model above was con-
firmed by linear regression analysis of the residuals.

Results

Measurements. Figures 2 to 11 show the plots of the
observed intracardiac dimensions versus body surface area.
Figure 2 shows the measurements from the parasternal
long-axis view of the anteroposterior dimensions at end-
diastole (Fig. 2A) and at end-systole (Fig. 2B). Figure 3
shows the parasternal short-axis, mitral level, anteroposte-
rior dimensions at end-diastole and end-systole. Figure 4
shows the corresponding measurements at the midlevel of
the papillary muscles. The mediolateral dimensions at the
mitral level are shown in Figure 5 and the mediolateral
dimensions at the midlevel of the papillary muscles in Figure
6. The apical four chamber lengths at end-diastole and
end-systole are shown in Figure 7, and the mediolateral
dimensions from that view in Figure 8. Figure 9 shows the
cross-sectional areas at the mitral level, Figure 10 shows the
cross-sectional areas at the papillary level and Figure 11
shows the areas subtended by endocardium in the apical four
chamber view. The solid line in each graph represents the
curve fit to exponential growth, and the dotted lines above
Figure 3. Parasternal short-axis mitral level anteroposterior dimensions. A, the anteroposterior dimension measured at the level of the mitral valve tips coaptation in the short-axis view at end-diastole (PSMAPD); and B, the same dimension measured at end-systole (PSMAPS). Graph symbols and units are as described for Figure 2.

and below represent the 90% confidence limits (see Discussion) based on the second order, or quadratic, model of variance as a function of body size.

The data also allow comparisons between corresponding measurements by different approaches. For example, the parasternal short-axis view, mitral level, anteroposterior dimension (Fig. 3) corresponds to the anteroposterior dimension measured from the parasternal long-axis view (Fig. 2). Likewise, the mediolateral dimension at mid-ventricular level is measured in both the parasternal short-axis view, midpapillary level (Fig. 6) and in the apical four chamber view (Fig. 8). Comparison of these measurements indicates that the normal values determined by the curve fits as a function of body size are in good agreement. Similarly, there is no significant difference between the mediolateral dimensions from the short-axis versus the apical four chamber views. Furthermore, comparison of the variances shows no appreciable differences in measurement spread for the corresponding measurements from perpendicular views.

With the use of the mediolateral and anteroposterior
dimensions to define an ellipse, those pairs of dimensions provide additional measures of cross-sectional area. Comparing the variance in the projected ellipse areas versus the corresponding areas determined by hand planimetry revealed distinctly narrower error bars with use of the calculated ellipse. For the mitral level at end-diastole, $F = 1.94$, $p = 0.0001$, whereas at end-systole, $F = 1.37$, $p = 0.01$. For the papillary level at end-diastole, $F = 1.74$, $p = 0.0001$, whereas at end-systole, $F = 1.21$, $p = 0.08$.

Discussion

Relation to prior studies. The finding that two-dimensional echocardiographic linear measurements increase as a function of body size is in agreement with previous studies based on earlier technology using blindly performed M-mode measurements (1–7). Furthermore, the exponential growth curvature that fits our data, also fits the data obtained by Roge et al. (4) and Henry et al. (6) for the left ventricular internal dimensions by M-mode study. Those studies also
examined age, weight and other factors and determined that body surface area was the best predictor of variance, and that differences between male and female subjects were negligible. Previous M-mode studies (3,5) have also noted an increase in variance with increasing body size but reported constant width limits to simplify the analysis. The present study differs in that 1) it reports normal dimensions by two-dimensional echocardiography (identifying perpendicular orientation for measurements), rather than by the older technologies; 2) it uses a larger sampling of nonhospitalized normal subjects (not referred to a cardiologist); and 3) the normal limits are based on modeling of variance as well as the linear dimensions as functions of body size, from infancy to full development.

Implications. The multitude of measurements attainable from a two-dimensional echocardiogram allows comparison
Figure 9. Parasternal short-axis mitral level areas. A, The cross-sectional area at the level of the mitral valve tips coaptation in the parasternal short-axis view perpendicular to the long axis at end-diastole (PSMAD); and B, the corresponding measurement at end-systole (PSMAS). Graph symbols and units are as described for Figure 2.

Figure 10. Parasternal short-axis papillary level areas. A, The cross-sectional area at the midlevel of the papillary muscles in the parasternal short-axis view perpendicular to the long axis at end-diastole (PSPAD); and B, the corresponding measurement at end-systole (PSPAS). Graph symbols and units are as described for Figure 2.

of corresponding measurements from different views. There was no significant difference in midnormal values nor in normal limits for comparable dimensions measured in orthogonal views. Furthermore, the anteroposterior and mediolateral dimensions of the left ventricle superimpose at each body size, consistent with circular cross section for normal subjects throughout growth and development.

In keeping with the current status of the technology, our data represent concurrent examinations on subjects whose ages ranged from 6 days to 76 years. Although this allowed determination of normal limits as well as some inferences regarding normal growth and development, it is likely to be less sensitive for analysis of growth and development than would be a serial study with each case serving as its own control.

Sources of variability. Echo quality was not a limitation in this normal study but may be expected to interfere with optimal plane selection and definition of measurements in a
NORMAL LEFT VENTRICULAR DIMENSIONS

Figure 11. Apical four chamber areas. A, The area subtended by the left ventricular endocardium in the apical four chamber view closed by the line connecting the hinge points of the mitral valve leaflets at end-diastole (AFAD); and B, the corresponding measurement at end-systole (AFAS). Graph symbols and units are as described for Figure 2.

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population that does not exclude ailments such as chronic obstructive pulmonary disease. Particularly when quality of images is a limiting factor, variance in results ascribable to technician and to observer become important considerations. Those factors will depend on the laboratory as well as the prevalent diseases, age distribution and other characteristics of the patient population examined and are beyond the scope of this study. The selection of 90% tolerance as the displayed limits of normality is based on selection of appropriate levels for type I and type II error (14). Wider bands representing higher levels of tolerance may be computed from the data in Table 1 based on the z score (14) corresponding to the level of confidence desired. For example, to calculate the 90% tolerance normal limits of the parasternal long-axis anteroposterior dimension in diastole for a subject of body size 1.70 m², Table 1 gives the parameter values \( a = 3.580 \), \( b = 0.418 \), \( P_2 = -0.091 \), \( P_2_1 = 0.247 \) and \( P_2_0 = -0.018 \). These values indicate that the mean for normal subjects of body surface area 1.70 m² is \( aX^b = 3.580(1.70^{0.418}) = 4.47 \) cm, and using the second-order polynomial model for the variance (P2),

\[
V(X) = P_2 X^2 + P_2_1 X + P_2_0 \\
= -0.091(1.70^2) + 0.247(1.70) - 0.018 = 0.14.
\]

One standard deviation is the square root of the variance, that is, \( 0.14^{1/2} = 0.37 \) cm. As 90% limits correspond to a z score of 1.645, the normal limits for this measurement with body surface area 1.70 m², based on 90% tolerance, are 4.47 ± 1.645(0.37), that is, 3.9 to 5.1 cm. These ranges differ somewhat from M-mode normal values.

Clinically, we favor the measurements based on two-dimensional images because blindly obtained M-mode measurements provide fewer landmarks and may overestimate lengths if the single axis is tilted or underestimate the true dimensions if the axis is misaligned entirely. Furthermore, M-mode normal ranges may be misleadingly small because of subjectivity in view selection, whereas views may be defined more objectively with two-dimensional echocardiography to establish perpendicular axes of measurement.

Conclusions. We studied 268 normal subjects to establish the normal limits for left ventricular internal dimensions by cross-sectional echocardiography and to model changes in the cardiac dimensions and in their variance representing normal growth and development. The data fit well to the exponential growth model (r values 0.85 to 0.95). Variance about the central values also depended significantly on body size; that relation was modeled well by a linear function of body surface area (r values 0.75 to 0.97) and better by a quadratic (r values 0.82 to 0.98). The model parameters allow calculation of normal limits at any desired level of confidence. Areas determined by hand planimetry have significantly greater variance compared with variance of cross-sectional areas using ellipses generated from the anteroposterior and mediolateral dimensions, implying that either biologic variations in the amount of infolding or errors in freehand planimetry constitute a significant source of variance (which may be remedied by filtering out high frequency oscillations of contour). There is no significant difference in midnormal values and confidence limits for corresponding dimensions measured from orthogonal views. Furthermore, the anteroposterior and mediolateral dimen-
**Table 1. Left Ventricular Length Dimensions and Areas in 268 Normal Subjects**

<table>
<thead>
<tr>
<th>Y</th>
<th>First-a</th>
<th>First-b</th>
<th>a</th>
<th>b</th>
<th>P32</th>
<th>P31</th>
<th>P30</th>
<th>P22</th>
<th>P21</th>
<th>P20</th>
<th>P12</th>
<th>P11</th>
<th>P10</th>
<th>P00</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFAD</td>
<td>0.726</td>
<td>0.826</td>
<td>20.786</td>
<td>0.827</td>
<td>-26.113</td>
<td>98.808</td>
<td>-83.838</td>
<td>24.478</td>
<td>12.305</td>
<td>2.071</td>
<td>-0.344</td>
<td>29.478</td>
<td>-12.566</td>
<td>18.552</td>
</tr>
<tr>
<td>AFAS</td>
<td>0.726</td>
<td>0.726</td>
<td>12.242</td>
<td>0.757</td>
<td>-15.564</td>
<td>60.467</td>
<td>-50.748</td>
<td>14.980</td>
<td>8.908</td>
<td>0.457</td>
<td>0.185</td>
<td>20.297</td>
<td>-8.663</td>
<td>12.764</td>
</tr>
<tr>
<td>AFMSAD</td>
<td>0.744</td>
<td>0.868</td>
<td>7.205</td>
<td>0.919</td>
<td>-5.441</td>
<td>15.690</td>
<td>-7.778</td>
<td>1.884</td>
<td>-2.183</td>
<td>9.781</td>
<td>-3.116</td>
<td>4.974</td>
<td>-1.012</td>
<td>4.124</td>
</tr>
<tr>
<td>AFPSAP</td>
<td>5.992</td>
<td>0.871</td>
<td>7.565</td>
<td>0.873</td>
<td>-15.642</td>
<td>46.958</td>
<td>-35.569</td>
<td>8.525</td>
<td>-3.099</td>
<td>11.979</td>
<td>-4.483</td>
<td>5.325</td>
<td>-1.677</td>
<td>3.444</td>
</tr>
</tbody>
</table>

The columns headed “first-a” and “first-b” show the values of a and b for the exponential growth model \( Y = a X^b \) obtained by first-pass nonlinear regression. The values a and b show the results of refitting the curve when data confidence is weighted inverse to the variance computed from the first fit. The remaining columns show the results of the polynomial fit to the variance about the growth curve. The values in the columns headed \( P_{32} \), \( P_{31} \), \( P_{30} \), \( P_{22} \), \( P_{21} \), and \( P_{20} \) are the values fit to a third-order polynomial (cubic model): \( P_{32} \) is the coefficient or multiplier of \( X^2 \), \( P_{31} \) is the coefficient of \( X^1 \), \( P_{30} \) is the constant (that is, multiplier of \( X^0 = 1 \)). Analogously, \( P_{22} \), \( P_{21} \), and \( P_{20} \) are the coefficients fit to the second-order or quadratic polynomial model of variance, with the subscript indicating the corresponding power of X. Similarly, \( P_{12} \), \( P_{11} \), and \( P_{10} \) are the coefficients fit to the first-order or linear polynomial and \( P_{00} \) is the result of modeling by a zero-order polynomial or constant (that is, \( P_{00} \) is the mean variance). On the basis of balancing improvement in curve fitting to complexity of the model, the second-order polynomial fit is recommended as one that explains the variance well at minimal cost in complexity. AFAD = apical four chamber, area diastole; AFAS = apical four chamber area, systole; AFLD = apical four chamber length, diastole; AMLS = apical four chamber length, systole; AFMLS = apical four chamber, mediolateral dimension, diastole; AFMLD = apical four chamber, mediolateral dimension, systole; P3P3 = parasternal long-axis, anteroposterior dimension, diastole; PLAPS = parasternal long-axis, anteroposterior dimension, systole; PSPAD = parasternal short axis, mitral, area, diastole; PSPAS = parasternal short axis mitral, area, systole; PSPMAD = parasternal short axis, mitral, anteroposterior dimension, diastole; PSPMAS = parasternal short axis mitral, anteroposterior dimension, systole; PSMAD = parasternal short axis, mitral, anteroposterior dimension, systole; PSMILAD = parasternal short axis, papillary, mediolateral dimension, diastole; PSMILS = parasternal short axis, papillary, mediolateral dimension, systole; PSMILMS = parasternal short axis, papillary, anteroposterior dimension, systole; PSMILPLS = parasternal short axis, papillary, mediolateral dimension, systole.


population with two-dimensional echocardiography (abstr). Clinical Research 1982;30:229A.


