Modeling the influence of body size and composition on M-mode echocardiographic dimensions

ALAN M. BATTERHAM AND KEITH P. GEORGE
Department of Exercise and Sport Science, Manchester Metropolitan University, Crewe and Alsager Faculty, Alsager, Cheshire ST7 2HL, United Kingdom

Batterham, Alan M., and Keith P. George. Modeling the influence of body size and composition on M-mode echocardiographic dimensions. Am. J. Physiol. 274 (Heart Circ. Physiol. 43): H701–H708, 1998.—The purpose of this study was to determine the optimal index for normalizing left ventricular (LV) echocardiographic dimensions for differences in body size. M-mode echocardiograms defined LV internal dimension at end diastole (LVIDD) and LV wall thickness (LVWT) in 107 adults (59 male, 48 female). Allometric relations were assessed between cardiac dimensions (Y) and body size variables (X) of fat-free mass (FFM), height (H), body surface area (BSA), and fat mass (FM). Further to confirmation of homogeneity of regression slopes, size exponents common to both genders were fitted by a log-linear model: ln Y = ln aXb + c·gender + b·ln X, where a is the proportionality coefficient, b is the size exponent, and c is the gender coefficient. For LVIDD, mean body size exponents (95% confidence interval) were FFM0.35 (0.22–0.47), H1.97 (0.32–1.03), and BSA0.44 (0.26–0.62). For LVWT, the derived exponents were FFM0.13 (0.20–0.65), H0.65 (0.1–1.3), and BSA0.36 (0.23–0.89). Body fatness (expressed by FM) had no influence on LV dimensions, with exponents not different from zero (P > 0.05). The root-mean-squares error from the separate regression models indicated that the FFM index was the optimal solution. Indexation of LV dimensions by H was associated with the greatest error. Because the 95% confidence interval for the FFM exponents included 0.33, we recommend that linear LV dimensions be indexed by the cube root of FFM. In the absence of FFM data, the root of BSA was found to be the best surrogate index.

allometric relations; heart size; log-linear models

DESPITE THE ADVENT of two- and even three-dimensional echocardiography (32), M-mode echocardiography continues to be a useful tool in the diagnosis and management of cardiovascular disease (26). In addition, M-mode techniques have been widely applied in the exercise and sport sciences to examine such issues as gender differences in cardiac dimensions (3) and the "athletic heart syndrome" (16, 40). Because of the strong relationship between heart size and body size, cardiac dimensions must be scaled for body size differences to establish reference standards for normality (35) and to permit meaningful intersubject or intergroup comparisons (3).

In the cardiology literature, a variety of different methods of normalizing heart size to account for the influence of body size have been proposed. Traditionally in clinical practice, cardiac dimensions have been divided by body surface area (BSA), although this "cardiac index" has been criticized on theoretical (19) and mathematical (44) grounds. To address these concerns, a number of cross-sectional studies have modeled echocardiographic dimensions using a general allometric equation (e.g., see Refs. 7–10, 23, 24, 30, 45, 47). The allometric model assumes a nonlinear relationship between the body size and heart size variables of the form Y = aXb (where Y is the cardiac dimension, X is the indicator of body size, b is the "dimensionless" size exponent, a is the proportionality coefficient, and e is the multiplicative residual error term). Derivation of b permits the construction of a power function ratio standard (Y/X), which is already size independent.

In studies of these allometric relations, "height" has been the most popular indicator of general body size because it is simple to use and allegedly a surrogate of lean body mass (24). In modeling left ventricular (LV) mass, a variety of different height exponents have been reported, including height1.97 in young, "apparently healthy" men and women from the Framingham Heart Study (23), height2.7 in a large population study of normotensive children and adults (9), and height3 in children and adolescents aged 6–17 yr (7). For linear echocardiographic dimensions, Lauer et al. (24) reported mean height exponents in males and females of 0.57 and 0.50, respectively, for LV internal dimension and 0.84 and 0.41, respectively, for LV wall thickness (LVWT; sum of posterior free wall (PWT) and interventricular septum (ST) thicknesses). It is clear that the majority of studies have focused on echocardiographically predicted LV mass, with less attention paid to LVWT and LV internal dimensions. Allometric relations between body size and linear echocardiographic dimensions, however, are of critical importance in establishing normal limits for quantification of specific disease states (35) and in comparative studies when attempting to differentiate between "concentric" (due to increased LVWT) and "eccentric" (due to increased LV internal dimension) LV hypertrophy (16).

Despite the apparent popularity of indexing cardiac dimensions according to their allometric relations with height, the most appropriate indicator of body size is yet to be defined and remains controversial. It has been suggested that height is superior to BSA normalization,
H 702

MODELING ECHOCARDIOGRAPHIC DIMENSIONS

because the latter masks the observed independent influence of obesity on heart size (22, 25). Others have suggested that the impact of obesity on cardiac dimensions is negligible (2, 8, 17). We believe that the controversy relates to how obesity is operationally defined. Lauer et al. (22, 24) and others (25) have represented obesity by threshold values for body mass index (BMI). It is well known, however, that BMI is influenced to an almost equal degree by the lean and fat compartments of the body (21), indicating that this ratio is unable to distinguish muscularity from adiposity (36). Because a strong link between cardiac and skeletal muscularity has been assumed (16), it is possible that the observed positive relationships between BMI and LV mass (22, 24, 25) are due to the influence of fat-free mass (FFM) rather than to obesity per se. On the basis of this critique, to assess the influence of overfatness or obesity on heart size, we suggest that it is more appropriate to model the influence of estimated fat mass (FM) on cardiac dimensions. Indeed, in contrast to the observed influence of BMI on LV hypertrophy, FM has been found to be of only minor importance in determining cardiac dimensions in children and adolescents (8) and in older adults (2).

Recently, Daniels et al. (8) and Roman (35) have suggested that FFM may indeed represent the optimal parameter for allometric normalization of cardiac dimensions. Estimated FFM has been found to be the strongest predictor of heart size in children and adolescents (7, 47), older adults (2), and younger adults (3, 11, 20, 29). Criterion methods for assessing body composition, such as dual-energy X-ray absorptiometry (DEXA), clearly offer greater precision and accuracy. Indeed, DEXA may be superior to the traditional gold standard of hydrodensitometry, because it is capable of separating the FFM into bone and bone-free compartments (28). Estimation of body composition using DEXA thus circumvents two key assumptions of the two-component model, that the density of the FFM is known and constant and that the components of the FFM normally exist in constant proportions (21).

In clinical practice, however, concerns have been voiced about the practicality of obtaining accurate measurements of FFM using criterion techniques that may be expensive and cumbersome and require highly skilled technicians (35). Methods that are safe, rapid, and acceptably precise and accurate are required for clinical and field testing. For the busy clinician, the choice falls between anthropometry and bioelectrical impedance analysis (BIA). In the field, percent body fat can be estimated using skinfold equations with acceptable accuracy [Ref. 27; standard error of the estimate (SEE) 3–4% fat]. Estimation of body composition using BIA, although rapid and noninvasive, may have limited general applicability because of the lack of appropriately cross-validated prediction equations (15). In a recent report (15), the prediction of body fat percentage using skinfolds (SEE 2.6% fat compared with the criterion derived from densitometry) was found to be more accurate than any of 10 published BIA equations in a population of young adult males. The authors considered that the BIA equations developed by Guo et al. (18) (SEE 2.9% fat) and Segal et al. (39) (SEE 3.3% fat) were acceptable alternatives to the skinfold method. However, both of these equations require additional anthropometry, along with resistance measures, to improve the predictive accuracy of the model. Indeed, the Segal fatness-specific BIA equations (39) require the a priori estimation of body fat percentage from skinfolds to determine which equation to apply. Moreover, results of multiple regression analyses including anthropometric and BIA variables (15, 18) indicate that anthropometric measures account for the majority of the variance in the prediction of body fat percentage. The addition of resistance measures from BIA contributes little to the explained variance and has a marginal effect on the SEE. On the basis of these findings, we believe that, despite the inherent and well-documented limitations (31), anthropometric estimates of FFM can be an extremely useful indicator of general body size. Recently, we have demonstrated (3) the utility of FFM, estimated by skinfolds, in allometric scaling of LV mass in adult males and females, and this is the preferred field method for the current study. In the absence of FFM estimates, an accurate body size surrogate of FFM is required to appropriately normalize cardiac dimensions. To date, insufficient attention has been paid to the determination and critical evaluation of these surrogates.

The aim of the current study was to determine the most appropriate and practical method of normalizing linear echocardiographic dimensions. We modeled the influence of general body size (FFM, BSA, and height) and “fatness” (FM) on LVWT and LV internal dimension. The best potential surrogate of FFM was predicted from a dimensional analysis of the allometric relations between the different body size indicators.

METHODS

Subjects. One hundred and seven Caucasian adults [59 males, age 23.5 ± 3.2 (mean ± SD) yr and 48 females, age 23.7 ± 2.7 yr] volunteered for the study. Subjects were screened medically with a standard laboratory questionnaire, and all were found to be apparently healthy, asymptomatic, and free from cardiovascular disease and major risk factors for coronary heart disease. Exclusion criteria also included the chronic use of medications that may influence resting echocardiographic dimensions. Previous testing in the same laboratory had revealed no evidence of resting or exertional hypertension or electrocardiographic abnormalities. Subject characteristics are displayed in Table 1. Institutional ethics approval for the project and written informed consent from all subjects were obtained.

A simple, “global” self-report assessment of habitual physical activity was obtained through personal interview. The instrument was modified from that used in the Allied Dunbar National Fitness Survey (1), with the frequency and intensity of ≥20-min exercise or activity sessions in the previous 4 wk documented. All subjects were found to be moderately recreationally active, with 49% of males and 46% of females reporting an average of three ≥20-min sessions per week at a “vigorous” exercise intensity (≥7.5 kcal/min). The remainder of the sample reported an equivalent frequency of “moderate” intensity activity (≥5 kcal/min). Male and female activity levels were not significantly different (P > 0.05). There was no relationship (P > 0.05) between physical activity status...
Allometric relationships were derived from technical quality (12). Measurements represented an average of held expiration, at the peak of a simultaneous electrocardio-

Allometric relationships were derived from natural log transformations (base $e$) of the absolute data. The general curvilinear allometric equation $Y = ax^b$ can be linearized by taking natural logarithms of both sides: $\ln Y = \ln a + \ln b \ln X + \ln \varepsilon$. The exponent $b$ is simply the slope of the log-linear plot, and $a$ is derived from the antilog of the $Y$-intercept. All exponents were calculated as mean point estimates, with 95% confidence intervals (CI). Statistical significance of the coefficients was tested at an $\alpha$ level of 0.05.

Allometric relations between body size indicators. To predict the optimal surrogate of FFM, a dimensional analysis was conducted of the allometric relations between the different body size variables. Estimated FFM was modeled as the dependent variable ($Y$), with H and BSA included separately as independent variables ($X$). To check whether a single model common to both genders could be identified, homogeneity of regression slopes (43) was confirmed by including gender ($G$, coded “0” for males, “1” for females), and a $G \times \ln$BSA (or $G \times \ln H$) interaction term in a multiple log-linear regression model

$$\ln FFM = \ln a + d(G \times \ln BSA, or G \times \ln H) + cG$$

$$+ b\ln BSA (or b\ln H) + \ln \varepsilon$$

The interaction terms ($d$) for both $\ln BSA$ and $\ln H$ were not significant ($P > 0.05$), indicating commonality of slopes between gender for the relationships between $\ln FFM$ and $\ln BSA$ and between $\ln FFM$ and $\ln H$. Single solutions, common to both males and females, could therefore be obtained from the following model, omitting the interaction term

$$\ln FFM = \ln a + cG + b\ln BSA (or b\ln H) + \ln \varepsilon$$

The separate BSA and H prediction models were evaluated by comparing the model $R^2$ and root-mean-squares error and the relative width and stability of the 95% CI surrounding the mean $b$, exponents.

Allometric relations between body size and cardiac dimensions. To evaluate whether allometric normalization models can reduce the between-gender variability of cardiac dimensions, it is necessary to derive a common power function ratio standard ($Y/X^c$). With this index, male and female cardiac dimensions can be compared in the same units of measurement. Clearly, this is possible only if homogeneity of regression slopes is confirmed, that is, there is no significant gender difference in the slopes of the log-linear relationships between body size indicators and cardiac dimensions. Therefore, allometric relations between the indicators of body size ($X$) and the echocardiographic dimensions ($Y$) were determined, as per the previous dimensional analysis

$$\ln LVWT (or \ln LVIDD) = \ln a$$

$$+ d(G \times \ln FFM, G \times \ln BSA, or G \times \ln H) + cG$$

$$+ b\ln FFM (or b\ln BSA, b\ln H) + \ln \varepsilon$$

All $G \times \ln X$ interaction terms were nonsignificant ($P > 0.05$), indicating that allometric models common to males and females could be fitted by omitting the interaction term

In $\ln$LVIDD = $\ln a$

$$+ cG + b\ln FFM (or b\ln BSA, or b\ln H) + \ln \varepsilon$$

In $\ln$LVWT = $\ln a + cG$

$$+ b\ln FFM (or b\ln BSA, or b\ln H) + \ln \varepsilon$$

By taking antilog of the constant ($\ln a$) and the constant plus gender coefficients ($\ln a + c$), the “proportionality coefficients” (a) in the allometric relationships $Y = ax^b$ were obtained for

<table>
<thead>
<tr>
<th>Variable</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>$n$</td>
<td>59</td>
<td>48</td>
</tr>
<tr>
<td>BM, kg</td>
<td>75.1 ± 8.4*</td>
<td>60.1 ± 8.5</td>
</tr>
<tr>
<td>BSA, m²</td>
<td>19.2 ± 0.12*</td>
<td>1.67 ± 0.13</td>
</tr>
<tr>
<td>FFM, kg</td>
<td>65.3 ± 5.6*</td>
<td>46.4 ± 5.0</td>
</tr>
<tr>
<td>H, m</td>
<td>1.77 ± 0.06*</td>
<td>1.66 ± 0.07</td>
</tr>
<tr>
<td>FM, kg</td>
<td>9.8 ± 3.9*</td>
<td>13.7 ± 4.8</td>
</tr>
<tr>
<td>%Fat</td>
<td>13.0 ± 4.0*</td>
<td>22.8 ± 5.0</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>24.0 ± 2.5*</td>
<td>21.8 ± 2.7</td>
</tr>
<tr>
<td>LVIDD, cm</td>
<td>5.3 ± 0.4*</td>
<td>4.8 ± 0.3</td>
</tr>
<tr>
<td>LVWT, cm</td>
<td>1.9 ± 0.2*</td>
<td>1.5 ± 0.2</td>
</tr>
</tbody>
</table>

Values are means ± SD; n, no. of subjects. BM, body mass; BSA, body surface area; FFM, fat-free mass; H, height; FM, fat mass; %Fat, body fat percentage; BMI, body mass index (BM/H²); LVIDD, left ventricular internal dimension at end diastole; LVWT, left ventricular wall thickness (sum of posterior wall and interventricular septum thicknesses). *Different from females ($P < 0.05$).
mas and females, respectively. Direct gender comparisons could then be made with respect to appropriately normalized cardiac dimension, to evaluate the reduction in between-gender variability due to each scaling model. Additional information regarding the optimal body size indicator was again obtained by comparing the model $R^2$ and root-mean-squares error from the separate regression models, together with the relative width and stability of the CI surrounding the mean size exponents.

The best surrogate of the optimal body size parameter was determined by comparing the 95% agreement limits (5) between the LVDD and LVWT values predicted by the obtained optimal model and the corresponding values predicted by the surrogate models.

**RESULTS AND DISCUSSION**

The physical and physiological characteristics of the subjects in the current study (Table 1) are remarkably consistent with those reported in the healthy, body size-restricted sample of men and women from the Framingham Heart Study (24). This suggests that our sample is adequately representative of a normal adult population. The prevalence of overweight and obesity in men in the current study compares well with that reported in the Allied Dunbar National Fitness Survey (1) for the equivalent age group. For women, the data indicate that the subjects in our sample were slightly leaner than the national average. Clearly, therefore, caution must be exercised in extrapolating the findings of the current study to populations with different body size and composition characteristics. All body size and heart size variables demonstrated significant gender differences. On average, females were 0.11 m shorter and 15 kg lighter, with 18.9 kg less FFM. In absolute terms, females possessed ~91% of the LVDD and 79% of the LVWT of males.

Kolmogorov-Smirnov one-sample tests revealed that the independent and dependent log-transformed variables, together with the allometric model residuals, were normally distributed ($P > 0.1$). In addition, no correlation was found between the absolute residuals and the predictor (independent) variables for any of the allometric models analyzed ($P > 0.05$), indicating that the model assumption of homoscedasticity had been satisfied.

Allometric relations between body size indicators. For estimated FFM modeled by BSA, the following solution was obtained

$$
\ln \text{FFM} = 3.33 (3.25–3.39) - 0.16 (-0.18 \text{ to } -0.14) \ln \text{BSA} + 1.32 (1.20–1.43) \ln \text{BSA}
$$

where model $R^2 = 0.96$, $P = 0.0000$, and model root-mean-squares error = 0.04. Separate $\beta$-coefficients for constant, gender, and BSA were all significant at $P = 0.0000$. Allometric relations between estimated FFM and H were best represented by the equation below

$$
\ln \text{FFM} = 3.24 (3.00–3.49) - 0.24 (-0.28 \text{ to } -0.20) \ln \text{H} + 1.63 (1.21–2.06) \ln \text{H}
$$

where model $R^2 = 0.84$, $P = 0.0000$, and model root-mean-squares error = 0.08. Separate $\beta$-coefficients for constant, gender, and H were all significant at $P = 0.0000$.

This simple dimensional analysis of the allometric relations between indicators of body size suggests that BSA is superior to H as a surrogate of FFM in young, moderately active adults of average-to-lean body fatness. This finding is in agreement with previous literature (42) in which stature was found to be an ineffective predictor of FFM when used alone. The BSA model is able to explain 12% more of the variance in FFM and has a much smaller root-mean-squares error. In addition, the width of the confidence interval around the mean body size exponent is much broader for H, suggesting that the H exponent is relatively less stable.

The mean exponent for BSA of 1.32 (95% CI 1.20–1.43) is representative of slight “negative allometry.” Simple dimensionality theory (38) predicts that FFM (a 3-dimensional construct) would be proportional to BSA (a 2-dimensional construct) to the power of 1.5, to maintain dimensional consistency or “isometry.” The upper limit of the 95% CI for the BSA exponent, however, excludes 1.5.

The mean exponent for H of 1.63 (95% CI 1.21–2.06) again indicates negative allometry. Dimensional consistency would require that FFM be proportional to the cube of height (a linear dimension), a value precluded in the current analysis. The 95% CI for the H exponent includes 2, indicating that in this sample FFM is approximately proportional to height squared. This result is remarkably consistent with previous findings in adults. In a population study of >3,000 adult males and females (age 16–64 yr), Nevill and Holder (33) reported that estimated FFM was proportional to the square of height in all groups except female subjects aged ≥55 yr (where the H exponent was <2). In contrast, Daniels et al. (7) reported that FFM, determined by DEXA, was proportional to height cubed in children and adolescents. Such differences in the reported allometric relations between FFM and H in different populations may well explain the wide range of H exponents obtained in allometric modeling of LV mass. Previously reported H exponents for LV mass of 1.97 in adults (23) and 3.0 in children and adolescents (7) are entirely consistent with the foregoing analysis. Clearly, these findings lend indirect support to the pivotal role of FFM in determining echocardiographic dimensions.

Allometric modeling of LVDD and LVWT. The findings from the specific allometric models are presented in Tables 2 (LVDD) and 3 (LVWT). All allometric models were successful in providing dimensionless size exponents, with no residual correlations evident ($P > 0.05$) between the power function ratio-scaled cardiac dimension variable ($Y/X^p$) and the body size variable ($X$). In addition, examination of the model residuals revealed no (linear or curvilinear) size-related distributional patterns ($P > 0.05$), indicating that the log-linear
Table 2. Body size exponent b derived from log-linear allometric models

<table>
<thead>
<tr>
<th>Size Variable (X)</th>
<th>b Exponent (95% CI)</th>
<th>ln a</th>
<th>c</th>
<th>Model 1 R²</th>
<th>Model 1 RMSE</th>
<th>P Value of Size Exponent</th>
</tr>
</thead>
<tbody>
<tr>
<td>FFM</td>
<td>0.35 (0.22–0.47)</td>
<td>0.22</td>
<td>0.023</td>
<td>0.48</td>
<td>0.0618</td>
<td>0.0000</td>
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<tr>
<td>BSA</td>
<td>0.44 (0.26–0.62)</td>
<td>1.38</td>
<td>-0.034</td>
<td>0.44</td>
<td>0.0640</td>
<td>0.0000</td>
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<tr>
<td>H</td>
<td>0.68 (0.32–1.03)</td>
<td>1.28</td>
<td>-0.054</td>
<td>0.40</td>
<td>0.0663</td>
<td>0.0003</td>
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<td></td>
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<tr>
<td>FM</td>
<td>0.02 (–0.017–0.06)</td>
<td>1.61</td>
<td>-0.103</td>
<td>0.32</td>
<td>0.0703</td>
<td>0.2650</td>
</tr>
</tbody>
</table>

Model is described by ln LVIDD = ln a + 0.35 ln X + ln e. RMSE, root-mean-squares error; G, gender (coded 0 for male, 1 for female); ln a, point estimate of constant term (Eq. 1); c, point estimate of coefficient for gender term (Eq. 1).

The derived body size exponents are consistent with the foregoing dimensional analysis. If LV mass (a 3-dimensional construct) is assumed to be directly proportional to the first power of FFM, as we have previously reported (3), then it follows that linear echocardiographic dimensions should relate to the cube root of FFM (FFM^{0.33}). The 95% CI surrounding the FFM exponents for LVIDD and LVWT both include 0.33 (Tables 2 and 3). Indeed, the point estimate for the FFM exponent for LVIDD is very close to 1/3. The dimensional analysis revealed that FFM in this sample was proportional to BSA to the power of 0.33 (Tables 2 and 3). For LVIDD (Table 2), the mean BSA exponent is exactly 0.44. For the LVWT model (Table 3), the 95% CI for the BSA exponent includes this value. In practice, however, because the 95% CI for the exponent also includes the value of 0.5, it would be more convenient to scale LVIDD and LVWT by the square root of BSA, as recommended by Gutsev and Rembold (19). Simple dimensionality theory would predict that linear cardiac dimensions should be indexed by the first power of height. However, this would only be so if FFM and LV mass were related to the cube of height. Because we have stated that in adults these variables appear to be proportional to height squared, it follows that LVIDD and LVWT should scale with height to the power of 2/3.

Consistent with this prediction, Tables 2 and 3 show that the mean H exponents for both LVIDD and LVWT are very close to 2/3. Within 95% confidence limits, however, these height exponents are not different from unity (P > 0.05) or from previously reported values for the equivalent cardiac dimensions in large population samples (24).

For both linear echocardiographic dimensions, the model including FFM as the body size indicator provides the highest R² and lowest root-mean-squares error. This finding supports the well-documented observation that FFM is the strongest univariate predictor of heart size (e.g., see Refs. 3, 8, 29, 47). Conversely, modeling echocardiographic dimensions by height results in the lowest R² and highest root-mean-squares error of the three general body size indicators. All size exponents are statistically significant, however, and the differences in variance of cardiac dimension accounted for are relatively modest. Additional insight can be gained from the width of the CI surrounding the size exponent. The relatively wide CI surrounding the equivalent cardiac dimensions, especially for the LVWT model, suggests that this point estimate is less stable and potentially less generalizable to other populations than either the FFM or BSA exponents.

Modeling of cardiac dimensions by FFM sheds light on the influence of body fatness on LV dimensions. Tables 2 and 3 reveal that FFM was not a significant determinant of LVIDD or LVWT in this sample, with b exponents not significantly different from zero. The magnitude of effect of FM on LV dimension can be quantified by an analysis of the mean exponents. The β-coefficient for FM signifies the predicted increase in the specific LV dimension, associated with a 1-unit increase in log e FM. Because the back-transformation of a log-transformed variable provides a ratio (4), a 1-unit increase in log e FM represents a 2.718-fold increase (antilog of 1 = 2.718, base e). For LVIDD, the mean β-coefficient of 0.35 indicates that a 2.718-fold increase in FM is associated with only a 2% increase in the cardiac dimension (antilog of 0.35 = 1.02). For LVWT, the equivalent increase in FFM is associated with only a 6% increase in the dependent variable (antilog 0.06 = 1.06). In contrast, the corresponding predicted increments in LV dimensions associated with a 2.718-fold increase in FFM are 42% for LVIDD (antilog 0.35 = 1.42) and 54% for LVWT (antilog 0.43 = 1.54). Modeling of echocardiographic dimensions by gender and FFM was associated with the lowest R² and highest root-mean-squares error overall. It would appear that in this sample of young, healthy adults, body fat has a negligible impact on LV hypertrophy, as has previously been reported in children and adolescents (8) and older adults (2). We urge caution in extrapolating this finding to larger and diverse population samples, however, in which a greater degree and a higher prevalence of overweight or obesity may influence the results.

As detailed in METHODS, the relative reduction in between-gender variability due to different scaling models can be evaluated by calculating the separate
proportionality coefficients (a) in the allometric equations for males and females, assuming a common size exponent (b). For comparison, findings are presented for FFM and H (the body size indicators associated with the lowest and highest root-mean-squares error, respectively) in modeling LVIDD and LVWT. For modeling of LVIDD by FFM, in males LVIDD (cm) = 1.25·FFM (kg)0.39 and in females LVIDD (cm) = 1.28·FFM (kg)0.35 (female/male percentage, 102%, P = 0.34). For modeling of LVIDD by H, in males LVIDD (cm) = 3.60·H (m)0.67 and in females LVIDD (cm) = 3.41·H (m)0.67 (female/male percentage 95%, P = 0.002). For modeling of LVWT by FFM, in males LVWT (cm) = 0.33·FFM (kg)0.43 and in females LVWT (cm) = 0.30·FFM (kg)0.43 (female/male percentage 91%, P = 0.03). For modeling of LVWT by H, in males LVWT (cm) = 1.33·H (m)0.65 and in females LVWT (cm) = 1.08·H (m)0.65 (female/male percentage 81%, P = 0.0000).

The findings confirm that indexation of cardiac dimensions by FFM, raised to its allometric power, is most effective in reducing between-gender variability. For LVIDD, significant absolute gender differences (females 91% of male value) disappear when the data are appropriately normalized for differences in FFM. For LVWT, although the differences in FFM-adjusted values remain significant, between-gender variability is considerably reduced. Females possess 91% of the male FFM-adjusted value compared with 79% in absolute terms. These results are concordant with previous findings reported in the literature. Devereux et al. (11) reported that scaling LV mass by lean body mass, estimated by 24-h urinary creatinine excretion, eliminated gender differences in absolute LV mass. Furthermore, we have previously demonstrated the ability of an allometric model using FFM, estimated by skinfolds, to reduce between-gender variability in LV mass (3). In contrast, the present results for height-adjusted cardiac dimensions illustrate that between-gender variability remains almost as high as the unadjusted absolute values, especially for LVWT.

FFM surrogates: Bland-Altman agreement limits. The preliminary dimensional analysis suggested that BSA would be the best surrogate of FFM for modeling echocardiographic dimensions. The LVIDD and LVWT predicted from the allometric models including gender and BSA, and gender and H as predictor variables, were compared with the predicted values from the criterion (optimal) model (including gender and FFM). Bland-Altman plots (5) revealed that for LVIDD, BSA was a more effective surrogate, with a 95% agreement limit of 98–102% of the FFM-predicted value. The corresponding agreement limits for H were 94–106%. For LVWT, a similar picture emerged. Agreement limits for BSA were 96–104% compared with 94–106% for H.

In the current study, the high values for goodness of fit, the low root-mean-squares error, the relatively narrow CIs and stable point estimates, and the demonstrably superior ability to reduce between-gender variability suggest strongly that estimated FFM is the optimal body size parameter for modeling echocardiographic dimensions. Therefore, despite the well-documented limitations (31), we believe that a simple anthropometric estimate of FFM may be more appropriate than height in accounting for the influence of body size on heart size. Future research, on larger samples and diverse populations, is obviously required to substantiate this assertion. Anthropometric variables can be measured rapidly, with acceptable precision, with relatively little specialized training (34), making estimation of FFM viable in clinical practice. If FFM estimates are unavailable or impractical, however, allometric indexation by BSA appears to be the most effective surrogate in young adults of average-to-lean body composition. Scaling by various powers of height has a negligible impact on between-gender variability in cardiac dimensions and demonstrates relatively weaker agreement with criterion modeling by FFM.

Because of the assumed close links between skeletal and cardiac musculature, with testosterone as the primary signal messenger (16), it is likely that measures of "skeletal muscle mass" (MM) would represent an improvement on FFM for modeling echocardiographic dimensions. Indeed, analyses from the Brussels Cadaver Study (6) have revealed that the proportion of adipose tissue-free mass that is composed of MM and bone mass demonstrates considerable intersubject variability. In 25 cadavers, bone mass ranged from 16.3 to 25.7%, and MM from 41.9 to 59.4% of adipose tissue-free mass. If this variability were present in the current sample, an important assumption of the existing allometric model, that MM represents a constant fraction of FFM, would be violated. Hence, in the current study, even indexation of cardiac dimensions by various powers of FFM may be prone to considerable error because of violation of the assumptions of the two-component (FM and FFM) body composition model. Unfortunately, methods such as DEXA and computerized axial tomography show great promise, criterion methods for the in vivo measurement of whole body MM have not been adequately developed and validated (46). At present, it would seem that measures of FFM, preferably by DEXA or alternatively by anthropometric techniques if a simple estimation is required in clinical practice, are the best compromise available.

In conclusion, based on the current findings, together with those of our previous study (3), we recommend indexation of LV mass by FFM to the first power (LVM/FFM) and of linear M-mode echocardiographic dimensions by FFM0.33. Alternatively, for indexation by BSA, the power function ratio standards LV mass/BSA1.3 and LVIDD/BSA0.5 (or LVWT/BSA0.5) seem most applicable, as originally proposed by Gutsev and Rembold (19). Further research is required to test the applicability of these findings to diverse population samples, with different age, racial/ethnic origin, and body size and composition characteristics.

Address for reprint requests: A. Batterham, School of Social Sciences, University of Teesside, Middlesbrough TS1 3BA, UK. E-mail: A.Batterham@ees.ac.uk.

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