The influence of body size on measurements of overall cardiac function

Paul D. Chantler, R. E. Clements, L. Sharp, K. P. George, L.-B. Tan, and D. F. Goldspink. The influence of body size on measurements of overall cardiac function. Am J Physiol Heart Circ Physiol 289: H2059–H2065, 2005. First published June 17, 2005; doi:10.1152/ajpheart.00022.2005.—The purpose of this study was to determine the best scaling method to account for the effects of body size on measurements of overall cardiac function and subsequently the interpretation of data based on cardiac power output (CPO). CPO was measured at rest (CPOrest) and at maximal exercise (CPOmax), on 88 and 103 healthy but untrained men and women, respectively, over the age range of 20–70 yr. Cardiac reserve (CR) was calculated as CPOmax – CPOrest, CPOrest, CPOmax, and CR were all significantly related to body mass (BM), body surface area (BSA), and lean body mass (LBM). The linear regression model failed to completely normalize these measurements. In contrast, the allometric model produced size-independent values of CPO. Furthermore, all the assumptions associated with the allometric model were achieved. For CPOrest, mean body size exponents were BM0.33, BSA0.60, and LBM0.47. For CPOmax, the exponents were BM0.41, BSA0.81, and LBM0.71. For CR, mean body size exponents were BM0.44, BSA0.87, and LBM0.79. LBM was identified (from the root-mean-squares errors of the separate regression models) as the best physiological variable (based on its high metabolic activity) to be scaled in the allometric model. Scaling of CPO to LBM is the scaling exponent) has been reported to be theoretically, physiologically, and statistically superior to RES and other methods of scaling (14, 22, 23, 36).

The most frequently used method of scaling simply divides a physiological variable (y) by body mass (x). However, this approach does not allow for the fact that the relationship between body size and physiological functions are often complex and nonlinear (23). When nonlinear, the linear regression model of RES will either underestimate or overestimate the impact of body size. This can lead to erroneous interpretations and conclusions, with possible therapeutic consequences in treating patients. In addition, RES assumes that the spread of scores around the regression line is constant throughout the range of x and y variables. This assumption of homoscedasticity is unlikely to be valid in subjects who vary greatly in body size (23). Therefore, normalizing physiological data using RES may not be appropriate, even when the least-squares regression line provides a better fit to the data. In contrast, the allometric model of y = axbε has been reported to be theoretically, physiologically, and statistically superior to RES and other methods of scaling (12, 23, 36).

It is also important to identify the most appropriate scaling variable, as well as the correct scaling model. Body mass (BM), BSA, and lean body mass (LBM) have all been used as scaling variables (5, 7, 26). Choosing the most appropriate variable should be based on its biological relevance and the accuracy of its measurement. For example, in cardiology, BSA, which incorporates both height and BM, is routinely used to scale for left ventricular mass (8, 11, 25). Despite the fact that BSA seems appropriate, its use has been criticized on both theoretical (14) and mathematical grounds (32). George et al. (13) have indicated that the best scaling variable for cardiac dimensions would be one that represents the most metabolically active tissues in the body, i.e., muscle or LBM. Although easily and accurately measured in exercise...
physiology, the use of BM to normalize physiological function [e.g., maximal oxygen consumption (VO₂ max), CO, etc.] will often be invalid, as the proportion of muscle mass to total BM will not be constant across different populations of subjects (13). It has been suggested that LBM (6, 13, 26, 27) and the allometric model (13, 23) represent the most appropriate normalization for cardiac structures and functions. Scaling for LBM will allow the independent isolation of a body dimension that relates to high levels of metabolic activity and blood flow (33). Given that CO and CPO are known to respond to the body’s demands for oxygen, it would seem theoretically sensible to scale both to LBM. However, establishing that LBM is the best dimension will depend on the accuracy with which it is measured. The emergence of dual-energy X-ray absorptiometry (DEXA) provides a potentially accurate method of determining LBM, as well as the proportions of adipose tissue and bone (16).

To date, the relationship between CPO, body size, and composition has not been investigated. If measurements of CPO are influenced by body dimensions, then the most appropriate scaling variable and modeling technique need to be identified before comparing and interpreting data between inter- and intragroups of subjects or patients. This study illustrates the impact and importance of normalizing data for differences in body composition before interpreting measurements of overall cardiac function (i.e., CPO) between different populations of subjects or patients.

METHODS

Subjects

Healthy subjects were recruited from the Merseyside community through the use of local media. Eighty-eight untrained healthy men and 103 women ranging from 20–70 yr of age were enrolled. All subjects underwent a medical history/lifestyle questionnaire and a treadmill ECG-exercise stress test. Subjects with any history of obesity, only subjects with a body mass index <35 kg/m² were included in the study. The study was approved by the Liverpool John Moores University Ethics Committee, and all subjects gave their written informed consent.

Power Analysis

The authors chose a prior power of 90% and a correlation coefficient of 0.3 as being of potential clinical relevance. This required a sample size of ~105 subjects. This target was readily met, and indeed surpassed, with 191 subjects eventually being studied, and thereby promoting adequate statistical power.

Protocol for Measuring CPO

Before attending the laboratory for exercise testing, all subjects refrained from consuming food, alcohol, or caffeine for 3 h and from undertaking any exercise (24 h). Measurements of CPO involved two stages separated by a 24-h recovery period.

Stage 1: aerobic capacity (VO₂ max). This stage involved an incremental exercise-stress test on a treadmill to uncover any asymptomatnic cardiovascular problems and the VO₂ max of each subject. For this, we used a ramping protocol, consisting of a preliminary 2-min warm-up stage at 2.2 km/h with no incline, followed by increments in both the speed and gradient of the treadmill at 1-min intervals until reaching volitional exhaustion. The VO₂ max achieved by the subjects will be subsequently used in stage 2 of the protocol to ensure that they were exercising at their physiological limit when CPO max was measured.

A 12-lead ECG was monitored throughout, and the subject’s heart rate (HR) was obtained from this. Blood pressure (BP) was measured at rest and at 2-min intervals up to, and including, maximal exercise by manual auscultation and sphygmomanometry. Breath-by-breath analysis of oxygen consumption (VO₂), carbon dioxide production (VCO₂), end-tidal partial pressure of carbon dioxide, tidal ventilation, and respiratory rate were all measured using the Medgraphics CPX-D system (Medgraphics, St. Paul, MN). VO₂ max was considered to have been reached when a minimum of two of the three following criteria were satisfied: a plateau in VO₂ despite further increases in workload, a HR > 95% of the age-predicted maximal value (220 – age), and a respiratory exchange ratio > 1.10.

Stage 2: measurements of CPO rest and CPO max. Resting CPO involved measuring both BP and CO in a seated position. CO at rest was measured using the CO₂ rebreathing technique of Collier (2) and calculated using the indirect Fick method. The concentrations of gases in the mixture that were rebreathed were 10% CO₂-35% O₂-55% N₂, and the volume was twice that of the subject’s resting tidal volume. Mean CO and MAP were calculated from triplicate measurements, separated by 4 min to allow for CO₂ washout from the circulation.

All subjects then exercised on the treadmill to 100% of their VO₂ max. When VO₂ max, maximal VCO₂, and maximal HR were reached (as established in stage 1), maximal BP was measured and a CO₂ rebreathing maneuver was performed to determine maximal CO. This time, the Defares (9) method and gas concentrations of 5% CO₂-35% O₂-60% N₂ were employed.

Calculations. CPO (in W) was calculated from the averaged CO (l/minute) and MAP (mmHg), i.e., by using

\[ \text{CPO} = (\text{CO} \times \text{MAP}) \times K \]

where \( K \) is the conversion factor \((2.22 \times 10^{-3})\) into watts (4). MAP was calculated as

\[ \text{MAP} = \text{DBP} + 0.412(\text{SBP} – \text{DBP}) \]

where SBP and DBP are systolic and diastolic blood pressures, respectively, measured in millimeters Hg (21).

Body composition. DEXA (Hologic, Horizon Park, Levenssteenweg, Belgium) was used to provide whole body, bone, adipose tissue, and lean body masses.

Scaling of physiological measurements. The relationship between various variable components of body size (e.g., total mass, surface area, lean mass) and CPO were examined using Pearson’s correlation.

Examination of Scaling Models

RES model. For the RES model, the physiological measurements \((y)\) were normalized using the equation (23)

\[ y = a + bx + \epsilon \]

where \( b \) represents the slope of the line of best fit, \( a \) the intercept on the \( y \)-axis, and \( \epsilon \) the additive residual error term.

Allometric model. The allometric equation can be represented as

\[ \ln y = ax^b + \epsilon \]

where \( a \) represents the physiological variable (e.g., CPO max), \( x \) represents the body size variable (e.g., BM), \( b \) represents the proportionality coefficient or constant multiplier, and \( a \) represents the multiplicative residual error term (23). The equation can be linearized by taking natural logarithms of both sides, giving

\[ \ln y = \ln a + b \ln x + \ln \epsilon \]

To evaluate whether a single allometric scaling model would apply to both genders, we sought to investigate whether a size-independent term, \( y a^b \), exists and is applicable to either gender. With this scaling model a
Gender-related differences in cardiac variables

Table 1. Gender-related differences in body dimensions

<table>
<thead>
<tr>
<th>Variables</th>
<th>Men (n = 88)</th>
<th>Women (n = 103)</th>
<th>Differences in Women Relative to Men, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>45.4 ± 1.8</td>
<td>44.3 ± 1.4</td>
<td>−2</td>
</tr>
<tr>
<td>BM, kg</td>
<td>81.5 ± 1.1</td>
<td>66.9 ± 1.0*</td>
<td>−18</td>
</tr>
<tr>
<td>Height, cm</td>
<td>175.9 ± 0.7</td>
<td>164.0 ± 0.6*</td>
<td>−7</td>
</tr>
<tr>
<td>BSA, m²</td>
<td>2.0 ± 0.02</td>
<td>1.7 ± 0.01*</td>
<td>−15</td>
</tr>
<tr>
<td>LBM, kg</td>
<td>59.6 ± 0.7</td>
<td>43.0 ± 0.5*</td>
<td>−28</td>
</tr>
</tbody>
</table>

Values are means ± SE; n = 191. BM, body mass; BSA, body surface area; LBM, lean body mass. *P < 0.05, significant differences between men and women.

approach, the values of male and female CPO no longer need to be compared separately according to gender but can be compared together. Clearly, this is possible only if similar regression slopes were compared separately according to gender but can be compared to - approach, the values of male and female CPO no longer need to be

Table 2. Gender-related differences in cardiac variables at rest and maximal exercise

<table>
<thead>
<tr>
<th>Variables</th>
<th>Men (n = 88)</th>
<th>Women (n = 103)</th>
<th>Difference in Women Relative to Men, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>( CO_{\text{rest}} ), l/min</td>
<td>4.8 ± 0.1†</td>
<td>3.8 ± 0.1†</td>
<td>−21</td>
</tr>
<tr>
<td>( CO_{\text{max}} ), l/min</td>
<td>19.6 ± 0.3</td>
<td>15.1 ± 0.2†</td>
<td>−23</td>
</tr>
<tr>
<td>CPOrest, W</td>
<td>1.0 ± 0.02</td>
<td>0.8 ± 0.02*</td>
<td>−20</td>
</tr>
<tr>
<td>CPOmax, W</td>
<td>5.3 ± 0.09</td>
<td>4.0 ± 0.06*</td>
<td>−25</td>
</tr>
<tr>
<td>CR, W</td>
<td>4.3 ± 0.08</td>
<td>3.2 ± 0.06*</td>
<td>−26</td>
</tr>
</tbody>
</table>

Values are means ± SE; n = 191. \( CO_{\text{rest}} \) and \( CO_{\text{max}} \), cardiac output at rest and at maximal exercise; CPOrest and CPOmax, cardiac power output at rest and at maximal exercise; CR, cardiac reserve. *P < 0.05, †P < 0.001, significant differences between men and women.

Table 3. Direct comparisons of the correlation coefficients for all relationships between cardiac power and body size

<table>
<thead>
<tr>
<th>Variables</th>
<th>CPOrest</th>
<th>CPOmax</th>
<th>CR</th>
</tr>
</thead>
<tbody>
<tr>
<td>BM</td>
<td>0.43*</td>
<td>0.59*</td>
<td>0.55*</td>
</tr>
<tr>
<td>BSA</td>
<td>0.46*</td>
<td>0.65*</td>
<td>0.61*</td>
</tr>
<tr>
<td>LBM</td>
<td>0.52*</td>
<td>0.75*</td>
<td>0.71*</td>
</tr>
</tbody>
</table>

Male and female data were pooled, with n = 191. Significant Pearson’s correlations: *P < 0.01.

that was not constant throughout the range of values. In addition, the ability of the linear or allometric model to provide a size-independent mass exponent was evaluated by correlating the scaled CPO values, obtained from the RES or allometric model, with the variables of body size. This correlation would not be significantly different from zero if the influence of body size has been fully accounted for (1).

Information regarding the most appropriate body dimension was obtained by comparing the model \( R^2 \) (i.e., the ratio of the variance due to treatment and the total variance) and root-mean-squares-error from separate regression models, together with the relative width of the confidence intervals surrounding the mean size exponents.

All the above analyses were carried out using the SPSS 11.0 for Windows statistical package (SPSS, Chicago, IL).

RESULTS

Anthropometric Details

Significant \( (P < 0.05) \) gender-related differences in body composition were found (Table 1). On average, men were 7% taller and possessed larger BM, LBM, and BSA by 18%, 28%, and 15%, respectively, compared with women (Table 1).

Cardiovascular Differences Between Men and Women

The sedentary men also possessed significantly greater hemodynamic values, both at rest and at maximal exercise, than their female counterparts (Table 2). The largest differences between men and women were found in maximal cardiac function with men possessing significantly \( (P < 0.001) \) 25% and 26% greater CPOmax and CR values, respectively, than the sedentary women.

Relationship Between Body Size and CPO

Pearson’s correlations \( (r) \) were significant \( (P < 0.01) \) for all variables of CPO and body dimensions (Table 3). However, LBM presented the strongest correlation with CPOrest \( (r = 0.52) \), CPOmax \( (r = 0.75) \), and CR \( (r = 0.71) \) compared with other body dimensions.

Scaling Model

RES model. Significant \( (P < 0.05) \) correlations were obtained between the absolute residuals and the independent
variables for the relationships analyzed between CPO_max, CR, and all variables of body size by the RES model (Table 4). These indicated that the error around the regression line was not constant. Therefore, the assumption of homoscedasticity was not satisfied. Instead, the error around the regression line increased as the independent variable increased (i.e., heteroscedasticity). However, no such significant correlations were identified between the absolute residuals and the independent variables, together with the allometric model residuals, were revealed that the log-transformed dependent and independent variables for resting CPO (Table 4).

Allometric model. Kolmogorov-Smirnov one-sample test revealed that the log-transformed dependent and independent variables, together with the allometric model residuals, were normally distributed. In addition, no significant correlations were identified between the absolute residuals and the predictor variable (e.g., natural logs of LBM, BM, or BSA) (Table 5), implying that there was homoscedasticity. The absence of correlation between residuals from the log-linear analysis of covariance confirmed the appropriate fit provided by the allometric model.

Analyses on the effects of gender on the relationships between body size and CPO showed that the slopes of the regression lines for male and female values were quantitatively similar. The exponents, b, for body size factors between the male and female subjects were not statistically significantly different (all P > 0.05), and the Δb values were negligible. This allows common exponents to be calculated for both genders and thus direct comparisons irrespective of gender can be made (Table 6).

To check whether the allometric model completely provided size-independent values, Pearson’s correlations were performed between the power functions and the various variables of body size. No significant correlations were found, indicating that the allometric model produced size-independent values of CPO (Table 7). In addition, examination of the model residuals revealed no size-related distribution pattern, indicating that the log-linear model was correctly specified, with the residuals randomly scattered around zero, thus confirming the appropriate fit provided by the allometric model.

Scaling variables. As the allometric model successfully provided dimensionless size exponents, theoretically all body dimensions could be used to scale measurements of CPO. However, when examining the strength of the b exponents, scaling to LBM gave the highest R² and lowest root-mean-squares error. Also, the width of the CIs was relatively narrow for CPO values measured at rest and at maximal exercise. By comparison, values were less precise when using either BM or BSA (Table 6).

The CPO data derived from men and women were reanalyzed by scaling to either BM, BSA, or LBM, with the aim of providing data that were independent of body size (Table 8). Highly significant (P < 0.01) gender-related differences (22–25%) remained for all values of CPO, scaled for BM or BSA (Table 8). The least differences were found when CPOs were normalized with LBM, although the CPOrest and CPOmax scaled to LBM showed 7% difference, with men still showing higher values than women, which remained significant (P < 0.05). In contrast, only when values of CR were scaled to LBM were the gender differences nonsignificant (Table 8).

**DISCUSSION**

More often than not, when cardiac function is assessed in exercise physiology or medical research, indexes of either blood flow (e.g., ejection fraction or cardiac output) or pressure (e.g., wedge pressure), but not both, are measured. As a hydraulic pump, the heart generates both blood pressure and

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**Table 5. Correlation coefficients of the absolute residuals from the allometric model and the independent variables**

<table>
<thead>
<tr>
<th>Size Variable</th>
<th>CPOrest</th>
<th>CPOmax</th>
<th>CR</th>
</tr>
</thead>
<tbody>
<tr>
<td>ln BM</td>
<td>0.09</td>
<td>0.10</td>
<td>-0.09</td>
</tr>
<tr>
<td>ln BSA</td>
<td>-0.06</td>
<td>-0.07</td>
<td>-0.08</td>
</tr>
<tr>
<td>ln LBM</td>
<td>-0.09</td>
<td>-0.03</td>
<td>-0.02</td>
</tr>
</tbody>
</table>

The independent variables are ln BM, ln BSA, and ln LBM; n = 191.

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**Table 6. Exponents of body dimension derived from log-linear allometric models**

<table>
<thead>
<tr>
<th>Size Variable</th>
<th>b Exponent (95% CI)</th>
<th>ln a</th>
<th>Model R²</th>
<th>Model RMSE</th>
<th>P Value for Size Exponent</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Female</td>
<td>Male</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPOrest</td>
<td></td>
<td>0.201</td>
<td>0.239</td>
<td>0.278</td>
<td>0.043</td>
</tr>
<tr>
<td>BM</td>
<td>0.33 (0.11–0.54)</td>
<td>0.201</td>
<td>0.239</td>
<td>0.278</td>
<td>0.043</td>
</tr>
<tr>
<td>BSA</td>
<td>0.60 (0.20–1.01)</td>
<td>0.566</td>
<td>0.664</td>
<td>0.277</td>
<td>0.043</td>
</tr>
<tr>
<td>LBM</td>
<td>0.47 (0.22–0.73)</td>
<td>0.143</td>
<td>0.134</td>
<td>0.275</td>
<td>0.040</td>
</tr>
<tr>
<td>CPOmax</td>
<td></td>
<td>0.714</td>
<td>0.872</td>
<td>0.504</td>
<td>0.023</td>
</tr>
<tr>
<td>BM</td>
<td>0.41 (0.25–0.57)</td>
<td>0.714</td>
<td>0.872</td>
<td>0.504</td>
<td>0.023</td>
</tr>
<tr>
<td>BSA</td>
<td>0.81 (0.52–1.10)</td>
<td>2.532</td>
<td>3.013</td>
<td>0.513</td>
<td>0.022</td>
</tr>
<tr>
<td>LBM</td>
<td>0.71 (0.53–0.89)</td>
<td>0.272</td>
<td>0.285</td>
<td>0.567</td>
<td>0.020</td>
</tr>
<tr>
<td>CR</td>
<td></td>
<td>0.505</td>
<td>0.620</td>
<td>0.435</td>
<td>0.032</td>
</tr>
<tr>
<td>BM</td>
<td>0.44 (0.25–0.62)</td>
<td>0.505</td>
<td>0.620</td>
<td>0.435</td>
<td>0.032</td>
</tr>
<tr>
<td>BSA</td>
<td>0.87 (0.53–1.22)</td>
<td>1.946</td>
<td>2.319</td>
<td>0.445</td>
<td>0.032</td>
</tr>
<tr>
<td>LBM</td>
<td>0.79 (0.57–1.00)</td>
<td>0.164</td>
<td>0.170</td>
<td>0.501</td>
<td>0.030</td>
</tr>
</tbody>
</table>

RMSE, root-mean-squares error; ln a, point estimate of constant term. 95% confidence intervals (CI) are shown in parentheses.

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**Table 7. Pearson’s correlation check for the normalization of cardiac power to variables of body dimension, for men and women**

<table>
<thead>
<tr>
<th>CPO Scaled to the Appropriate b Exponent for Body Size</th>
<th>CPOrest</th>
<th>CPOmax</th>
<th>CR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BM</td>
<td>-0.13</td>
<td>0.09</td>
<td>-0.08</td>
</tr>
<tr>
<td>BSA</td>
<td>-0.09</td>
<td>0.06</td>
<td>-0.07</td>
</tr>
<tr>
<td>LBM</td>
<td>-0.05</td>
<td>-0.01</td>
<td>-0.01</td>
</tr>
<tr>
<td>Women</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BM</td>
<td>-0.05</td>
<td>0.09</td>
<td>-0.08</td>
</tr>
<tr>
<td>BSA</td>
<td>-0.09</td>
<td>0.06</td>
<td>-0.07</td>
</tr>
<tr>
<td>LBM</td>
<td>-0.05</td>
<td>-0.01</td>
<td>-0.01</td>
</tr>
</tbody>
</table>

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SCALING OF CARDIAC POWER OUTPUT

Table 8. Gender-related comparisons of normalized cardiac power output

<table>
<thead>
<tr>
<th></th>
<th>Men</th>
<th>Women</th>
<th>Difference in Relative to Men, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>45.4±1.8</td>
<td>44.3±1.4</td>
<td>-2</td>
</tr>
<tr>
<td>Absolute data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPOrest, W</td>
<td>1.0±0.02</td>
<td>0.8±0.02*</td>
<td>-20</td>
</tr>
<tr>
<td>CPOmax, W</td>
<td>5.3±0.09</td>
<td>4.0±0.06*</td>
<td>-25</td>
</tr>
<tr>
<td>CR, W</td>
<td>4.3±0.08</td>
<td>3.2±0.06*</td>
<td>-26</td>
</tr>
<tr>
<td>CPO scaled to BMb</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPOrest, W/kg BM0.33</td>
<td>0.24±0.01</td>
<td>0.21±0.01†</td>
<td>-13</td>
</tr>
<tr>
<td>CPOmax, W/kg BM0.44</td>
<td>0.88±0.01</td>
<td>0.72±0.01†</td>
<td>-18</td>
</tr>
<tr>
<td>CR, W/kg BM0.44</td>
<td>0.63±0.01</td>
<td>0.51±0.01†</td>
<td>-19</td>
</tr>
<tr>
<td>CPO scaled to BSAb</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPOrest, W/m² BSA0.60</td>
<td>0.7±0.01</td>
<td>0.6±0.01†</td>
<td>-14</td>
</tr>
<tr>
<td>CPOmax, W/m² BSA0.81</td>
<td>3.1±0.05</td>
<td>2.6±0.04†</td>
<td>-16</td>
</tr>
<tr>
<td>CR, W/m² BSA0.87</td>
<td>2.4±0.04</td>
<td>2.0±0.03†</td>
<td>-17</td>
</tr>
<tr>
<td>CPO scaled to LBMb</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPOrest, W/kg LBM0.47</td>
<td>0.15±0.003</td>
<td>0.14±0.003*</td>
<td>-7</td>
</tr>
<tr>
<td>CPOmax, W/kg LBM0.71</td>
<td>0.29±0.004</td>
<td>0.27±0.004*</td>
<td>-7</td>
</tr>
<tr>
<td>CR, W/kg LBM0.70</td>
<td>0.17±0.003</td>
<td>0.17±0.003</td>
<td>0</td>
</tr>
</tbody>
</table>

Data are expressed as means ± SE; n = 191. *P < 0.05, †P < 0.001, significant differences between men and women.

flow, and as such, both components need to be determined if a comprehensive measure of overall cardiac function is to be obtained (4, 29, 35). This is one advantage derived by measuring CPO. Also, because CPO is measured both at rest and during maximal exercise, the functional reserve capacity of the heart can be determined by subtraction of these two values.

This is the first study that has examined the relationship between CPO and various body dimensions and composition. It is clear from the strong positive correlations (Table 2) that body size affects both peak and resting values of CPO. These novel findings highlight the importance of normalizing data appropriately before making comparisons between different populations of individuals or patients.

For data on CPO to become independent of body size, the correct scaling technique must be selected and applied. Frequently when attempting to normalize various physiological variables for differences in body size, many investigators routinely use the linear regression model. The assumption that this model adequately corrects for differences in body size is not always true. Although the use of the allometric scaling model for normalizing cardiac dimensions and functions has become more popular within recent years, its advantages have not yet become widely appreciated. In this study we have shown that the allometric model is superior to the RES model, as only the former fully accounts for differences in body size when comparing data on CPO between men and women (Table 7). In contrast, significant correlations still remained when using the RES model. Hence, it is highly likely that the use of the RES model for scaling CPO data will lead to less precise and possibly erroneous conclusions (e.g., with smaller individuals receiving an arithmetic advantage over larger ones). By way of example, if a man and woman possess the same CPOmax (e.g., 5 W) and BM (e.g., 60 kg), but the man has 10% body fat (LBM = 63 kg) and the woman 25% body fat (LBM = 52.5 kg), the RES model results in a gender difference of 25% in CPOmax. In contrast, when scaled allometrically to the power of 0.71, the difference in CPOmax is only 14%. That is, the RES model produces an error of 11% compared with the allometric model for scaling CPOmax and when comparing these values in men and women. Therefore, for data on CPO to be independent of body size, the correct scaling technique must be selected and applied.

In addition to the scaling model, it is important to establish the body size variable that is the most relevant to normalize CPO. Although for convenience in exercise physiology BM is routinely used as a variable, the contribution that LBM makes toward BM will vary between individuals and between different populations. BM is therefore likely to be less satisfactory as a scaling factor than LBM (13). In contrast, in a clinical setting BSA continues to be the choice of scaling variable for normalizing cardiac structures and function. Its popularity, however, does not necessarily mean that it represents the best method. Here we have examined BSA along with other body size variables. We have clearly shown that BM is the main determinant of CPO, whether measured at rest or during exercise. In addition, the statistical evidence highlights that LBMb was the best variable of body size to scale CPO. Furthermore, like BM, changes in BSA failed to distinguish between differences in body composition, (e.g., as caused by changes in muscularity or obesity). Hence, it is probably an inappropriate scaling variable, especially in populations where changes in body composition occur. Other authors have shown that BSA is not the best variable for normalizing cardiac variables (34). Thus scaling CPO to LBMb effectively reduced the between-gender variability in CPO and CR in particular (Table 8). However, in the absence of research tools such as DEXA that accurately measure LBM, BM or BSA may be used in a clinical or field setting to generate body size-independent CPO data. These can provide alternatives to scaling to LBM, but the limitations of these approaches should be appreciated and noted. However, in a purely experimental setting, we would strongly encourage the determination of LBM, if possible by DEXA.

We are only aware of one previous study in which the relationship between body size and component aspects of cardiac function was examined using the allometric scaling model. In that study, de Simone et al. (7) examined the relationship between CO and body size. However, CO was only measured using M-mode echocardiography and cubing unidimensional measurements under resting conditions, and not during exercise. With a similar subject population to that used here, de Simone et al. (7) scaled CO at rest for BM to the power of 0.41. They concluded that this normalization of CO was essential to establish the effects of obesity on cardiac function. The value of their b exponent was higher than that calculated here for CPOrest, when scaled to either BM (b = 0.33) or LBM (b = 0.47).

According to the theory of geometric similarity, CPO should be related to BM (and therefore to LBM) to the power of 0.67 (15). In our study, CPOrest, CPOmax, and CR were scaled against LBM raised to the power 0.47, 0.71, and 0.79, respectively. Although the exponents b for CPOmax and CR differed slightly, the 95% confidence limits suggest that they were not significantly different from 0.67 (Table 6). The exponent 0.67 was also included in the 95% confidence limits for CPOrest. However, unlike maximal exercise, where all relevant body functions are working close to their limits, it is difficult to attain a uniform basal state. Hence more scatter is often found.
in resting measures. Thus it was not surprising that the $b$
exponent for $\text{CPO}_{\text{rest}}$ was lower than that for $\text{CPO}_{\text{max}}$ or CR. Although we have calculated specific power function ratios for $\text{CPO}$, whether at rest or at maximal exercise, it is important that further empirical studies determine their own scaling
exponents as by their nature they are specific to the population from
which they are determined.

Although the use of LBM represents an improvement on the
conventional approaches of scaling physiological functions to
BM or BSA, it is not perfect because LBM is composed of both
metabolically active (e.g., skeletal and cardiac muscle, etc.)
and less active (e.g., tendons, ligaments, etc.) tissues or organs.
Although under basal conditions, the liver, kidneys, and gastro-
intestinal tract possess high metabolic rates (22), during
vigorous exercise the demands of striated muscles predom-
inate. Therefore, an ideal scaling variable for $\text{CPO}$ would be
one that solely takes into account the most metabolically active
tissues under defined physiological conditions (e.g., skeletal and
cardiac muscles during exercise).

The use of LBM is further dependent on the accuracy by
which it can be measured. In this study, DEXA was used as a
precise technique for measuring various elements of body
composition (17–19). Unfortunately, in practical terms, the
scaling of $\text{CPO}$ data to LBM may be limited by the availability
of appropriate equipment and hence the accuracy with which
LBM can be measured. Calipers have been used extensively to
measure skinfold thickness, and bioelectrical impedance has
been used to measure adipose mass. However, although more
readily available, these methods possess more inherent errors
and do not measure the body’s bone content.

In conclusion, this study has yielded novel findings that
highlight the fact that $\text{CPO}$ is significantly affected by body
size and composition, particularly the amount of metabolically
active lean tissue. If differences in body size, specifically LBM,
are not accounted for before data between inter-and intragroups of subjects or patients are compared and inter-
preted, erroneous conclusions are likely to be made. Therefore,
whenever practically possible, measurements of $\text{CPO}$ should
be scaled for differences in body size, specifically to LBM, and
the allometric model of scaling used. However, further re-
search is required to test the applicability of these findings to
diverse samples of the population to establish the normal range
of exponents for the allometric scaling of $\text{CPO}$. Once the
normal range of exponents has been determined for the diverse
populations (i.e., heart failure), then $\text{CPO}$ can be scaled allo-
metrically on an individual basis.

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