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Sex-specific lean body mass predictive equations are accurate in the obese paediatric population

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Abstract

Background—The clinical assessment of lean body mass (LBM) is challenging in obese children. A sex-specific predictive equation for LBM derived from anthropometric data was recently validated in children.

Aim—The purpose of this study was to independently validate these predictive equations in the obese paediatric population.

Subjects and methods—Obese subjects aged 4–21 were analysed retrospectively. Predicted LBM (LBMp) was calculated using equations previously developed in children. Measured LBM (LBMm) was derived from dual-energy x-ray absorptiometry. Agreement was expressed as [(LBMm-LBMp)/LBMm] with 95% limits of agreement.

Results—Of 310 enrolled patients, 195 (63%) were females. The mean age was 11.8 ± 3.4 years and mean BMI Z-score was 2.3 ± 0.4 . The average difference between LBMm and LBMp was -0.6% (-17.0% , 15.8%). Pearson's correlation revealed a strong linear relationship between LBMm and LBMp ($r=0.97$, $p<0.01$).

Conclusion—This study validates the use of these clinically-derived sex-specific LBM predictive equations in the obese paediatric population. Future studies should use these equations to improve the ability to accurately classify LBM in obese children.

Keywords

Lean body mass; obesity; paediatric cardiology

Introduction

Measurement of lean body mass (LBM) is becoming increasingly recognised as useful in the assessment of obese children. As children become more obese, they not only have increased adipose tissue, but LBM as well. In fact, as LBM is known to be one of the main drivers of

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

energy expenditure, recent equations to estimate energy expenditure needed to be modified for children with a BMI above the 95th percentile (Trumbo et al., 2002).

The relationship between adiposity and LBM complicates many other biologic relationships, as kidney function and cardiac size are known to correlate strongly with LBM. For example, abnormal left ventricular (LV) mass is an independent risk factor for death in many adult and paediatric disease processes (Cuspidi et al., 2015; Fisher et al., 2005; Manyari, 1990; Suda et al., 1997). LV mass is routinely measured in children during echocardiography and magnetic resonance imaging to assess for LV hypertrophy. However, LV mass is proportional to body size. There is controversy regarding the ideal method for which to normalise LV mass (de Simone et al., 2005; Dewey et al., 2008; Foster et al., 2008; Kuch et al., 2001). Numerous normalisation methods have been studied. The most common body size variables in which to index LV mass are height^{2.7} or body surface area (BSA) (de Simone et al., 1992; National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents, 2004). However, these methods have known limitations in the obese population. Scaling to BSA results in under-estimation of relative LV mass among overweight subjects, while scaling to height^{2.7} leads to over-estimation of LV mass in the same population (Foster et al., 2013). The ideal body size variable to which LV mass should be scaled is lean body mass (LBM). Many studies have shown that LBM is the main determinant of LV mass as it explains more of the variance in LV mass than height or weight and also scales best to cardiac output (Bella et al., 1998; Chantler et al., 2005; Collis et al., 2001; Daniels et al., 1995b; Dewey et al., 2008; George et al., 2009; Hense et al., 1998; Kuch et al., 2000).

It is especially important to accurately account for LBM when assessing for cardiac and renal disease in the obese paediatric population due to their increased risk for obesity sequelae, such as hypertension and diabetes mellitus that lead to LV hypertrophy and renal insufficiency. The reference-standard method to measure LBM is by dual-energy X-ray absorptiometry (DXA). However, DXA is not practical to utilise in a clinical setting. In an effort overcome this barrier, Foster et al. (2012) developed and validated a predictive equation for LBM in the paediatric population based on anthropomorphic measures. A limitation to its use is that it has not been independently validated in obese children, the population that has the most to gain from accurate assessment of LV mass. The objective of this study was to independently assess the accuracy of these LBM predictive equations vs measures of LBM derived from DXA in the obese paediatric population.

Methods

This was a retrospective, secondary analysis of a previously performed prospective cross-sectional study whose goal was to assess for racial differences in cardiometabolic risk profiles in obese children. All tests were conducted during a single assessment using a standardised protocol. The protocol was approved by the institutional review board. Informed consent was obtained from the parents or legal guardians of minors or from participants aged 18 years.

Subject population

Obese subjects [body mass index (BMI) >95th percentile] aged 4–21 were recruited from the Medical University of South Carolina's childhood obesity management clinic. Inclusion criteria of the initial study were (1) body mass index (BMI) >95th percentile, (2) aged 4–21 years and (3) white or African-American population ancestry. Subjects who were pregnant, were taking insulin or were taking oral steroids were excluded. Patients were enrolled consecutively as long as they met inclusion criteria. For the purposes of the secondary analysis, patients were excluded if they had a diagnosis of hypertension, diabetes mellitus or structural/ congenital heart disease.

Procedures

Patients' anthropomorphic assessments were performed at the Clinical and Translational Research Centre. Body composition variables included total body fat, percentage body fat and measured lean body mass (LBMm) and were quantified using DXA. Whole body DXA scans were performed on a Hologic Discovery A DXA scanner (Hologic Inc., Waltham, MA) and analysed with the software program Hologic APEX software, version 3.0. This version of the software does account for the over-estimation of LBM found on previous versions (Schoeller et al., 2005). During the scan, the participant was asked to lie supine on the scanning bed with their arms at their sides. The scanner was calibrated daily with a spine phantom and its performance was monitored as per a quality assurance protocol.

Calculations

Previously developed sex-specific equations for predicted lean body mass (LBMp) in children and adolescents were used (Foster et al., 2012). Two sets of equations were developed in the previous study, one set with and one without population ancestry inclusion. They concluded that population ancestry improved the accuracy of the equation by such a small amount that either set of equations could be used. Therefore, we tested both sets of equations.

Equations without population ancestry as a co-factor

$$\begin{aligned} \text{Males:ln (LBM)} &= -2.899 + 0.8064 \times \ln(\text{height}) \\ &\quad + 0.5674 \times \ln(\text{weight}) + 0.0000185 \\ &\quad \times \text{weight}^2 - 0.0153 \times \text{BMIz}^2 \\ &\quad + 0.0132 \times \text{age.} \\ \text{Females:ln (LBM)} &= -3.8345 + 0.954 \times \ln(\text{height}) \\ &\quad + 0.6515 \times \ln(\text{weight}) \\ &\quad - 0.0102 \times \text{BMIz}^2. \end{aligned}$$

Equations with population ancestry as a co-factor

$$\begin{aligned}
 \text{Males:ln (LBM)} &= -2.9585 + 0.8208 \times \ln(\text{height}) \\
 &\quad + 0.5607 \times \ln(\text{weight}) + 0.0000184 \\
 &\quad \times \text{weight}^2 - 0.0159 \times \text{BMIz}^2 \\
 &\quad + 0.0135 \times \text{age} + 0.0225 \\
 &\quad \times \text{African American.} \\
 \text{Females:ln (LBM)} &= -3.9361 + 0.9786 \times \ln(\text{height}) \\
 &\quad + 0.6431 \times \ln(\text{weight}) - 0.0118 \\
 &\quad \times \text{BMIz}^2 + 0.029 \\
 &\quad \times \text{African American.}
 \end{aligned}$$

Statistics

Differences between sexes were tested using independent *t*-tests or chi-square tests. Agreement was reported in the difference between LBMm and LBMp expressed as a percentage error of LBMm (LBMp–LBMm)/LBMm with 95% limits of agreement (mean difference $\pm$ 1.96*standard deviation). Systematic bias in LBMp compared to LBMm was tested using a one sample *t*-test to determine if the percentage error of the mean was statistically significantly different from zero. Differential bias was assessed by performing linear regression percentage error of LBMm vs LBMm, BMI *Z*-score and age to look for evidence of differential bias. Pearson correlation was then performed to evaluate for a linear relationship between measured and calculated LBM. Differences of percentage error of LBMm between sexes was assessed using independent *t*-tests. A *p* value less than 0.05 was considered statistically significant. All statistics were performed using IBM® SPSS® Statistics software v. 22.

Results

A total of 310 patients were included in this secondary analysis, 195 (63%) of whom were female. Demographic information can be found in Table 1.

Agreement between LBMm and LBMp in females

Using calculations that did not include population ancestry, the percentage error of LBMm was 1.4% (95% limits of agreement=–11.0% to 13.8%). LBMp did systematically over-estimate LBMm ($p<0.01$). Pearson's correlation revealed a strong relationship between LBMm and LBMp ($r=0.98$, $p<0.01$).

Using calculations that did include population ancestry, the percentage error of the LBMm was 2.1% (95% limits of agreement=–9.9% to 14.1%) (Figure 1). LBMp did systematically over-estimate LBMm ($p<0.01$). Pearson's correlation revealed a strong relationship between LBMm and LBMp ($r=0.98$, $p<0.01$) (Figure 2). This relationship was stronger than that between LBMm and both BSA ($r=0.97$, $p<0.01$) and height^{2.7} ($r=0.90$, $p<0.01$). It should be noted that the correlation between LBMm and height^{2.7} is identical to that of LBMm vs height ($r=0.90$, $p<0.01$). There was no evidence of differential bias in percentage error of LBMm by age ($R^2=0.00$, $p=0.58$). There is weak positive evidence of differential bias due to LBM ($R^2=0.07$, $p<0.01$) and level of adiposity as measured by BMIz ($R^2=0.07$, $p<0.01$).

Agreement between LBMm and LBMp in males

Using calculations that did not include population ancestry, the percentage error of LBMm was -5.2% (95% limits of agreement= -22.1% to 11.8%). LBMp did systematically under-estimate LBMm ($p<0.01$). Pearson's correlation revealed a strong relationship between LBMm and LBMp ($r=0.98$, $p<0.01$).

Using calculations that did include population ancestry, the percentage error of the LBMm was -4.7% (95% limits of agreement= -21.6% to 12.2%) (Figure 3). LBMp did systematically under-estimate LBMm ($p<0.01$). Pearson's correlation revealed a strong relationship between LBMm and LBMp ($r=0.98$, $p<0.01$) (Figure 4). This relationship was stronger than that between LBMm and both BSA ($r=0.96$, $p<0.01$) and height^{2.7} ($r=0.91$, $p<0.01$). The correlation between LBMm and height^{2.7} is identical to that of LBMm vs height ($r=0.91$, $p<0.01$). There was evidence that LBMp under-estimates LBMm as LBMm ($R^2=0.19$, $p<0.01$) and age ($R^2=0.27$, $p<0.01$) increase. There is no differential bias due to level of adiposity as measured by BMIz ($R^2=0.01$, $p=0.33$). Percentage error of LBMm was statistically significantly different between males and females, $p<0.01$.

Discussion

This study externally validates previously developed sex-specific predictive equations for LBM in obese children and adolescents. We found good agreement between predicted and measured LBM in both obese males and females. We also determined that the equations that included racial ancestry were very slightly superior to those that did not.

These LBM predictive equations were developed in a large paediatric population (Foster et al., 2012). Although only a small number of obese patients were included in their development, the equations accounted for variability in the extremes of BMI. Equations that only include height and weight are often inaccurate at the low and high ends of the BMI spectrum. At higher BMI, additional weight is often adipose tissue. Conversely, at lower BMI additional weight is often LBM. The inclusion of BMIz² helped account for these changes at the far ends of the spectrum with a negative coefficient. For example, when BMIz was positive, indicating a higher BMI and an associated high fat tissue content, the BMIz² was subtracted from the LBM. This decreases the impact of adipose weight to the calculation of LBM and accounts for the accuracy of the predictive equations in this study's obese population.

Our results differ slightly than those from Foster et al. (2012). First, the mean difference between LBMm and LBMp in their obese cohort ($n=70$) was -1.05% for males and -0.68% for females. In contrast, we found that LBMp under-estimated LBMm in males vs over-estimated LBMm in females. In addition, the degree of under-estimation worsened in males as LBMm increased. It is feasible that males have a higher rate of lean body mass acquisition with increasing weight than do females as obesity severity worsens, leading to differential bias. This may be detected in our study, and not by Foster et al., due to the higher levels of obesity seen in the current study. Second, the agreement between LBMm and LBMp in the current study is slightly lower than that found by Foster et al. (2012), although still clinically acceptable. The decreased agreement in our study was again likely due to the

fact that our cohort had an increased severity of obesity compared with the previous study. This likely resulted in increased heteroscedasticity, leading to increased measurement variability in the most obese patients (Sluysmans & Colan, 2005).

The success of the predictive equation has numerous strengths. First, this is a non-invasive predictive model that only requires height, weight and sex. In paediatrics, this is especially important because of the difficulty and morbidity that can be associated with more invasive procedures. Second, in the era of rising healthcare costs it provides an inexpensive modality to calculate LBM. In addition, the ability to assess LBM has important ramifications in many disease processes. It is well known that several clinically important parameters correlate with LBM, such as resting energy expenditure, kidney function and drug dosing (Foster et al., 2012). Clinicians may use these formulae to assess the impact of lifestyle or medical interventions on body composition in obese children. For example, LBM may be used to accurately assess LV mass in children and adolescents. Daniels et al. (1995b) demonstrated that LBM is independently associated with LV mass. Another study demonstrated that LV mass was more strongly related to LBM than to adipose tissue mass or other surrogates for LBM (Bella et al., 1998). It is clear that the ideal body size variable for which to scale LV mass is LBM. Differences in LV mass between males and females disappear when LV mass is expressed relative to LBM (Daniels et al., 1995a). Differences between population ancestries are also eliminated when LBM is accounted for in other cardiovascular measurements, such as carotid intima-media thickness, in obese children (Chowdhury et al., 2014). Validation of these LBM predictive equations will allow researchers to further evaluate the influence of LBM on cardiovascular health in obese children—those who are at most risk for future cardiovascular disease.

Limitations

These equations were developed in those patients 5 years old or greater—their accuracy is unknown in younger children. In addition, since population ancestries other than white and African-American were not included in the analysis, the accuracy of the equations is unknown in other population ancestries. Ideally, this study would have included both non-obese and obese patients so that the accuracy of these equations could be assessed simultaneously in both groups. Unfortunately, a control group is not available currently. The DXA scanner used in this study vs Foster et al.'s was a slightly different model. However, both groups accounted for the over-estimation of LBM using these models of DXA scanners (Foster et al. (2012) did so manually, while our data accounted automatically via software update). These equations may not apply to those patients with an LBM that is unusually high (athletes) or low (chronic disease). While DXA is known to be reasonably accurate and is the reference standard method to assess body composition in the majority of paediatric studies, it is not the true gold-standard.

Conclusion

This study validates the use of these clinically-derived sex-specific LBM predictive equations in the obese paediatric population. Future studies should use these equations to

further study the relationship of cardiovascular structures to LBM in order to improve our ability to accurately classify abnormalities of LV mass in obese children.

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Figure 1.

Bland-Altman plot: LBMm vs LBMp in females. Bland-Altman Plot: Measured vs predicted lean body mass. LBM=lean body mass; % error of LBMm=(Measured LBM–Predicted LBM)/Measured LBM.

Figure 2. Pearson correlation of measured LBM and predicted LBM in females. Pearson's correlation plot. LBMm=measured lean body mass; LBMp=predicted lean body mass.

Figure 3.

Bland-Altman Plot: LBMm vs LBMp in males. Bland-Altman Plot: Measured vs predicted lean body mass. LBM=lean body mass. % error of LBMm=(Measured LBM–Predicted LBM)/Measured LBM.

Figure 4. Pearson correlation of measured LBM and predicted LBM in males. Pearson's correlation plot. LBMm=measured lean body mass, LBMp=predicted lean body mass.

Table 1

Patient demographics.

Measure	Whole group	Males (<i>n</i> =115)	Females (<i>n</i> =195)	<i>p</i> Value [*]
Age (years)	11.8±3.4	11.9±3.0	11.8±3.6	0.53
White, <i>n</i> (%)	144 (46%)	52 (45%)	92 (47%)	0.74
Height (cm)	155±15	159±15	153±15	50.01
Weight (kg)	82.4±28.8	86.7±29.3	79.7±28.2	0.03
BMI (kg/m ²)	33.0±7.4	33.4±7.0	32.8±7.6	0.36
BMI <i>z</i> -score	2.3±0.4	2.4±0.4	2.3±0.4	50.01
% body fat	40.7±5.4	39.6±5.8	41.4±5.0	0.01
LBM index (kg/m ²)	18.5±3.3	19.1±3.5	18.1±3.2	0.01

^{*} *p* Values compare for differences between males and females. Values reported are mean±standard deviation. BMI, body mass index; LBM, lean body mass.