Limitations of Expressing Left Ventricular Mass Relative to Height and to Body Surface Area in Children

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Background: Left ventricular (LV) mass varies in proportion to lean body mass (LBM) but is usually expressed relative to height or body surface area (BSA), each of which functions as a surrogate for LBM. The aims of this study were to characterize the adiposity-related biases associated with each of these scaling variables and to determine the impact of these biases on the diagnosis of LV hypertrophy (LVH) in a group of children at risk for LVH.

Methods: In a retrospective study, LV mass was estimated using M-mode echocardiography in 222 healthy nonoverweight reference children and 112 children "at risk" for LVH (48 healthy overweight children and 64 children with hypertension). LBM was estimated for all children using validated predictive equations and was considered the criterion scaling variable. *Z* scores for LV mass for LBM, LV mass for height, and LV mass for BSA were calculated for each child relative to the reference group. The performance of height-based and BSA-based *Z* scores were compared with that of LBM-based *Z* scores at different levels of adiposity (estimated by the *Z* score for body mass index for age [BMIz]).

Results: Among healthy normotensive children, LV mass–for–height *Z* scores were greater than LV mass–for–LBM *Z* scores at higher values of BMIz and lower than LV mass–for–LBM *Z* scores at lower values of BMIz (R^2 = 0.52, $P < .0001$). LV mass–for–BSA *Z* scores for agreed well with LBM-based *Z* scores at BMIz < 0.7 but were lower than LV mass–for–LBM *Z* scores for at BMIz > 0.7 (R^2 = 0.31, $P < .0001$). Compared with 13% of at-risk children classified as having LVH on the basis of LV mass for LBM > 95th percentile, 30% and 11% had LVH when LV mass was scaled to height and BSA, respectively.

Conclusions: Scaling LV mass to BSA in children results in less misclassification with respect to LVH than does scaling to height. (J Am Soc Echocardiogr 2013;26:410-8.)

Keywords: Left ventricular hypertrophy, Pediatric, Percentile curves, *Z* scores, Indexing, Scaling

Left ventricular (LV) mass is routinely measured during echocardiography in an effort to determine whether LV hypertrophy (LVH) is present. Normally, LV mass should be proportional to body size, so measures of LV mass must be normalized to determine appropriateness relative to body size. This is particularly important in children, among whom variability in body size is large. There has been some controversy regarding the best method of normalizing LV mass,[1-3] and there have been calls to develop a standardized approach.[4] When deciding how best to normalize LV mass for body size, two separate factors must be considered: the normalization method and the most appropriate body-size variable against which to normalize LV mass measurements.[5]

Most prior studies considering the question of how best to normalize LV mass for body size conflated the two issues of normalizing variable and normalizing method.[1,6] Allometric methods (in which LV mass is divided by a body-size variable raised to a power) applied to one scaling variable were compared with ratiometric methods (in which LV mass is simply divided by a body-size variable) applied to another variable, making it impossible to separate the importance of the scaling method from that of the scaling variable. Even when a consistent scaling method was applied, comparisons did not include all the most physiologically relevant scaling variables.[7] The

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Abbreviations
BMIz = Body mass index *Z* score
BSA = Body surface area
LBM = Lean body mass
LMS = Lambda mu sigma
LV = Left ventricular
LVH = Left ventricular hypertrophy
2D = Two-dimensional

question of the most appropriate body-size variable against which to normalize LV mass measurements has not yet been adequately addressed. This issue has become increasingly important as the prevalence of obesity has increased. The most commonly used LV mass scaling variables (height and body surface area [BSA]) may introduce important bias in the setting of overweight or obesity. Several studies concluded that LVH is significantly associated with childhood obesity, without fully accounting for the potential impact of the choice of LV mass scaling variable on diagnosis of LVH.[8,9]

It has been demonstrated repeatedly that LV mass is strongly determined by lean body mass (LBM).[2,5,10-15] LBM explains more of the variability in LV mass than either height or weight alone,[3,11-14] and when LV mass is expressed relative to LBM, sex differences are eliminated.[10] Cardiac output also scales best to LBM.[15] However, LBM is not easily measured in the clinical setting. Therefore, other measures, including height, weight, and BSA,[16,17] have been used as surrogates for LBM. However, these LBM surrogates have important limitations.

BSA is estimated from height and weight using predictive equations. BSA depends strongly on weight and thus has been criticized as a scaling variable for LV mass, particularly among obese individuals.[6] Because adipose tissue makes up a greater proportion of the weight in obese than in nonobese individuals, there is concern that scaling LV mass to BSA may result in underestimation of relative LV mass among overweight subjects. This theory is based on the observation that compared with lean tissue, fat is less metabolically active and therefore creates less cardiac demand.[11]

In recognition of this potential problem, height has been advocated as a more appropriate variable against which to normalize LV mass.[6,18] However, height alone may be a suboptimal surrogate for LBM. There is considerable variability in LBM among individuals of the same height. Importantly, an overweight individual will have not just a higher fat mass but a higher LBM than a normal-weight individual of equal height.[14,19,20] As a result, expressing LV mass relative to height may result in overestimation of the relative LV mass among overweight individuals.

We hypothesized that expressing LV mass relative to height would result in increasing overestimation of relative LV mass with increasing adiposity and that expressing LV mass relative to BSA would result in increasing underestimation of relative LV mass with increasing adiposity. We sought to characterize the adiposity-related biases associated with using each of height and BSA as scaling variables for LV mass and to compare the performance of each scaling variable with that of LBM with respect to the ability of each to identify LVH in a group of children at risk for LVH; LBM was considered a "reference standard" scaling variable. To increase the accessibility of LBM as a potential scaling variable, we developed and validated predictive equations to estimate LBM from easily measured variables; details of the development of these equations are published elsewhere.[21] We applied the same normalizing method to each scaling variable to ensure that observed differences were due to scaling variable and not to method.

METHODS

This was a retrospective study, conducted using echocardiograms of children seen for clinical evaluation in the echocardiography laboratories at Boston Children's Hospital and Montreal Children's Hospital. Only children free of congenital lesions were included in this study.

Healthy Normotensive Subjects

Healthy, nonoverweight children (body mass index for age < 85th percentile[22]; $n = 222$; age range, 5–21 years) and otherwise healthy overweight children ($n = 48$) were all evaluated in Boston. These subjects were included in a prior research study conducted at Boston Children's Hospital[23] (the protocol was approved by the institutional review board, and all subjects or their guardians gave written informed consent when required). All subjects were free of systemic disease; none had a family history of cardiomyopathy. All subjects were reevaluated 1 year later to verify that they remained free of any identifiable systemic disorder, including hypertension. The 222 nonoverweight children formed the reference group used to generate the reference centile curves. Overweight subjects were not included in the reference group, because of concern that overweight may be a risk factor for LVH, even in the absence of hypertension.[8,9] Race was not recorded.

Subjects "at Risk" for LVH

A group of 112 children considered to be "at risk" for LVH was assembled by combining the 48 healthy overweight children from Boston with 64 hypertensive children studied at Montreal Children's Hospital. To identify hypertensive children, we reviewed the medical records of all children evaluated in the Montreal Children's Hospital Division of Nephrology between July 1999 and June 2006 and identified all those assessed for hypertension; all children assessed for hypertension for whom cardiac echocardiography was done, and who were free of congenital lesions, were included. Race was not recorded.

Figure 1 illustrates the composition of each of the reference, healthy overweight, healthy normotensive, and "at risk for LVH" groups.

Echocardiography

Echocardiography was performed using commercially available cardiac ultrasound scanners and recorded on videocassettes. Each study was reviewed by a single pediatric cardiologist at each site for the purposes of this study. We measured septal, free wall, and LV ventricular chamber dimensions at end-diastole, where end-diastole is defined as maximum dimension. M-mode echocardiograms were recorded from parasternal short-axis views using the tissue-blood interface (inner edge to inner edge), and values were calculated as the average of three successive heartbeats. At the Boston site, the LV surface of the ventricular septum and the endocardial and epicardial borders of the LV posterior wall were hand digitized with a computer-based digitizing station using custom software. LV septal, free wall, and chamber dimensions were calculated from the digitized borders as continuous variables throughout the cardiac cycle. In Montreal, electronic calipers were used for all measurements. LV mass was estimated using the Devereux equation.[24] We used M-mode rather than two-dimensional (2D) images because this is the method used most frequently in quantitative echocardiographic research in children.[8,9,16,17,25]