Left Ventricular Mass Indexing in Infants, Children, and Adolescents: A Simplified Approach for the Identification of Left Ventricular Hypertrophy in Clinical Practice

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Objective To determine a simplified method to identify presence of left ventricular hypertrophy (LVH) in pediatric populations because the relationship between heart growth and body growth in children has made indexing difficult for younger ages.

Study design Healthy children (n = 400; 52% boys, 0-18 years of age) from 2 different European hospitals were studied to derive a simplified formula. Left ventricular mass (LVM) was calculated according to the Devereux formula. The derived approach to index LVM was tested on a validation cohort of 130 healthy children from a different hospital center.

Results There was a strong nonlinear correlation between height and LVM. LVM was best related to height to a power of 2.16 with a correction factor of 0.09. Analysis of residuals for LVM/[(height$^{2.16}$) + 0.09] showed an homoscedastic distribution in both sexes throughout the entire height range. A partition value of 45 g/m$^{2.16}$ was defined as the upper normal limit for LVM index. As opposed to formula suggested by current guidelines (ie, LVM/height$^{2.7}$) when applying the proposed approach in the validation cohort of 130 healthy participants, no false positives for LVH were found (0% vs 8%; $P < .01$).

Conclusions Our data support the possibility to have a single partition (ie, 45 g/m$^{2.16}$) value across the whole pediatric age range to identify LVH, without the time-consuming need of computing specific percentiles for height and sex. *(J Pediatr 2016;170:193-8)*.

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Presence of left ventricular hypertrophy (LVH) has been shown to be associated with increased morbidity and mortality in both adults and children over a wide range of medical conditions including overweight, systemic hypertension, dilated cardiomyopathy, and kidney failure.[1-10] However, LVH in children is important not only for cardiovascular risk stratification in hypertension, obesity, and/or acquired renal dysfunction, but also to identify patients at high cardiovascular risk in the presence of neonatal diseases as metabolic disorders and/or neonatal acute renal failure.[11-13] Although cardiac magnetic resonance imaging has gained increasing popularity in evaluating left ventricular mass (LVM), the echocardiographic measurement of LVM remains the preferred method in clinical practice because of the combination of accuracy, low cost, and high accessibility.[14] To identify abnormalities of ventricular mass, the relationship between heart and body size should be taken into account. Accordingly, ventricular weight is usually normalized for measures of body size. However, the complex relationship between heart growth and body growth in children has made indexing difficult for younger ages. In fact, the relationships among body surface area (BSA), height, and cardiac mass are not linear, thus, different LVM indexing methods have been proposed in pediatric patients. Indexing LVM measurement by height (traditionally raised to the power 2.7) or by BSA allows comparisons across individuals of varying body sizes.[15] In adults, studies have shown that height raised to the power of 2.7 may be the best indexing method because it most closely approximates lean body mass.[16,17] The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents delivered by the National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents recommends using the index

BSA	Body surface area
LV	Left ventricular
LVH	Left ventricular hypertrophy
LVM	Left ventricular mass

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by LVM/height$^{2.7}$.[18] This method has been used widely used in recent years, and previous studies have proposed pediatric-specific single partition values for LVH.[7] In contrast, in other studies, the use of a single specific partition values has been discouraged, given the nonlinearity of the relationship between LVM and height$^{2.7}$ in the youngest children and the resulting significant overestimation of LVH in children with height <140 cm.[19] Thus, the definition of specific quantile (percentile) curves for LVM/height$^{2.7}$ to identify the presence of LVH, has been suggested, with the drawback of making its clinical use very limited.

Therefore, our purpose was to use echocardiographic data from the Echocardiography Laboratory of the Bambino Gesù Pediatric Hospital and the Department of Pediatrics of the University of Heidelberg, Germany, to determine a simplified method to correctly identify presence of LVH in a large pediatric population from 0-18 years of age.

Methods

Caucasian children (n = 400; 52% boys, 0-18 years of age) were prospectively or retrospectively enrolled in the study from 2 different European pediatric hospitals (Rome and Heidelberg). All patients were children referred to the echocardiography laboratory for the evaluation of innocent murmurs or chest pain who were then determined by echocardiography to have normal hearts. Specific exclusion criteria included systemic disease, arrhythmias, structural heart disease, cardiac dysfunction, valve regurgitation above the physiological trivial grade, body mass index for age and sex >85th percentile, hematologic disease, Kawasaki disease, renal dysfunction, and/or genetic syndromes. Hypertension was excluded according to the criteria proposed by the fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents delivered by the National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents.[18] Research protocol was approved by the institutional review board, and all subjects or their guardians gave written informed consent when needed.

The formula derived from the aforementioned 400 children was then tested in a validation cohort of 130 consecutive healthy children evaluated at the Pediatric Cardiology Outreach Clinic, Bambino Gesù Pediatric Center Basilicata, San Carlo Hospital, Potenza, Italy. The indication to perform the echocardiogram and the exclusion criteria were identical to those applied to the study population previously described in details.

Echocardiograms in all 3 centers were performed on commercially available cardiac ultrasound scanners equipped with S-5, S-8, and S-12 probes. Examinations were performed according to the guidelines of the American Society of Echocardiography.[20] All studies were recorded in Digital Imaging and Communications in Medicine format and reviewed on digital review stations by a pediatric cardiologist with long-standing experience in echocardiographic research measurement. Studies performed for clinical purposes were re-examined for the purposes of the present study. Mean left ventricular (LV) internal diameters, septal thickness, and posterior wall thickness were derived from measures on 3 cardiac cycles. LVM was estimated by the Devereux equation.[21]

For the analysis of the validation cohort, LVH was defined by different reported methods: (1) using single partition values of LVM/height$^{2.7}$ for both sex and all ages (LVM/height$^{2.7}$>38g/m$^{2.7}$,[7] and the more conservative LVM/height$^{2.7}$ >51/m$^{2.7}$ [18]); (2) applying age- and sex-specific partition values for LVM/height$^{2.7}$ [19]; (3) using LVM-for Lean Body Mass z-scores[22]; and (4) by the partition value proposed by the present study.

Statistical Analyses

Data were analyzed using commercially available statistical software (Excel 2007; Microsoft, Redmond, Washington, and SPSS 21.0; SPSS Inc, Chicago, Illinois). Data are expressed as mean ± SD.

Relationships of LVM to measures of body size were assessed by linear regression analysis. Multivariate analyses were performed by partial correlation and by forward stepwise multiple linear regression procedure. Nonlinear regression analysis was performed to assess the allometric (growth) relationship of LVM to measures of body size. Best-fit procedure was used to obtain allometric equations so that the sum of all the observations of the squared differences between the observed and predicted LVM values was minimized. Residuals were standardized (ie, residuals/square root of mean sum of squares for the error in the regression model) to approximate standard normal deviates.

Results

Of the 400 patients, 24% were infants or toddlers (0-3 years of age), 21% preschoolers (3-6 years of age), 33% children (6-11 years of age), and 22% adolescents (12-18 years of age). Except for the group of infants and toddlers in which there were more males (60%), both sexes were equally represented in all groups. Anthropometrics and clinical details of the study population are shown in Table I.

Table I. Clinical characteristics of study population (n = 400)

	Mean	SD
Age (y)	9.6	4.3 (range 0-18)
0-3	24%	
3-6	21%	
6-12	33%	
12-18	22%	
Male	52%	
Height (cm)	136	26
Weight (Kg)	36	17
SBP (mm Hg)	104	10
DBP (mm Hg)	60	9
Heart rate (bpm)	81	13

DBP, diastolic blood pressure; *SBP*, systolic blood pressure.