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Editorial Comment

Left Ventricular Mass in Children and Adolescents*

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Electrocardiographic left ventricular hypertrophy and radiographic cardiac enlargement have long been known to be strong predictors of cardiovascular morbidity among adults with hypertension (1,2) and in the general population (3,4). Recent studies using echocardiographic methods that have been validated anatomically in adults (5–7) have shown that echocardiographic left ventricular mass is a major risk factor for cardiovascular morbidity among adults with hypertension (8,9) and in the general population (10), independent of and possibly stronger than elevated blood pressure or other standard risk factors.

Accordingly, increasing attention is being devoted to the early stages of increases in left ventricular mass during childhood, with the goal of devising strategies to prevent development of left ventricular hypertrophy. Comparison of children and adolescents with relatively high versus low blood pressure has revealed greater left ventricular wall thickness and mass (11–16) or enhanced myocardial performance (16,17) among those with higher blood pressure. Of particular importance, Mahoney et al. (18) found that, among children studied longitudinally in the Muscatine study, initial left ventricular mass added independently to the value of baseline measurements of blood pressure for prediction of systolic blood pressure measured at follow-up evaluation >3 years later. These data indicate that, in childhood, left ventricular mass increases with even subtle elevation of blood pressure and also suggest that, as in adults (19,20), such increases may be a better reflection of pressure responses to exercise or recurring stresses than are clinical blood pressure measurements. Despite increasing evidence of the significance of left ventricular mass, echocardiography has not been used to detect abnormal ventricular mass in childhood because of the lack of age-appropriate upper normal limits for left ventricular mass.

Echocardiographic calculation of left ventricular mass in normal children. The report by Daniels et al. (21) in this issue of the Journal addresses this deficiency by providing necropsy validation in children of the formula most widely used for echocardiographic measurement of left ventricular mass and by establishing gender-specific upper normal limits for left ventricular mass in children, adolescents and young adults. However, before the proposed criteria for left ventricular hypertrophy are accepted as definitive, it is important to critically examine aspects of study design as well as of the relation between body size and left ventricular mass.

Because of the fundamental importance of necropsy validation of echocardiographic left ventricular mass measurements, this aspect of the study deserves special attention. Although not stated in the report of Daniels et al., measurements made at necropsy by use of ruler and twine in hearts from 23 normal children among a previously reported series of 51 hearts (22) were utilized to calculate left ventricular mass by the Penn Convention echocardiographic formula (5,7) (Bove KE, personal communication). The close correlation (r = 0.89, $p < 0.001$) between calculated left ventricular mass and left ventricular weight by the chamber partition method (23) thus constitutes a *theoretical* validation because no echocardiographic measurements were made of these hearts. However, the correlation coefficient of 0.89 in this study actually falls slightly below the 0.90 and 0.96 obtained in two previous studies of adults (5,7), suggesting that calculation of left ventricular mass from in vivo echocardiographic measurements approaches the theoretical limit of accuracy of the formula. The fact that ventricular mass estimated by using anatomic measurements in the Penn formula falls along the line of identity with necropsy mass (Fig. 1 of Daniels et al. [21]) also suggests that echocardiographic measurements by the empirically derived Penn convention correspond closely to true anatomic measurements. However, comparison of Figure 1 of the present report with Figure 3 of reference 23 suggests that a further increase in accuracy of left ventricular mass measurements may be achieved at least theoretically by use of two-dimensional echocardiographic measurements in more complex formulas, as proposed by Schiller et al. (24).

Development of normal confidence limits also depends on correct selection of a normal reference population. The children and adolescents studied by Daniels et al. (21) appear appropriate with regard to adequate population size (n = 334), age range (6 to 23 years), representation of important subgroups (equal numbers of male and female subjects, approximately 25% black) and freedom from apparent cardiovascular disease. However, limitations are also apparent.

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No indication is given as to inclusion or exclusion of subjects who are obese or have borderline high blood pressure (albeit below levels mandating drug therapy in childhood), although studies in adults suggest that "normal" confidence limits are widened by inclusion of such subjects (25–28). Of even greater importance, no information is given as to whether the reported confidence limits are equally applicable to younger as well as older children and adolescents. The fact that normal blood pressure increases throughout this age range makes this unlikely to be the case, as a compensatory increase in left ventricular mass out of proportion to body size would be expected.

A final important issue concerns the method for relating left ventricular mass to body size. In this (21) as in previous studies in both adults and children (16,18,25,26,29), left ventricular mass was more closely correlated with body surface area than with other measures of body size. Earlier investigators (25,26), have taken this into account by indexing left ventricular mass by body surface area or by relating left ventricular mass to body surface area (29), its component parts (height and weight) (18) or both body surface area and ponderal index (16). On the basis of recent evidence that obesity is a powerful stimulus to left ventricular hypertrophy (28,30) and that obesity-induced hypertrophy may be masked by indexing ventricular mass by body surface area, Levy et al. (30) suggested, and Daniels et al. (21) accepted, that left ventricular mass should be indexed by dividing it by height.

Implications. Implicit in this suggestion is the unstated premise that the three-dimensional volume of the heart is directly proportional to the linear measurement of body height, whereas most available data suggest that the volume of the body and its organs is related to the second power of height, as is body surface area, or its third power (31). If this reasoning is correct, the ratio of left ventricular mass to height should be greater in tall normal individuals than in short ones, whereas this should be less true for the ratio of left ventricular mass to body surface area. This should result in wider normal confidence intervals for left ventricular mass/height rates than for left ventricular mass/body surface area ratio when the range of heights is great, as it is in children (range from the 5th percentile among 8 year olds to the 95th percentile among 18 year olds = 69.5 cm in male and 56.7 cm in female children) but to a lesser degree in adults (range of 21.9 and 20.0 cm, respectively, among 18 year old men and women) (32). In accord with these predictions, the dispersion of normal values—as assessed by the ratio of the 95th percentile to the mean for each measure—is greater for left ventricular mass/height ratio than for mass/body surface area ratio, for both male (159 versus 146%) and female (153 versus 139%) subjects. This widening of confidence intervals would result in upper normal limits that are too high in smaller children, but that might also be slightly low for adolescents of large body size. Therefore, further data are needed demonstrating that the mean and dispersion of values of left ventricular mass/height ratio do not vary between different age groups before a single upper normal limit for this measurement is accepted for recognition of left ventricular hypertrophy in children and adolescents.

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