Editorial Commentary

Controversies in the Assessment of Left Ventricular Mass

Samuel S. Gidding

With the recognition that left ventricular (LV) mass (LVM) contributed to the prediction of cardiovascular morbidity and mortality, independent of conventional risk factors, including those that partially determined LVM (body size, blood pressure, and tobacco), interest in better understanding the clinical and epidemiological roles of LVM measurement accelerated. Over the last 2 decades, substantial progress has been made in this regard. For example, clinical trials have been designed to demonstrate the independent contribution of pharmacological LVM reduction, beyond blood pressure reduction in hypertensive patients, to improvement in cardiovascular outcomes. The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents incorporates LVM measurement in its evaluation algorithm with intensification of antihypertensive management recommended in the presence of LV hypertrophy.

Despite this success, the role of LVM in clinical practice has not been firmly established. There are a number of controversies surrounding the measurement of LVM. These include the fact that LVM is principally determined by body size so that some component of LVM is adaptive rather than pathological, that LVM can be increased by healthful behaviors (eg, physical training) and cardiovascular risk factors, that there are significant problems in standardizing echocardiographic measurement of LVM by echocardiography across laboratories, that MRI provides more accurate measurement of LVM than echocardiography, and that a firm definition of LV hypertrophy based on the calculation of heart weight has not been established by consensus. Historically, one method for overcoming these several limitations has been indexing LVM to body size. Most commonly this is done by dividing LVM by body surface area or height elevated to some power, usually height$^2$ or height$^{2.7}$. Driving these analyses has been a concern for accommodating the strong relationship of LVM to lean body mass (and normal growth in analyses that include children) while not compensating for the potential pathological effect of obesity on heart size. An additional goal driving these analyses has been the identification of a single indexing method that can be applied across age, sex, and ethnic lines.

These issues are not trivial. LVM occupies a unique place among cardiovascular risk factors in that it is both determined by established risk factors (principally obesity and blood pressure but also tobacco) but has a strong independent effect on cardiovascular outcomes. In fact, these predictors explain less than half of the variation in LVM with a wide SD around the regression equation line. In an analysis from the Coronary Artery Risk Development in Young Adults Study that stratifies a healthy population by categories of LV mass and LV relative wall thickness, we have shown that high LVM and abnormal LV relative wall thickness are typically found at the upper end of the normal distribution of risk rather than confined to obese and hypertensive individuals. Genetic studies have not significantly enhanced our understanding of the wide variation in LVM around a predicted mean. Thus, being able to accurately use LVM in risk algorithms may have prognostic importance for patients.

In this issue of *Hypertension*, Chirinos et al re-examine the question of the optimal way to index LV mass to body size. First, the distribution of optimal LVM is determined by defining the distribution in a low-risk cohort (ie, free of hypertension, obesity, tobacco use, and other factors associated with increased LVM). Second, they use 2 separate methods of calculating LVM (echocardiography and MRI). Third, they support their analysis by relating the performance of the various indexing methods to potential biases in identification of elevated LVM. Fourth, they compare the usefulness of the different methods in predicting cardiovascular outcomes. Driving their analysis is a concern that sex differences confound previous efforts to accomplish an effective indexing strategy. They suggest that there are inherent biases in methods that do not account for sex, particularly those using body surface area and height$^2$ as indexing strategies. They conclude in sex-specific analyses that height$^{1.7}$ is the preferred indexing coefficient, that this coefficient can be used in both echocardiographic and MRI-based measurements, that other methods of indexing do have inherent biases, and that all of the methods of indexing perform equally in relating to future cardiovascular outcomes.

The methodology used in this study provides a model to come to a determination on the optimal method for LVM indexing, which is to first determine the distribution of LVM in a low-risk cohort and then to test the performance of the method by determining the usefulness of the method in predicting outcomes. Foster et al have used a low-risk pediatric cohort to try to optimize the best method of indexing LVM in children and adolescents to body size, but this study is necessarily limited by the absence of outcomes in a young population. Examples of studies that have compared different methods of indexing LVM and relating this measure to outcomes include the work of Liao et al and Ristow et al; these studies have shown that the method of indexing LVM...
does not have significantly impact the ability to predict future CVD outcomes, but these studies are limited by the fact that the cohorts studied had identified cardiovascular disease at study entry and, thus, may not be generalizable to an otherwise healthy population and do not provide analyses of a normal distribution of LVM.

How then should LV mass be indexed? All 3 strategies are well related to outcomes. The advantages of the strategy of Chirinos et al9 with regard to misclassification are presented. The advantage of using height2.7 is that it has been used for many years and was developed to be generalizable across all age groups and both sex. However, the risk of misclassification is highest with this strategy. Body surface area–based strategies seem to be preferable for children, but thresholds that are outcomes based are not available, and there seems to be a risk of misclassification in the obese. A limitation of the 3 strategies compared in the article by Chirinos et al9 is the complexity of dividing by height elevated to a power or calculating body surface area for every patient. This can be overcome by having a table of height raised to the relevant power available in the echo laboratory or having calculations performed in algorithms provided at the echo reading station. The final answer to this question should be provided by further outcome studies that compare several indexing strategies in diverse cohorts. These studies could include simpler calculations as well; these strategies can be evaluated in an evidence-based fashion to determine the best method and to make recommendations regarding the definition of LV hypertrophy.4,5,9

From a clinical standpoint, at the current time, it is important that clinical echocardiography laboratories provide an estimate of LVM and normal ranges consistent with the indexing method chosen by the individual laboratory to allow this information to inform clinical decision making. In follow-up assessments of adults, raw LVM can be used. In the absence of change in height, any change downward from a value defined previously as LV hypertrophy can be considered beneficial.

A further reassuring finding in this study is that LVM measurements using echocardiography and MRI produce comparable results, although those using echocardiography are slightly less accurate, an outcome that is predictable based on the need to use more assumptions regarding LV shape using echocardiography. Because echocardiography is more easily obtained in serial studies, this finding supports the continued use of echocardiography for this purpose.

Better understanding of the relationship of echocardiographic and MRI measures of cardiac size and function will become increasingly important in cardiovascular medicine in the near future. The obesity epidemic, with comorbidities of diabetes mellitus and hypertension, is a known predecessor of heart failure. Studies such as the one by Chirinos et al9 that link outcomes with assessment of LVM and contrast different methods of indexing LVM will allow the development of a sufficient evidence base so that meaningful definitions of LV hypertrophy, based on outcomes rather than arbitrary thresholds, can be developed. Additional work looking at left atrial size, LV geometry, and the linkage of LV size measurements with cardiac function may add further precision to risk estimates.

New insights into apoptosis, myocardial regeneration, and cardiac fibrosis suggest that the heart is not a static organ. Cardiac size and function are dynamic responding to the stressors of daily life but also having a chronic evolution. For example, the Multi-Ethnic Study of Atherosclerosis has shown that, from age 45 years onward, heart size in otherwise healthy individuals changes with declines in LV internal dimension.12 Risk factors present in young adulthood may predispose to myocardial dysfunction later in life independent of myocardial infarction.13 Just as atherosclerosis is recognized as a chronic condition with events occurring after decades of vascular injury, heart failure may soon be recognized to have similar chronic antecedents. LV hypertrophy is recognized in adolescence and young adulthood, particularly in association with obesity and hypertension.14 Better definitions of LV hypertrophy and early markers of cardiac dysfunction may allow for better risk stratification and earlier treatment to prevent myocardial dysfunction. Clinical trials may wish to incorporate measures of LV mass and other imaging-determined LV and left atrial assessments to correlate with outcomes, testing this hypothesis. Without clear insights into the best ways to measure cardiac structure and function, preventive research cannot move forward.

What then is the research agenda for studies of LVM and other cardiac structure parameters that can be measured by echocardiography and MRI? As suggested by the work of Chirinos et al,9 studies of the large population-based cohorts should link measures of cardiac size with outcomes using different methods of adjusting for body size so that the best indexing methods can be ascertained. These relationships may be complex, because many of the factors governing LVM remain undiscovered; both risk factors (eg, obesity and hypertension) and healthful factors (physical training) can contribute to LV size. More longitudinal data, across the age spectrum, on the evolution of cardiac structure will be needed to more accurately understand the evolution of myocardial structure. This should occur both in population-based cohorts and in clinical trials so that the independent impact of improvement in myocardial structure on outcomes can be understood. Finally measures of cardiac structure should be linked to systolic and diastolic measures of cardiac function to determine optimal risk stratification algorithms.

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Disclosures


References


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