Editorial

Value and Challenges of Measuring Left Ventricular Mass in Clinical Research
Implications for the Practitioner

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The relationship of left ventricular (LV) hypertrophy (H) to abnormality of the arterial circulation was noted almost a century and a half ago by the great French physician Auguste Laennec who noted1 that “When affecting the left ventricle, I have seen its parietes more than an inch thick...the septum between the two ventricles becomes also notably thickened in the disease of the left ventricle....Symptoms are - a strong full pulse, strong and obvious pulsation of the heart...”

Since Laennec’s observation, the importance of LVH to cardiac outcomes, including heart failure, myocardial infarction, and cardiovascular death, has been well established.2,3 Moreover, LV mass (actually weight) even at values below those used to define LVH, as well as normal geometry (increased proportion of wall thickness to diastolic LV dimension, ie, concentric geometry), is also associated with adverse outcomes. Given the evidence that reduction of LV mass may vary based on selected therapy and population characteristics, it has been suggested that specific targeting of LV mass reduction may confer benefits over and above those that accrue with blood pressure lowering, per se.3

However, given the well-demonstrated efficacy of blood pressure lowering on improving cardiovascular outcomes, without measuring its effects on LV mass or other potential surrogate outcome measures, treatment guidelines in hypertension have placed little emphasis on measurement of LV mass and its change with therapy. Measurement of LV mass and its change over time confers technical challenges attributable to what can be substantial measurement variability.4 Alternate methods, specifically magnetic resonance imaging, confer high cost and logistic difficulty in large population studies and clinical trials. Hence, relatively few studies have successfully examined how LV mass changes during long periods of time either in population studies or in clinical trials.

In this issue of Circulation: Cardiovascular Imaging, Gidding et al5 evaluated changes in LV mass during an interval of 20 years in participants in the Coronary Artery Risk Development in Young Adults (CARDIA) study, an National Heart, Lung, and Blood Institute (NHBLI)-sponsored study of 5,115 community dwelling young adults 18 to 30 years old at enrollment between 1985 and 1986 and evaluated periodically at 4 sites throughout the United States. Echocardiography was performed at years 5, 10, and 25 after enrollment, and data were collected on blood pressure, lipids, glucose and other blood chemistries, physical measures, lifestyle factors, and family history.

They found that LV mass and relative wall thickness increased over time, and the proportion of individuals with normal LV geometry decreased. Importantly, both initial body mass index and increase in body mass index were associated with increase in LV mass, while increase in body mass index was associated with the development of abnormal LV geometry. Black women who had the highest proportion of LV structural abnormality (ie, LVH, or concentric remodeling) at baseline were the most likely to have still greater prevalence of LV structural abnormality 20 years later. Of those who maintained cardiovascular health during the 20 years between echocardiograms, there was minimal increase in LV mass compared with participants who did not maintain cardiovascular health. The present study complements a previous publication6 from CARDIA evaluating 5-year interval change in LV mass and geometry where there was relatively little change in LVM other than in black women. Moreover, the exceptional length of follow-up in the present study allowed determination of the importance of tobacco use, diabetes mellitus, and need for antihypertensive medication on LV mass and geometry.

The authors point out some of the limitations of using echocardiography for the measurement of LV mass and its change during long intervals. Echocardiography is a performance-based technique, where the quality of image acquisition may vary according to the skill and experience of the sonographer, as well as with patient characteristics such as age, obesity, and chronic lung disease, which affect echogenicity. Moreover, during the 20-year interval between the echocardiograms in this study equipment, recording format and personnel have changed. Even individual readers may change their measurement styles over time. Given that the primary measurements of LV cavity dimension, septum, and posterior wall thickness used in calculation of LV mass are cubed in the calculation of LV mass, errors as small as a few millimeters can result in large errors in calculated LV mass. As an example, the greater LV wall thicknesses that are recorded with harmonic imaging, done in year 25 but not the

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612
year 5 baseline echo, could have resulted in overestimation of LV mass increases on the follow-up studies. The authors commendably used rigorous quality control measures. Nonetheless, in rereading an aliquot of year 5 echos 2 decades later, the average LV mass read originally at year 5 was on average 21 gm less when remeasured by different readers 2 decades later. This difference was likely because of tape degradation. However, if it were because of differences in reading styles, as can occur, there would have been an underestimation of the increase in LV mass on the follow-up studies relative to the baseline. This would have decreased the power of the study to find significant relationships between subject characteristics (such as obesity and race) and change in LV mass. Nonetheless, the study was adequately powered to overcome even this potential difficulty.

The exclusion of participants because of poor quality echocardiograms, however, would remove from evaluation those with particularly high risk profiles, resulting in underestimation of increases in LV mass and LV hypertrophy but also producing biased estimates of associations of LV mass change with those very characteristics that lead to study dropout. Although the effects of even fairly large random errors can be reduced by adequate sample size, this latter source of error cannot be addressed by increasing statistical power.

It should also be noted that the prevalence of LV hypertrophy will be dependent on the criteria used. The authors used commonly used, guideline-recommended partition values normalized for height that were obtained in other study populations with potentially different characteristics than CARDIA, at different times and using different personnel than CARDIA. Published normal values in guidelines are commonly determined in those free of overt disease rather than healthy individuals free of even subclinical disease. An alternative, and perhaps preferable, approach would have been to derive partition values derived from the CARDIA study itself based on predictive models for LV mass in healthy individuals identified by well-defined phenotypic characteristics, studied contemporaneously, using the same equipment, and by the same personnel.

These technical issues notwithstanding, the principal findings of the article are unequivocally clear, and of importance in public health approaches to improving cardiovascular outcomes, particularly in the high risk individuals described.

There are, of course, other questions which remain to be addressed possibly in CARDIA and other large cohort studies. In particular, the mechanisms by which adiposity promotes increase in LV mass are still not defined, and other factors such as renal and endocrine function may be important. Obesity, tobacco use, and hypertension are common in adolescents who are still growing, and the interaction between physiologival influences on LV mass and geometry with these and other unhealthy exposures remains to be determined. Much of the between individual variability of LV mass is not explained by its pathophysiological correlates, and there is mounting evidence that genetic factors are important. It is hoped the modern genomic techniques using stored DNA in large epidemiological studies may provide useful information on how genetic–environmental interactions effect LV mass and related clinical outcomes.

However, the message of this and other studies is quite clear. Although technical considerations may make LV mass measured by echocardiography an inappropriate way to risk stratify and follow therapy in individual patients, longitudinal studies of change in LV mass in CARDIA and other epidemiological and clinical studies have clearly documented the long term and continued risk of adiposity as well as race and sex for pathological increases in LV mass and adverse cardiovascular outcome.

Disclosures

None.

References


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