Left Ventricular Mass
Reliability of M-Mode and 2-Dimensional Echocardiographic Formulas

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Abstract—The study of left ventricular (LV) hypertrophy is hindered by problems with LV mass measurement by echocardiography. Both the M-mode and 2D area-length formulas for calculating LV mass assume a fixed geometric shape, which may be a source of error. We examined this hypothesis by using cardiovascular magnetic resonance images to eliminate the confounding effects of acoustic access and image quality. LV mass was measured directly in 212 healthy subjects by means of a standard 3D cardiovascular magnetic resonance technique. LV mass was also calculated by using the cube-function and area-length formulas with measurements from the magnetic resonance images. A comparison of serial measurements was made by examining the changes in LV mass by all 3 techniques in those completing an exercise program (n = 140). The cube-function technique showed a consistent underestimation of LV mass of 14.3 g, and there were wide 95% limits of agreement (±57.6 g and ±46.3 g for cube-function and area-length techniques, respectively) when compared with 3D measurement. There were similarly wide limits of agreement for the change in mass (±55.2 g and ±44.8 g for cube-function and area-length, respectively). The assumption of geometric shape in the cube-function and area-length formulas resulted in significant variation in LV mass estimates from direct measurement by using a 3D technique. The technique cannot be recommended either at a single time point or for serial studies in small populations; 3D imaging techniques, such as cardiovascular magnetic resonance, are preferable. (Hypertension. 2002;40:6-11.)

Key Words: myocardium • hypertrophy • magnetic resonance imaging • echocardiography

Left ventricular (LV) hypertrophy is an independent cardiovascular risk factor associated with significant excess and morbidity and mortality rates.1-3 There is now evidence for the effectiveness of antihypertensive agents, particularly ACE inhibitors, in reducing LV mass,4-6 and this reduction in LV mass appears to carry a favorable prognosis.7-8 However, studying the prognostic implications of LV mass reduction is hindered by the poor accuracy and reproducibility of LV mass measurement by M-mode and 2D echocardiography. The high 95% confidence limits for accuracy (±57 to 190 g for M-mode,9-12 ±61 to 80 g for 2D techniques11-13) and interstudy reproducibility (±45 to 78 g for M-mode,10,14-17 poorly assessed for 2D) result in the need for large numbers of subjects in research studies.

The principal sources of error are considered to be image quality, beam positioning, and the assumption of a uniform geometric shape of the left ventricle, with LV mass calculated from measurements made at 1 or 2 positions. Both M-mode and 2D echocardiography assume a prolate ellipsoid shape, with a ratio of long- to short-axis lengths of 2:1, which provided the best simplified geometric model for LV mass estimation.18 Formulas were developed for the calculation of LV mass based on the regression equations of the calculated mass to autopsy findings for M-mode9,10 and 2D echocardiography.12,19-21 The cubing involved in the formulas means that small (<1 mm) differences in measurement can have large effects on the calculated mass. Additionally, the assumption of shape may not be appropriate, even for normal hearts, in which a substantial natural variation in shape may exist, though the specific influence of this assumed geometry on accuracy has not previously been examined. We examined the M-mode and 2D formulas under the best possible circumstances of good image quality and normal hearts by applying them to cardiovascular magnetic resonance (CMR) images and comparing the results with direct measurement of the LV mass by using the standard 3D CMR technique.

Methods

Subjects

The study group comprised 212 male British Army recruits, free from cardiovascular disease, who had CMR scans performed at the start of military training, as part of a separate study.22 After a 10-week physical training program as part of standard training, 140 completed the course and had follow-up scans. In this way, both the measurement of LV mass at a single time point and the detection of changes over time could be compared.
Cardiovascular Magnetic Resonance (3D Method)
Studies were performed with a custom-built mobile CMR scanner situated at the military base for the study (0.5 Tesla; imaging software: Surrey Medical Imaging Systems). All imaging was ECG-gated and acquired in a standard manner as previously described. Briefly, a stack of contiguous short-axis cine images covering the whole LV were obtained, and the myocardial volume from each slice was summed to obtain the total volume, by using Simpson’s rule. Multiplying this volume by the specific density of myocardial tissue (1.05 g/cm³) gives the mass. This technique is well validated, with high accuracy and reproducibility.

M-Mode Measurements
From the CMR image set, the short-axis image slice just basal to the papillary muscles was used, reproducing measurements obtained at the level of the chordae tendineae, according to the American Society of Echocardiography (ASE) guidelines for M-mode measurement. Measurements were made of the septal wall thickness (SWT) and posterior wall thickness (PWT) and LV internal diameter (LVID) from this slice. These were used in the cube-function formula for ASE guidelines to calculate LV mass (the ASE-cube formula):

\[ \text{LV mass (g)} = 1.05 \times \left( \frac{5}{6} \times (PWT \times LVID - SWT) ^ 3 - LVID ^ 3 \right) + 0.6 \]

Two-Dimensional Measurements
The area-length method was selected for comparison because it is a simpler formula with easily obtainable measurements; it is commonly used and has been shown to be closer to the true LV mass than other 2D methods. Measurements were made of the epicardial (A_Epi) and endocardial (A_Endo) areas from the same short-axis slice as the M-mode calculations, just basal to the papillary muscles. This is close as possible to the high papillary muscle level suggested, given the limitations of the CMR slice thickness (10 mm). The ventricular long axes (epicardial, L_Epi; and endocardial, L_Endo) were measured from the horizontal long-axis slice (equivalent to the echocardiographic 4-chamber view), maximizing accuracy of the apex position. LV mass was calculated by using the following area-length formula:

\[ \text{LV mass (g)} = 1.05 \times \left\{ \frac{5}{6} \left( \frac{A_{Epi} \times L_{Epi} - A_{Endo} \times L_{Endo}}{1.05} \right) \right\} + 0.6 \]

Statistical Analysis
The difference in LV mass measurement between methods was calculated for each subject at baseline and for the change in LV mass. Bland-Altman plots were performed to determine the 95% limits of agreement between methods. Group means were compared with an unpaired Student t test and the within-group change in means by paired t test. Values are shown as mean±1 SD. Percentage changes are shown using the standard 3D LV mass measured by CMR as the reference. Although scatterplots are shown, correlation coefficients were not calculated because these are a measure of the linearity of the relation between 2 variables and do not indicate the strength of agreement between techniques, for which Bland-Altman plots are more appropriate.

Results
Mean LV mass measurements at baseline were 168.8±35.4 g, 180.5±32.8 g, and 183.1±26.4 g for the M-mode, 2D, and 3D methods, respectively, though there was considerable scatter when the methods were compared (Figure 1). The mean difference between M-mode and 3D techniques was −14.3 g (7.8%, P<0.0001), with 95% limits of agreement of ±57.6 g (31.5%). The mean difference between the 2D area-length formula and 3D techniques was −2.6 g (1.4%, P<0.0001), with 95% limits of agreement of ±46.3 g (25.3%). Bland-Altman plots for these differences are shown in Figure 2.

LV mass changed with training by a mean of +8.3±14.0 g (4.3%, P<0.0001) by 3D compared with +7.8±28.2 g (P<0.0001) and +8.9±22.5 g (P<0.0001), with the use of the M-mode and 2D echocardiographic methods, respectively. Although the mean change was similar for all groups, there was considerable scatter in the results when comparing the methods (Figure 3) and the Bland-Altman plots showed wide 95% limits of agreement (+5.5.2 g and ±44.8 g for M-mode and 2D echocardiography, respectively; Figure 4).

Discussion
Despite the excellent image quality used here, calculations of LV mass with the use of the ASE-cube (M-mode) and 2D formulas showed considerable variation from the reference standard of direct 3D imaging of the whole ventricle. The ASE-cube method showed a consistent underestimation of LV mass by −14 g, though the mean values of the 2D method were little different from 3D measurement. In addition, the scatter of values was high for both formulas, indicating high absolute differences between these techniques and 3D measurement (95% confidence intervals ±46.3 g for 2D; ±57.6 g for ASE-cube), which represent significant clinical differences. Group studies with M-mode and 2D methods are still feasible, and our understanding of the dangers of LV hypertrophy come from several of these, but the increased variability means that much larger sample sizes are needed.
The mean values for the change in LV mass with training were not significantly different between techniques, suggesting no systematic bias in serial measurements with the use of the formulas. It also demonstrates that with large enough group sizes, similar mean changes can be observed with all 3 techniques. However, the wide confidence limits for both formula methods result in a reduced ability to detect changes in smaller groups and the loss of the ability to detect individual changes in LV mass below this level (45 to 55 g). With direct measurements using 3D techniques, the same change in LV mass can be detected with much smaller sample sizes, or, alternatively, using the same sample size, smaller degrees of change can be identified. This has a substantial impact on the costs of performing studies.

**Validity of Reference Standard**

CMR LV mass may deviate slightly from the true LV mass, and it lacks the gold-standard comparison of human autopsy LV mass with in vivo data, but it has been shown to be highly accurate and reproducible (95% confidence intervals ±15 to 19 g)\(^{16,17,24}\) and no better in vivo method exists. The purpose of this study was to allow a direct comparison of the differences between directly measured 3D quantification and calculated values with an assumed geometric shape, using the same data set to minimize image quality problems, and the CMR data perform this function well. Furthermore, the confidence intervals obtained here for the 2D and M-mode methods are similar to previously published values for accuracy\(^{9,10,12}\), and reproducibility\(^{14}\) of LV mass with the use of the same formulas, suggesting that these differences are mostly due to errors in the calculations rather than an incorrect reference standard of 3D CMR.

**Possible Reasons for Errors in LV Mass Calculation**

The use of a single geometric model to estimate LV mass appears inappropriate. The original studies determining the equations\(^{9,10,12}\) involved relatively few subjects (34, 52, and 21 subjects), with a wide age range (23 to 82 years) and marked variation in LV mass (77 to 625 g). Although the wide range studied facilitated a “best-fit” model, it is difficult to expect equations drawn from small numbers to be applicable to all sections of the population. The LV mass derived from these equations may be useful in large population studies that have demonstrated prognostic differences\(^{1}\); however, it does not appear to predict LV mass accurately for individuals nor to be good at detecting changes in individuals and small groups. Previous studies have quoted a good correlation of echocardiography-derived LV mass with post-mortem values,\(^{9,10,12}\) but this is a poor measure of the strength.
of agreement between techniques and indicates only the linearity of the relation—the trend for one variable to increase proportionately to another. If the variables are actually 2 different techniques measuring the same parameter, it is expected that the 2 variables will be proportional to each other, and little inference can be made about the accuracy of either technique or their strength of agreement. Considerable differences may exist in the absolute values from 2 techniques despite a very high correlation.26 Given that the prolate ellipsoid correlated better than other simple models in the original comparison studies,18 it is unlikely that any fixed geometric shape will give an adequate representation of left ventricular mass. These were also normal hearts, and altered cardiac shape, slice positioning problems, and poor image quality will all add to the error from fixed geometric formulas.

Limitations
The study population involved only young men free from cardiovascular disease. They were physically fit but not athletes, and the LV mass index was toward the upper end of the normal range for a population (96.8±16.9 g/m² before training). It is unlikely that the LV shape or variability in shape in this group differs substantially from the rest of the normal population. In addition, the absence of any cardiac disease makes this a good group for study because it is likely that results in patients with abnormal ventricles would increase the variances we have shown between directly measured and calculated techniques.

The CMR short-axis image slice used for M-mode and 2D analysis was as close as possible to the positions recommended for echocardiographic analysis, but the greater slice thickness of CMR may encompass a wider area than the echocardiographic equivalent, with averaging of the myocardial border positions. In practice, the degree of error is likely to be small and is offset by the true short-axis alignment (some misalignment is possible using echocardiography) and good image quality.

CMR has the same limitations as any MRI, with a small minority of people unable to undergo scanning for a variety of reasons, and limited availability. These are covered in more detail in a previous review.23

Perspectives
The use of improved techniques for the measurement of LV mass and in particular, greater reproducibility for the changes in mass, is likely to aid the study of LV hypertrophy and the effect of pharmaceutical agents and other interventions on its regression. It may also be possible to determine whether it is the LV mass per se or some other factor for which LV mass is a marker that is responsible for the serious adverse health consequences of LV hypertrophy.

All 3 dimensional techniques—CMR, 3D echocardiography, and electron-beam computed tomography—share the advantages of direct LV mass measurement, avoiding the use of formulas, and may be used for the above studies. Each has limitations: for 3D echocardiography, problems with limited acoustic access and operator skill; for electron-beam computed tomography, ionizing radiation and limited slice positioning; and for CMR, the unsuitability of a minority of patients, for example, with pacemakers. All share the problem of limited availability. It is suggested, however, that for the majority of subjects, CMR is the preferred method, with a free choice of imaging planes, uniformly excellent image quality, and lack of ionizing radiation.

Conclusions
With normal hearts and good image quality, calculated values for LV mass with the use of echocardiographic formulas and an assumed geometric shape of the left ventricle resulted in significant variation from direct measurement with the use of a 3D technique. The confidence limits of ±45 to 55 g represent significant clinical differences and are sufficiently large to prevent routine use of these techniques either at a single time point or for serial studies in small populations, where 3D imaging techniques are preferable. Irregularities in shape and reduced image quality will increase these errors.

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Figure 4. Bland-Altman plot showing 95% limits of agreement between 3D-CMR and ASE-cube LV mass (a) and 2D area-length LV mass (b) for change in LV mass over 10-week physical training program. Note substantial limits of agreement.


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