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CME

iREVIEWS

STATE-OF-THE-ART PAPER

LV Mass Assessed by Echocardiography and CMR, Cardiovascular Outcomes, and Medical Practice

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CME Objective for This Article: At the end of this activity the reader should be able to: 1) evaluate the role of LV mass to predict cardiovascular events in different populations; 2) understand the differences between assessment of LV mass by echocardiography and cardiac magnetic resonance; and 3) identify the role of indexing LV mass to body size, understanding limitations and strengths of height-derived and BSA-derived methods.

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LV Mass Assessed by Echocardiography and CMR, Cardiovascular Outcomes, and Medical Practice

The authors investigated 3 important areas related to the clinical use of left ventricular mass (LVM): accuracy of assessments by echocardiography and cardiac magnetic resonance (CMR), the ability to predict cardiovascular outcomes, and the comparative value of different indexing methods. The recommended formula for echocardiographic estimation of LVM uses linear measurements and is based on the assumption of the left ventricle (LV) as a prolate ellipsoid of revolution. CMR permits a modeling of the LV free of cardiac geometric assumptions or acoustic window dependency, showing better accuracy and reproducibility. However, echocardiography has lower cost, easier availability, and better tolerability. From the MEDLINE database, 26 longitudinal echocardiographic studies and 5 CMR studies investigating LVM or LV hypertrophy as predictors of death or major cardiovascular outcomes were identified. LVM and LV hypertrophy were reliable cardiovascular risk predictors using both modalities. However, no study directly compared the methods for the ability to predict events, agreement in hypertrophy classification, or performance in cardiovascular risk reclassification. Indexing LVM to body surface area was the earliest normalization process used, but it seems to underestimate the prevalence of hypertrophy in obese and overweight subjects. Dividing LVM by height to the allometric power of 1.7 or 2.7 is the most promising normalization method in terms of practicality and usefulness from a clinical and scientific standpoint for scaling myocardial mass to body size. The measurement of LVM, calculation of LVM index, and classification for LV hypertrophy should be standardized by scientific societies across measurement techniques and adopted by clinicians in risk stratification and therapeutic decision making. (J Am Coll Cardiol Img 2012;5:837–48)

Left ventricular mass (LVM) is an independent risk factor for prediction of cardiovascular events. However, the best way to incorporate LVM into clinical decision-making algorithms has not been established (1). Even in a range usually considered normal for healthy adults, LVM is positively related to systolic blood pressure, body mass index, and coronary calcium score by cardiac computed tomography (2,3). Elevation in myocardial mass may not be an inevitable consequence of aging, but better predicted by blood pressure, diabetes status, tobacco use, and body weight over time (4–8). Values of myocardial mass have also been shown to be associated with previous aneurysm of the abdominal aorta, subscapular skinfold thickness, left atrial size, resting heart rate, and physical activity (5,7,9–11). Increase in LVM, as related to cardiac remodeling, can be consequent to both an adaptive and a maladaptive process (12). The absence of an identifiable, pathological turning point for cardiac remodeling assessment from adaptive to maladaptive creates a challenge to the definition of normal LVM.

The distribution of LVM values is wide in a healthy population, with distinct patterns according to sex and ethnicity. Moreover, absolute values of myocardial mass are limited by not taking into account physiological variations related to body size. To adjust for these particularities, indexing LVM for anthropometry allows comparisons among different individuals. Several methods have been suggested for the normalization of LVM values—usually involving height, weight, or both. Indexing is also important because it affects who will be classified as having left ventricular hypertrophy (LVH) (1,13–19).

Echocardiography and cardiac magnetic resonance (CMR) are the best-documented imaging modalities used to assess myocardial mass. In both cases, scientific societies have elaborated guidelines discussing appropriate technical procedures, validation aspects, and clinical indications (20,21). Accurate quantification of cardiac dimensions is crucial for distinguishing disease states from normal variants (22). LVM is calculated using different algorithms for each modality and gives different average values for LVM with different degrees of accuracy (1).

Assessment of LVM in epidemiological studies has shown prognostic value (1). The importance of LVM and hypertrophy for clinical purposes is best evidenced for hypertensive populations. LVH is recognized by current guidelines as target-organ damage that influences the prognosis in hypertensive populations. However, recommendations for incorporation of LVM or LVH into hypertension treatment algorithms vary in different guidelines (23–25). This partly

explains why on a daily basis the clinical use of LVM measurements has not been firmly established—although extensively used as a surrogate endpoint in clinical trials (20,26).

In this review, we investigate 3 important points related to clinical use of LVM measurements: 1) comparison of LVM assessment by echocardiography and CMR; 2) outcomes prediction power of LVM; and 3) the different normalization methods used to index LVM. Our aim is to evaluate the strength of the evidence regarding the use of LVM measurements in clinical practice, as a predictor of events and as a therapeutic target.

LVM Assessment by Echocardiography and by CMR

Echocardiography. Although LVM may be assessed using 2-dimensional (2D) or 3-dimensional (3D) echocardiography, M-mode was the first noninvasive imaging technique developed and remains the recommended method (20,27). Whether using M-mode, 2D, or 3D measurements, LVM estimation by echocardiography is based on subtraction of the left ventricular (LV) cavity volume from the volume enclosed by the correspondent epicardium to obtain the myocardial volume, then multiplying by the myocardial density (taken to be 1.05 g/ml) (20). At the present time, the lack of long-term follow-up information using 2D or 3D echocardiography estimations of LVM as event predictors limits further discussion in this review.

In patients without major cardiac geometry distortions, the American Society of Echocardiography (ASE) recommends a formula to estimate LVM from linear dimensions based on the assumption of the LV as a prolate ellipsoid of revolution (Fig. 1). Linear measurements of interventricular septum wall thickness (IVST), as well as left ventricular internal diameter (LVID) and posterior wall thickness (PWT), should be done from the parasternal acoustic window in end-diastole at the level of the LV minor axis (mitral valve leaflet tips) using 2D-targeted M-mode or directly from 2D images (20). Although wall dimensions are used to assess LVM by echocardiography, regional increase in wall thickness seen in hypertrophic cardiomyopathy is a specific disease and will not be addressed in this review.

The first challenge to echocardiographic assessment of LVM is the correct identification of interfaces between the cardiac blood pool and the endocardium, as well as between the epicardium and pericardium. The correct M-mode reference beam orientation perpendicular to the septum can also be challenging. Poor acoustic windows and operator experience are also major concerns for echocardiography measurements. The LVM algorithm is performed cubing values of the primary linear measurements, which therefore magnifies measurement errors.

The need to calculate myocardial volume cubing linear dimensions—due to the geometric assumption of the prolate ellipsoid—is the major limitation for LVM estimated by M-mode echocardiography as related to accuracy and reproducibility (28–31). PRESERVE (Prospective Randomized Enalapril Study Evaluating Regression of Ventricular Enlargement) assessed intrapatient reliability (interscan reproducibility) of echocardiographic LVM measurements, repeating echocardiograms in 183 hypertensive subjects with LVH. The intraclass correlation coefficient (ICC) for the linear measurements was 0.87 for LVID, 0.85 for IVST, and 0.83 for PWT (32). Bottini et al. (33) also assessed interscan reproducibility, repeating echocardiograms in 22 hypertensive subjects, and reported an average mean difference of 0.3 g between exams, with 95% limits of agreement from −96.3 g to 96.9 g. The same authors also had 2 readers independently assessing 24 echocardiography images, finding mean differences (95% limits of agreement) of 1.83 g (−48.8, 52.5) (33). Intrareader reproducibility for LVM by echocardiography was evaluated in 735 children of HIV-infected mothers in the prospective P(2)C(2) HIV study (34). Echocardiograms were analyzed in 10 clinical sites and then reassessed at a central facility. The internal LVID showed the highest agreement (ICC = 0.97), but lower correlation was found for PWT (ICC = 0.65) and IVST (ICC = 0.50) (34). Also for intrareader reproducibility, 21 subjects were assessed by Missouris et al. (29), showing a mean coefficient of variation (95% confidence interval [CI]) of 6.1% (3.9 to 8.3). Using 20 hypertensive male subjects, Spratt et al. (35) investigated echocardiography inter-reader reproducibility and found mean differences (95% limits of agreement) for LVM/body surface area (BSA) between 4.5 g/m^2 (−24.9, 33.9) and 6.4 g/m^2 (−23.0, 35.8) for harmonic imaging (HI) and fundamental imaging (FI), respectively.

The ASE-recommended algorithm is based on the formula first described by Devereux et al. in 1977, adding modifications (20,27,36,37). Due to the ability

ABBREVIATIONS AND ACRONYMS

BSA = body surface area
FI = fundamental imaging
GRE = gradient-echo
HI = harmonic imaging
ICC = intraclass correlation coefficient
IVST = interventricular septum thickness
LV = left ventricular/ventricle
LVH = left ventricular hypertrophy
LVID = left ventricular internal dimension
LVM = left ventricular mass
LVMi = left ventricular mass index
PWT = posterior wall thickness
SSFP = steady-state free precession

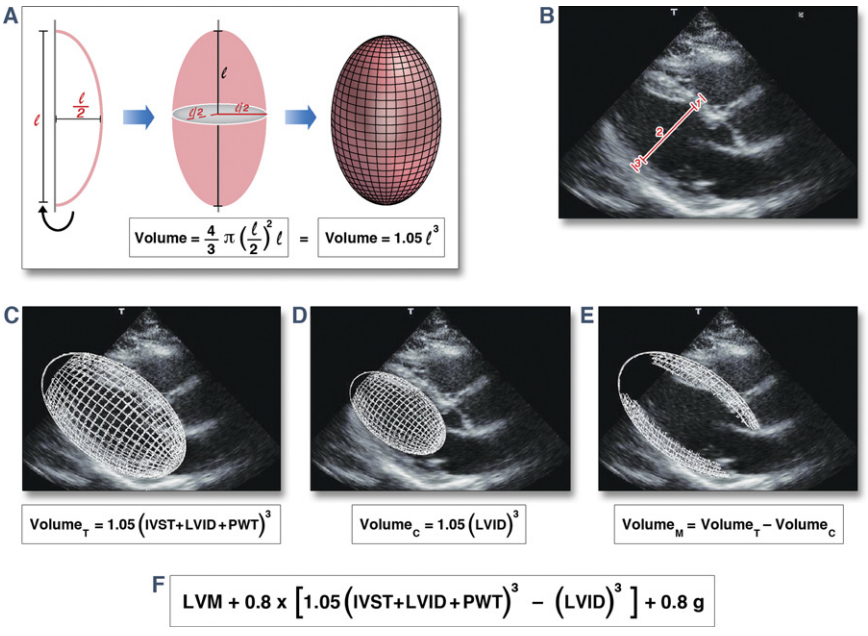

Figure 1. Principles for the Assessment of LVM by Echocardiography, as Recommended by the ASE

(A) A prolate ellipsoid of revolution, or prolate spheroid, is a 3-dimensional figure formed by revolving an ellipse about its major axes. The American Society of Echocardiography (ASE)-recommended formula assumes that the left ventricle has a prolate ellipsoid of revolution shape, with minor radii that are half the major radius. **(B)** Schematic representation of the linear measurements for the assessment of LVM by echocardiography (parasternal view), according to the ASE recommendations. 1 = interventricular septum thickness (IVST); 2 = left ventricular internal dimension (LVID); 3 = posterior wall thickness (PWT). **(C to E)** Images refer to a schematic representation of the steps for the estimation of left ventricular myocardial volume, as initially proposed by Devereux et al. (28). Left ventricular mass (LVM) is then calculated by multiplying the myocardial volume by the specific gravity of myocardium (1.05 g). **(C)** Calculation for the total left ventricular volume ($Volume_T$). **(D)** Calculation for the left ventricular internal cavity volume ($Volume_C$). **(E)** Calculation for the left ventricular myocardial volume ($Volume_M$). **(F)** The current ASE-recommended formula for the assessment of LVM. It is based on the initial concepts, but includes correction factors derived from regression analysis (20,35).

to improve definition of pericardial and endocardial borders, HI replaced FI in clinical practice. In the past, FI was limited to a fixed frequency for output and receiving (usually ~2.5 mHz), but the advent of HI allowed the emission of low-frequency ultrasound for good penetration and the reception of signal 2 octaves higher (38). When assessed by M-mode echocardiography, HI shows higher values for LVM compared with FI, but seems to correlate better to CMR measures (30,35,38,39).

Cardiac magnetic resonance. LVM evaluation by CMR permits a 3D high-resolution modeling of the LV free of cardiac geometric assumptions, contrast infusion, acoustic window dependency, or ionizing radiation. Both short-axis and long-axis techniques are highly accurate for quantification of LVM (40). The best-documented technique, however, uses a set of contiguous short-axis slices covering the entire LV from the atrioventricular ring down to the apex, acquired from a cine sequence. A combination of body matrix/torso radio frequency coils is used for the acquisition, using a 2D cardiac-gated pulse sequence. Ideally, images are acquired at resting lung volume. Myocardial volume is the area occupied between the endocardial and epicardial border multiplied by the interslice distance. By convention, LVM is measured at end-diastole. Similar to echocardiography, LVM is the product of this volume and the density of the myocardium (Fig. 2).

Early controversies were related to contour differences in LV quantification by CMR, with small studies favoring inclusion of papillary muscles in the calculation of myocardial mass (41–43). In fact, the measurement technique significantly influences the estimation of LVM (44). However, MESA (Multi-Ethnic Study of Atherosclerosis) enrolled the largest population with CMR assessment and showed better reproducibility when papillary muscles were excluded (45).

Technical developments in CMR image acquisition and post-processing influence LVM measurements. Black-blood techniques were previously used to assess LVM by CMR, moving to cine bright-blood techniques. More recently, steady-state free precession (SSFP) has replaced fast gradient-echo (GRE) se-

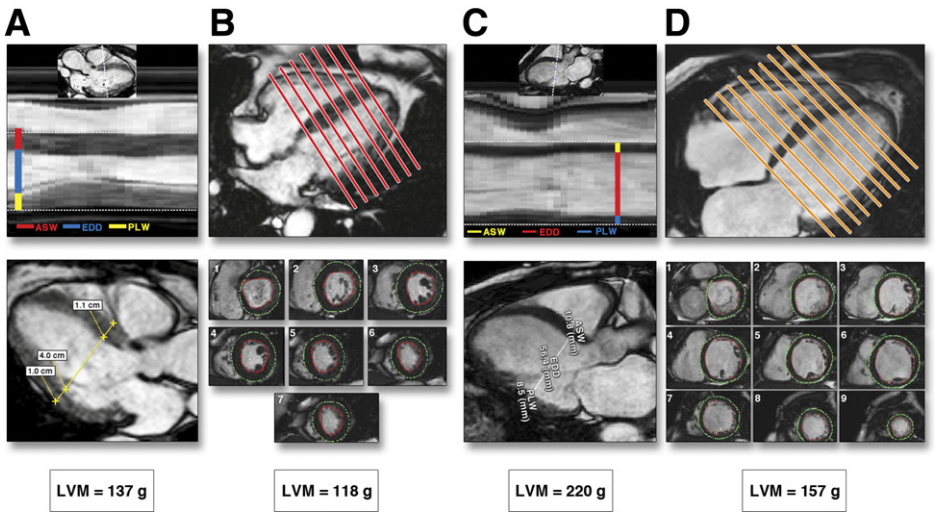

Figure 2. Images From CMR of 2 Patients With Chagas Cardiomyopathy

Case 1 has preserved cardiac geometry, but case 2 shows left ventricular remodeling. The usual assessment of LVM by cardiac magnetic resonance (CMR) does not require cardiac geometry assumptions, as opposed to linear measurements used in echocardiography. (Courtesy of Dr. Gustavo Volpe.) **(A and C)** CMR-derived images representing usual echocardiography views for linear measurements assessing LVM. The anterior septal wall (ASW) corresponds to the interventricular septal thickness; the end-diastolic dimension (EDD) corresponds to the left ventricular internal dimension; and the posterior lateral wall (PLW) corresponds to the posterior wall thickness. At the **bottom**, the ASE-recommended formula was used to calculate LVM (see Fig. 1 for a full description). **(B and D)** Usual CMR assessment for LVM, using contiguous short-axis slices covering the entire left ventricle from the atrioventricular ring to the apex (1 to 9). The estimated LVM is displayed at the bottom. Abbreviations as in Figure 1.

quences as the preferable CMR cine bright-blood technique. Compared with GRE techniques, SSFP sequences have substantially higher signal-to-noise and contrast-to-noise ratios and shorter acquisition times (46). SSFP sequences improve homogeneity of the blood pool signal and definition of the endocardial border throughout the cardiac cycle, improving the performance of automatic and manual delineation of contours for assessment of LVM (47). Studies comparing SSFP and GRE for calculation of LVM demonstrated a lower mass measured by the SSFP sequence, but both methods demonstrated good reproducibility (47,48).

In healthy participants, LVM assessed by CMR shows susceptibility to interobserver variation (49). Using 9 normal young volunteers, Missouris et al. (29) found CMR intrareader reproducibility between LVM estimations of 0.5% with 95% limits of agreement of ±11%. Bottini et al (33). assessed intrareader reproducibility in a population of 34 hypertensive subjects, finding mean differences (95% limits of agreement) of 0.32 g (−20.1, 21.7). Gandy et al. (50) showed that intrareader reproducibility of LVM measurements by CMR are dependent upon the clinical cardiac condition under investigation, with intraobserver coefficients of repeatability of 4.6 g for healthy volunteers, 6.7 g for post-myocardial infarct patients, 8.3 g in patients with congestive heart failure, and 9.8 g in patients with LVH. Moreover, Bellenger et al. (51) investigated 15 healthy adult volunteers and 15 patients with chronic stable heart failure that underwent 2 CMR scans 7 days apart, with correlation coefficient for the assessment of LVM of 0.99 and interscan average difference (95% limits of agreement) of 0.7 g (−6.3, 9.7) and 0.7 g (−11.9, 13.3) for normal and heart failure patients, respectively.

In fact, among the evaluations of LV volume, mass, and function by CMR, LVM appears to be the least reproducible and most variable parameter (44). This is because LVM is derived from the difference of 2 volumes (total LV volume and end-diastolic volume). Although gradually less significant over time, additional important limitations for wide clinical use of CMR include the following: elevated operational cost, time to acquire and analyze cine data, breath-hold dependency, hazards associated with ferromagnetic metal devices, and issues related to claustrophobia in susceptible patients.

Echocardiography versus CMR. Although CMR and echocardiographic LVM measurements show high correlation, absolute values of LVM differ between these techniques (Fig. 2) (29,30). The difference among estimates by echocardiography and CMR

indicates that the 2 methods cannot be used interchangeably in the assessment of LVM (33). Echocardiography is less expensive and has superior versatility, acceptability, and availability compared with CMR. These are practical issues that support clinical use of LVM assessed by echocardiography as an outcome predictor, as recommended by the most recent American Heart Association statement on cardiovascular risk assessment (52).

However, LVM determined by CMR is more accurate and precise than that provided by M-mode echocardiography (33). Interstudy reproducibility of CMR-derived parameters for LVM is also superior to 2D echocardiography for normal, dilated, and hypertrophic hearts (53). In fact, research studies using this method require substantially smaller sample sizes to assess outcome measures (51,53). The variability of echocardiography for evaluation of serial LVM changes has generated concerns (54). The previously reported probability of a true biological change in observed/predicted LVM over time was maximized for a single-reader difference >22% (55). Three-dimensional echocardiography improves accuracy and reproducibility compared with CMR, but is strongly dependent on equipment and technical conditions such as acoustic window quality (56–61).

LVM as a Predictor of Events

Longitudinal studies present in the MEDLINE database that investigated LVM, LVM index (LVMi), or LVH assessed by echocardiography or CMR as predictors of death or major cardiovascular outcomes were included in this analysis. The following criteria were applied to select articles: 1) echocardiographic studies using the ASE recommendations for chamber quantifications by M-mode technique (20,37); 2) survival analysis studies reporting hazard ratios and 95% CI; and 3) reports from multivariate analyses adjusted for at least 2 other traditional risk factors. In each study, analysis adjusted for the highest number of traditional cardiovascular risk factors was included. Analyses using covariates derived from other graphic/imaging diagnostic methods such as electrocardiography, ejection fraction, and LV volumes were excluded. Analyses that included pooled LVM data were excluded unless a classification of hypertrophy was clearly defined. For each study, we describe the mean follow-up time.

We included 26 longitudinal echocardiographic studies (Online Table 1) in our review. From those, 11 reported non-normalized LVM or LVMi as predictors of clinical outcomes (Online Fig. 1); 12 reported LVH (Online Fig. 2); and 8 reported serial changes in LVM or LVH status over time (Online Fig. 3). We included 5 studies for LVM assessed by CMR (Online Table 2). All CMR studies reported LVMi as outcome predictor; 2 also reported non-normalized LVM; and 1 additionally evaluated LVH. In the echocardiography group, a remarkable predominance of studies was oriented toward investigating hypertensive populations. For the CMR group, 4 of the 5 studies were based on participants from MESA, a population free from known cardiovascular disease at inclusion, using different outcomes and diverse methods for indexing LVM. Online Tables 1 and 2 also show the vast number of different LVH definitions used in these studies.

In Online Figure 4, the hazard ratios and 95% CI for the CMR group of studies are displayed according to the method used to index LVM, hypertrophy classification, and predicted outcomes. The 5 longitudinal CMR studies provide hazard ratios from 33 models. A direct comparison of events predictors is difficult due to the use of different clinical endpoints. Regardless of which method is used for normalization of LVM, however, most models demonstrated significant ability to predict events. For LVMi, the overall hazard ratio ranged from 1.0 (95% CI: 0.9 to 1.1) for prediction of coronary heart disease (62) to 2.2 (95% CI: 1.4 to 3.4) for prediction of a combined endpoint, including coronary heart disease or stroke (18).

Hazard ratios for the ability to predict events reported for LVM and LVMi in the echocardiography studies are shown in Online Figure 1, along with the mode of indexing and endpoint definitions. The 11 studies reported hazard ratios from 33 models. The hazard ratios ranged from 1.0 (95% CI: 0.99 to 1.02) for LVM indexed by BSA among subjects with diabetes—predicting a combined endpoint of cardiovascular death, ischemic heart disease, heart failure, end-stage renal disease, peripheral arterial disease, and stroke (63)—to 2.8 (95% CI: 1.6 to 4.7) for LVM predicting all-cause deaths among patients with heart failure (64).

The ability to predict events according to myocardial hypertrophy status by echocardiography is displayed in Online Figure 2. From the 10 included studies, 30 hazard ratios were reported. The hazard ratios ranged from 1.01 (95% CI: 1.0 to 1.02) for inappropriate LVM (>28% of excess, obtained by dividing LVM by predicted values based on a reference sample), predicting a composite endpoint (65) (see "composite 1" in the Online Fig. 2 legend for a full description) to 4.14 (95% CI: 1.8 to 9.7)

for LVH in patients without coronary artery disease, predicting all-cause mortality (66). Few studies are comparable, however, due to methodological differences. The majority of the studies report significant power to predict events for LVM, for LVMi, and for hypertrophy.

We assessed the ability to predict cardiovascular events by changes in LVMi or LVH classification over time using only echocardiography. Hazard ratios for serial changes in LVM or LVH status are displayed in Online Figure 3, with predicted outcome and mode of normalization. A total of 23 hazard ratios were reported in the 8 studies providing information on LVM and LVH status changes. In summary, the risk gradually increased according to LVM at baseline, with an increasing LVM or hypertrophy grading. When LV mass regressed after treatment, the hazard ratio was favorable, predicting an extensive composite endpoint (hazard ratio: 0.18, 95% CI: 0.05 to 0.7) (67) (see "composite 5" in the Online Fig. 3 legend for a full description). A maintained LVH status, however, significantly predicted a different composite endpoint (hazard ratio: 3.52, 95% CI: 2.5 to 4.6) (68) (see "composite 2" in the Online Fig. 3 legend for a full description).

Indexing Process

During the review process, we assessed several criteria used to normalize LVM. Online Figures 1, 3, and 4 display the wide variety of methods used to calculate LVMi. Heart size scales with the size of the body (22). Several different methods have been suggested for indexing LVM to anthropometric measures, usually based on height and/or weight, but the optimal way to normalize myocardial mass has not been established (20). Alternatively, procedures where measured LVM is indexed by dividing by expected LVM (based on a reference population free of major cardiovascular risk factors) have also been proposed, adding complexity to the calculation of LVMi. The most commonly used formula for computing BSA—the Dubois and Dubois regression ($BSA = 0.007184 \times \text{weight [Kg]}^{0.425} \times \text{height [cm]}^{0.725}$)—is based on an assessment of 9 cadaveric subjects reported in a 1916 publication, and its validity has been questioned (18,22,69).

Indexing LVM to BSA was the first normalization process used, but it seems to underestimate the prevalence of LVH in obese as well as in overweight hypertensive patients (17). Conversely, the prevalence of hypertrophy is higher in obese individuals for height-based indices that do not account for weight in overweight individuals (18). The purpose of indexing LVM for height with an allometric exponent is to attempt to approximate lean body mass and to possibly adjust for the impact of growth during childhood (70). Compared with LVM/BSA and LVM/height, indexation of LVM by height$^{2.7}$ appears to adjust better for the relations between height and LVM in hypertensive, obese individuals and to reduce the variability among normal subjects, providing a more sensitive cutoff for LVH (70,71). Comparing LVM indexed by BSA and height$^{2.7}$, LVM/height$^{2.7}$ has a better performance as a unique criteria to detect LVH prevalence in obese subjects (72). Also, in acromegaly, LVM indexed for height$^{2.7}$ appears to be the most appropriate method to identify LVH—particularly in patients who are also overweight (73).

Using a population of hypertensive subjects with low prevalence of obesity, de Simone et al. (74) (Online Table 1) compared indexing methods for LVM assessed by echocardiography as predictors of cardiovascular events. After adjustment for age and sex, indexing by height, height$^{2.7}$, or height$^{2.13}$ performed as well as BSA as outcome predictors (Online Fig. 1). de Simone also investigated American Indians free of cardiovascular disease, but with a high prevalence of obesity (Online Table 1) (75). Adjusted for age and sex, the presence of LVH identified by LVM normalized by height$^{2.7}$ and height$^{2.13}$ was associated with a higher proportion of outcomes than was LVH detected using LVM normalized by BSA (Online Fig. 1). In a cohort of patients undergoing dialysis (Online Table 1), more subjects were classified with LVH by LVM/height$^{2.7}$ compared with LVM/BSA (76). In this population, LVH classified either by normalization to BSA or height$^{2.7}$ predicted total and cardiovascular mortality. However, LVM/height$^{2.7}$ demonstrated better predictive ability compared with LVM/BSA (Online Fig. 1).

For LVM assessed by CMR, 2 studies used MESA (15) participants to compare indexing methods in their ability to predict clinical events (Online Table 2) (18,19). Chirinos et al. (19) initially included MESA CMR data and echocardiography data from the Asklepios Study (77) to compare LVM indexed by BSA, height, height$^{1.7}$, or height$^{2.7}$ in relation to the LVH classification. The authors conclude that indexation by height$^{1.7}$ would provide the best description of the relationship between LVM and body size in both echocardiography and CMR assessments. However, only

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the white and Chinese participants from MESA and white European subjects from the Asklepios Study were included in the analyses for the allometric exponent comparisons. In this study, survival analysis to establish the best indexation procedure was shown only for the MESA population. LVH defined by LVM/height$^{1.7}$ was reported to be related to all cardiovascular events, to hard cardiovascular events, and to all-cause mortality. Normalization by either height$^{2.7}$ or BSA, however, failed to predict all-cause mortality (Fig. 1) (19). Also using MESA participants, Brumback et al. (18) investigated LVM indexed by BSA, height^2, height$^{2.7}$, and 2 other allometric indices (percent-predicted LV mass based on height and sex; and percent-predicted LVM based on height, weight, and sex). The study found a higher prevalence of hypertrophy for indices that do not account for weight, but no significant difference was detected between indices for the outcomes prediction ability (18).

Gaps in Knowledge

An increase in LVM is the most important component of cardiac remodeling, resulting from an incompletely understood balance between cardiac stressors and compensatory mechanisms (12,28,78). However, the exact point when the increase of myocardial mass turns from an adaptive process to pathology is unknown. Obesity may be related to both adaptive and pathological increases in LVM. Future studies should address whether indexing methods can not only adjust for body size, but also account for adaptive changes in the obese and whether they influence clinical decision making.

The appropriate consideration of body size in the evaluation of cardiovascular structure affects recognition and treatment of cardiovascular disease states in pediatric and adult patients (22). The best approach seems to be normalization of LVM by height to some allometric power, specifying cutoff values of normality according to sex and ethnicity. When considering the definition of the appropriate height allometric exponent, the current literature still has important gaps in knowledge. Although height$^{1.7}$ seems to be promising to establish the best description for the relation between myocardial mass and body size, there are still strong limitations related to the cutoff definitions and to the limited longitudinal data available—especially for echocardiographic assessment of LVM. In this regard, most of the longitudinal scientific evidence is still related to normalization by height$^{2.7}$.

A reduction in intervertebral disk diameter occurs with aging, possibly accounting for artifactual individual changes over time in indexed parameters. Cumulative height loss from age 30 to 70 years may decrease approximately 3 cm of the original height for men and 5 cm for women (79). It affects the calculation of BSA, but should have higher impact on methods adjusted uniquely to height to an allometric power. However, the implications on LVMi of height changes related to aging are still unknown.

The majority of longitudinal studies assessing CMR-derived LVM predicting outcomes are from the MESA study (Online Table 2). Although addressing a large multiethnic population, the MESA results should be tested in other populations to assess how universal are these findings. There are also unclear aspects related to the assessment of LVM by CMR regarding the LV basal slices. Including or not including a more basal slice can be a major source of variability in the final LVM calculation, but this issue is not properly addressed in the literature. On the basis of the experience with the MESA study, a slice-by-slice analysis considering base when myocardium is present in more than 50% of the short-axis circumference appears to be appropriate. MESA also set the normality range for functional CMR and showed clinical event prediction for LVM assessed by resonance (15,19,62). However, these assessments were done with the GRE technique. The fact that GRE has been replaced by SSFP urges the necessity of new standard cutoff values for normality that account for technical differences.

Although CMR showed better performance than echocardiography for accuracy and precision in LVM evaluation (33), no direct comparison of the 2 methods has been performed for the ability to predict clinical events, the agreement for hypertrophy classification, or the cardiovascular risk reclassification. It is unknown how concordant CMR and echocardiography are regarding hypertrophy classification—especially when different indexing methods are considered. Additionally, there is a lack of knowledge regarding the risk reclassification for LVM when compared with traditional risk assessments (52,80).

Recommendations and Future Perspectives

We showed that LVM assessed by echocardiography has a good event prediction power, but has major limitations related to the need for cardiac geometric assumptions. Therefore, the ASE-recommended formula should be reported in all

echocardiograms performed in patients without major LV remodeling. To improve accuracy and reproducibility across laboratories, strict quality control recommendations should be enforced. In this regard, the Intersocietal Accreditation Commission for Echocardiography requires the measurement of IVST, PWT, and LVID by 2D or M-mode imaging, but has no special recommendation for LVM assessment (81). Laboratories should have technicians regularly perform intraobserver and interobserver reliability assessments to improve measurement accuracy.

The currently preferable method for LVM assessment by CMR is based in the scientific evidence collected by the MESA study, leading to the short-axis evaluation, with exclusion of papillary muscle. In addition, to include basal slides when myocardium is present in more than 50% of the short-axis circumference would be consistent with the MESA protocol. The Intersocietal Accreditation Commission for Magnetic Resonance has not made specific recommendations on LVM as criteria for quality control (82). Recommendations on standard reports and quality assessment should be consented by scientific societies.

For echocardiography, indexing LVM by height to the allometric power of 1.7 or 2.7 has shown the best relation to body size and events prediction. However, normal reference values have not been firmly established. Cutoff values endorsed by the ASE are based on FI technique and thus may not be applicable to the HI era. Values are not standardized for different ethnicities. For CMR, most of the longitudinal scientific evidence is based only on the MESA cohort of participants using GRE sequences. Standard recommendations for indexing and cut-points for hypertrophy across imaging modalities are needed to match current technologies used in daily practice.

The National Heart, Lung, and Blood Institute's Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents (24) recognizes LVH as the most prominent clinical evidence of target-organ damage caused by hypertension in children and adolescents. The guidelines incorporate LVM measurement in the evaluation algorithm, recommending intensification of antihypertensive management if there is presence of LVH. However, the role of periodic echocardiographic determination of LVMi is restricted to patients who have established LVH (24). The Eighth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-8) is expected to be released in 2012 (83). The previous edition also lists LVH as target-organ damage for the heart and an independent risk factor. Aggressive blood pressure management is described as a strategy for LVH regression. However, echocardiography is not included among the routine or even in the optional tests and procedures (25). The European Society of Cardiology Guidelines for management of arterial hypertension uses LVH as criteria of subclinical organ damage influencing prognosis (23). In this context, echocardiography is recommended during diagnostic evaluation for more precise stratification of overall risk and for checking the status of organ damage during follow-up visits. In a therapeutic view, effects of different drugs on LVM and LVH are discussed. However, LVMi variation is not stated among therapeutic goals (23).

The way clinicians use LVM in their practice may not reflect the scientific recommendations from medical societies. An important issue related to LVM is its restricted clinical use in daily practice in contrast to the regular use of measurements of cardiac systolic function (20). In a multicenter survey performed in Italy, hypertension accounted for approximately 30% of echocardiographic examinations in outpatient hospitals or academic echocardiography labs (84). However, a large majority of echocardiographic examinations routinely performed on hypertensive patients did not report data on LVM, and if reported, the results were usually not indexed to anthropometric variables (84,85).

Conclusions

In the assessment of LVM, no superiority between echocardiography and CMR may be stated at this time, due to the absence of studies directly comparing the methods. Assessed by both echocardiography and CMR, LVM, and LVH are reliable cardiovascular event predictors. LVM assessed by echocardiography is more practical on a clinical basis. CMR would be preferable for research and specific clinical conditions requiring higher accuracy and reproducibility. Dividing LVM by height to some allometric power is the most promising indexing method for scaling myocardial mass to body size. The measurement of LVM and a definition of LVH based on outcomes should be agreed upon by scientific societies considering all available techniques.

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Key Words: cardiac magnetic resonance ■ cardiovascular events ■ echocardiography ■ LVH ■ LVM.

▶APPENDIX

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