Fast Measurement of Left Ventricular Mass With Real-Time Three-Dimensional Echocardiography Comparison With Magnetic Resonance Imaging

Victor Mor-Avi, PhD; Lissa Sugeng, MD; Lynn Weinert, BS; Peter MacEneaney, MD; Enrico G. Caiani, PhD; Rick Koch, MS, MD; Ivan S. Salgo, MS, MD; Roberto M. Lang, MD

Background—Left ventricular (LV) mass is an important predictor of morbidity and mortality, especially in patients with systemic hypertension. However, the accuracy of 2D echocardiographic LV mass measurements is limited because acquiring anatomically correct apical views is often difficult. We tested the hypothesis that LV mass could be measured more accurately from real-time 3D (RT3D) data sets, which allow offline selection of nonforeshortened apical views, by comparing 2D and RT3D measurements against cardiac MR (CMR) measurements.

Methods and Results—Echocardiographic imaging was performed (Philips 7500) in 21 patients referred for CMR imaging (1.5 T, GE). Apical 2- and 4-chamber views and RT3D data sets were acquired and analyzed by 2 independent observers. The RT3D data sets were used to select nonforeshortened apical 2- and 4-chamber views (3DQ-QLAB, Philips). In both 2D and RT3D images, LV long axis was measured; endocardial and epicardial boundaries were traced, and mass was calculated by use of the biplane method of disks. CMR LV mass values were obtained through standard techniques (MASS Analysis, GE). The RT3D data resulted in significantly larger LV long-axis dimensions and measurements of LV mass that correlated with CMR better ($r = 0.90$) than 2D ($r = 0.79$). The 2D technique underestimated LV mass (bias, 39%), whereas RT3D measurements showed only minimal bias (3%). The 95% limits of agreement were significantly wider for 2D (52%) than RT3D (28%). Additionally, the RT3D technique reduced the interobserver variability (37% to 7%) and intraobserver variability (19% to 8%).

Conclusions—RT3D imaging provides the basis for accurate and reliable measurement of LV mass. (Circulation. 2004;110:1814-1818.)

Key Words: imaging ■ echocardiography ■ hypertrophy, left ventricular

Received February 3, 2004; de novo received March 17, 2004; revision received May 24, 2004; accepted May 26, 2004.

From the Noninvasive Cardiac Imaging Laboratory, University of Chicago, Chicago, Ill (V.M.-A., L.S., L.W., P.M., E.G.C., R.K., R.M.L.); Dipartimento di Bioingegneria, Politecnico di Milano, Milan, Italy (E.G.C.); and Philips Medical Systems, Andover, Mass (I.S.S.).

Correspondence to Victor Mor-Avi, PhD, University of Chicago MC5084, 5841 S. Maryland Ave, Chicago Illinois 60637. E-mail vmoravi@medicine.bsd.uchicago.edu

© 2004 American Heart Association, Inc.
Methods
Twenty-one consecutive patients (age, 48±16 years; 13 men, 8 women) referred for CMR imaging were enrolled in the study, including 7 patients with suspected coronary artery disease, 7 with dilated cardiomyopathy, 2 after myocardial infarction, 3 with aortic abnormalities, 1 with right atrial mass, and 1 with mitral valve disorder. Exclusion criteria were dyspnea precluding a 12-second breathhold, atrial fibrillation, pacemaker or defibrillator implantation, claustrophobia, and other well-known contraindications to MRI. Also, patients with cardiac arrhythmias, left bundle-branch block, and prior sternotomy were excluded. Echocardiographic imaging, including 2D and RT3D data acquisition, was performed on the same day as the CMR study. The Institutional Review Board approved the study.

CMR Assessment of LV Mass
CMR images were obtained with a 1.5-T scanner (General Electric) with a phased-array torso coil. ECG-gated localizing spin-echo sequences were used to identify the LV long axis. Steady-state free-precession dynamic gradient-echo cine loops were obtained during 12-second breathholds. Data were reconstructed to give 20 frames per cardiac cycle. In all patients, 6 to 10 short-axis cine loops were obtained from the AV ring to the apex (9-mm slice thickness, no gaps). CMR cine loops were analyzed offline with commercial software (MASS Analysis, General Electric). In each short-axis slice, endocardial and epicardial contours were manually traced at end diastole, while including the papillary muscles in the LV cavity. All tracings were performed by an investigator experienced in the interpretation of CMR images who had no knowledge of the echocardiographic measurements. For each patient, the traced contours were used to calculate LV mass, which served as the reference for comparisons against 2D and RT3D echocardiographic data.

2D Echocardiographic Assessment of LV Mass
The 2D harmonic imaging was performed by use of a commercial ultrasound system (SONOS 7500, Philips) with an S3 transducer from the apical window with the patient in the left lateral decubitus position. Five consecutive heartbeats were acquired at held respiration from each 4- and 2-chamber views while care was taken to avoid foreshortening. Images were stored digitally and analyzed offline (EnConcert, Philips). For both apical views, end-diastolic frames were selected as those captured at the peak of the R wave. In each view, endocardial and epicardial contours, including the papillary muscles in the LV cavity, were traced manually (Figure 1, top). The points of insertion of the mitral leaflets into the annulus were connected by a straight line, and the LV long-axis dimension was measured as the distance between the center of this line and the most distal point at the apical endocardium. The traced contours were used to calculate endocardial and epicardial LV volumes from Simpson’s formula.8,9 The difference between the epicardial and endocardial volumes was computed for each view and multiplied by the specific mass of myocardial tissue (1.05 g/mL) to represent a biplane estimate of LV mass. The accuracy of these estimates was determined by comparing them with the CMR values.

RT3D Echocardiographic Assessment of LV Mass
Harmonic RT3D imaging was performed in the same setting with the fully sampled matrix-array transducer (X4, 2 to 4 MHz) that uses ∼3000 elements to obtain a pyramidal volume data set from a single window. Gain and compression controls, as well as the time gain compensation settings, were optimized for quality of 3D images. Care was taken to include the entire LV cavity within the pyramidal volume. RT3D data sets were then acquired with the wedge-shaped subvolumes (93°×80°) mode in which 4 wedge-shaped subvolumes (93°×20° each) were obtained from 4 different cardiac cycles during held respiration. Acquisition was triggered to the R wave of every other cardiac cycle to allow time for storage of each subvolume, resulting in a total acquisition time of 8 heartbeats.

The RT3D data sets were analyzed with commercial software (3DQ-QLab, Philips). The pyramidal volume data (Figure 2, bottom right) were displayed in 3 different cross sections that could be modified interactively by use of the following color-coding convention. Apical 4-chamber view displayed in a green box (Figure 2, top left) could be controlled by manually shifting or rotating a green line shown in the apical 2-chamber view (Figure 2, top right) and the
short-axis view (Figure 2, bottom left). Apical 2-chamber view displayed in a red box (figure 2, top right) could be controlled by shifting or rotating a red line shown in the apical 4-chamber and the short-axis views. The short-axis view displayed in a blue box (Figure 2, bottom left) could be controlled by shifting or rotating a blue line in both apical views.

Using this convention, we selected the anatomically correct 2- and 4-chamber views with the largest long-axis dimensions as follows. First, the orientation of the long axis of the 2-chamber view (Figure 2, top right) was determined by positioning the red line along the LV long axis in the 4-chamber view (Figure 2, top left). Then, the orientation of the long axis of the 4-chamber view (Figure 2, top left) was determined by positioning the green line along the LV long axis in the 2-chamber view (Figure 2, top right). Then, the midpapillary short-axis plane (Figure 2, bottom left) was defined by positioning the blue lines in both apical views (Figure 2 top) at the midpapillary level perpendicular to the long axis of the ventricle determined in the previous 2 steps. The final selection of the apical views was achieved by changing the position of the green and red lines in the short-axis view (Figure 2, bottom left). The green line was forced to pass near the center of the LV cavity and the most distant point on the right ventricular endocardium. Similarly, the red line was forced to pass near the center of the LV cavity perpendicular to the green line. We made these last 2 fine-tuning steps while carefully ensuring that the resulting apical views have the largest long-axis dimension of the ventricle; thus, they represent the anatomically correct apical views.

In these 2 planes, endocardial and epicardial contours were traced manually at end diastole with the papillary muscles included in the LV cavity (Figure 1, bottom). The LV long-axis dimension was measured the same way as in 2D. The traced contours were then used to calculate LV volumes by use of the biplane Simpson formula with 20 slices\(^9\) incorporated into the analysis software. The accuracy of these RT3D-derived LV mass values was determined by comparing them with the CMR values.

**Interobserver and Intraobserver Variability**

To determine the interobserver variability in the 2D and RT3D evaluations of LV mass, all measurements were repeated by a second observer blinded to the values obtained by the first observer. Interobserver variability was calculated for each patient as the absolute difference between the 2 observers in percent of their mean. To assess intraobserver variability, all measurements were repeated 1 month later by an observer blinded to the results of the previous measurements. Intraobserver variability was calculated as the difference between the 2 measurements in percent of their mean.

**Statistical Analysis**

All values were expressed as mean±SD. Agreement between each technique, 2D and RT3D, and CMR was evaluated by use of a paired \( t \) test and linear regression analysis with Pearson’s correlation coefficient. In addition, Bland-Altman analysis was used to determine the bias and 95% limits of agreement between the echocardiographic measurements and their CMR counterparts. These analyses were performed for each observer individually and for the 2 observers’ measurements combined. The differences between LV long-axis dimension in the 2D and RT3D techniques were tested with a paired \( t \) test. Interobserver and intraobserver variability values were averaged for all patients and tested by use of a paired \( t \) test for significance of differences between techniques. Values of \( P<0.05 \) were considered significant.

**Results**

Acquisition of RT3D data sets was feasible in all but 2 patients whose heart sizes exceeded that of the pyramidal scan volume. These patients were excluded from analysis. In the remaining 19 patients, the end-diastolic volume was 153±69 mL (range, 56 to 353 mL) measured from 2D echocardiographic images and 172±74 mL (range, 79 to 390 mL) measured from CMR images. The CMR value of LV mass was 126±39 g (range, 57 to 222 g).

The 2D technique yielded an LV mass of 103±39 g (range, 38 to 165 g) by observer 1 and 72±22 g (range, 30 to 107 g) by observer 2, which were significantly lower than the CMR values (\( P<0.05 \)). The combined readings of the 2 observers resulted in a correlation of \( r=0.79 \) with CMR values, a regression slope of 0.54, and an intercept of 19 g (Figure 3, left). Bland-Altman analysis (Figure 4, left) confirmed the underestimation by the 2D technique by demonstrating a bias of 39 g (39% of the mean) with 95% limits of agreement at ±58 g (±52% of the mean). The LV long-axis dimension was 9.2±0.7 cm in the 4-chamber view and 8.9±0.8 cm in the 2-chamber view.

Identification of nonforeshortened apical views from the RT3D data sets was achieved in all 19 patients, in most cases within 20 seconds. The RT3D-based technique yielded an LV mass of 120±35 g (range, 57 to 183 g) by observer 1 and 123±39 g (range, 57 to 213 g) by observer 2, which were similar to the CMR values (\( P=\text{NS} \)). The combined readings of the 2 observers resulted in a correlation with CMR values of \( r=0.90 \), a regression line slope of 0.86, and an intercept of 14 g (Figure 3, right). Bland-Altman analysis (Figure 4, right) showed no significant underestimation by the RT3D-based technique as reflected by only a minimal bias of 4 g (3% of the mean) with 95% limits of agreement at ±34 g (±28% of the mean). The LV long-axis dimension was 9.4±0.7 cm in the 4-chamber view and 9.4±0.8 cm in the 2-chamber view. These values were significantly larger than in the 2D measurements (Figure 5).

The interobserver variability was 37±19% of the measured LV mass values, ranging between 5% and 66% between patients, for
the 2D technique and 7±7%, ranging between 0% and 23%, for the RT3D-based technique (P<0.05 between techniques). The intraobserver variability was 19±11% of the measured LV masses, ranging between 2% and 37% between patients, for the 2D technique and 8±5%, ranging between 1% and 22%, for the RT3D-based technique (P<0.05 between techniques).

Discussion
Since the predictive value of increased LV mass in patients with systemic hypertension was recognized, echocardiography has played a leading role in the quantification of LV mass because of its noninvasive nature, portability, and relatively low cost. In fact, studies that involve serial LV mass measurements have been the most common echocardiographic application in epidemiology and in clinical trials of antihypertensive agents. Quantification of LV mass has traditionally been based on M-mode measurements of myocardial thickness, coupled with geometrical modeling of the ventricle, or model-based calculations from manually traced endocardial and epicardial contours obtained from 2D images. Because overestimation of M-mode LV mass measurements as a result of inadvertent use of oblique cuts and underestimation by the 2D techniques as a result of foreshortening of apical views have been reported, 3D methods have been proposed to improve the accuracy of LV mass measurements. Several studies have demonstrated that 3D techniques based on offline reconstruction from multiple planes, including rotational acquisition and free-hand scanning with locator devices and more recently followed by the early real-time volumetric imaging system, were more accurate than the conventional M-mode or 2D methods. These studies and others have endorsed the use of 3D data as a more accurate way to evaluate LV mass on the basis of validation in animal experiments and explained human hearts, with comparisons against true anatomic mass, and in vivo validation with CMR imaging. In addition, several studies demonstrated that the 3D-based techniques are more reproducible and have less variation between observers than conventional techniques.

Despite these obvious advantages, LV mass measurements from 3D data have not become standard in clinical laboratories because of cumbersome and time-consuming data acquisition and analysis; thus, 3D assessment of LV mass remained limited mainly to the research arena. The recent development of the matrix-array transducer offers an opportunity for real-time imaging and online rendering of the heart without reconstruction, thus bringing the RT3D imaging into the mainstream.

Our goal was to explore the potential of this new technology for quantitative evaluation of LV mass. We hypothesized that data sets acquired with the matrix-array transducer could be cross sectioned offline to allow selection of anatomically correct apical views. Specifically, we assumed that tracing endocardial and epicardial boundaries on anatomically correct, nonforeshortened apical views would result in improved accuracy in the quantification of LV mass. We tested this hypothesis by acquiring and analyzing RT3D data in a group of consecutive patients referred for CMR imaging. This study design automatically provided us with validation of our measurements using an accepted standard reference method for LV mass. The interactive technique we used to identify anatomically correct, nonforeshortened apical views was based on that routinely applied to scout CMR images to identify anatomically correct short-axis views for imaging LV function.

We found that RT3D data sets obtained with commercially available equipment provided images with sufficient detail to allow easy offline selection of nonforeshortened apical views, with the exception of 2 patients (10%) who were excluded because their hearts were too big to fit into the scan volume. This may indicate a limitation of this technique in patients with dilated cardiomyopathies.

The accuracy of the 3D technique could likely be improved further by increasing the number of planes used to trace the endocardial and epicardial boundaries, although adding planes beyond 3 was shown to have little if any added benefit in normally shaped ventricles. Another related limitation of this study is that no patients with nonconcentric hypertrophic cardio-
myopathy were included. It is likely that in such patients, the RT3D measurements would have yielded lower levels of agreement with the reference method, because these measurements were performed in 2 orthogonal planes only. A more comprehensive approach such as detection of the endocardial and epicardial surfaces would be beneficial in these patients.

Nevertheless, to allow fair intertechnique comparisons, we used the same biplane method of disks to calculate LV mass from endocardial and epicardial boundaries traced on the 2D images and those selected from the RT3D data sets. Although this strategy might have compromised to some extent the accuracy of the 3D measurements compared with potentially more accurate albeit more complex and time-consuming multiplane analysis, it resulted in a quick, simple, and intuitive technique.

Despite these limitations, our RT3D-derived estimates of LV mass resulted in higher levels of agreement with the conventional 2D measurements obtained in the same subjects. Our measurements of the LV long-axis dimension showed that offline cross sectioning of the RT3D data sets resulted in significantly less foreshortened and thus more anatomically correct apical views than the conventional 2D measurements, thus explaining the improved accuracy of the former technique. In addition, our results indicate that the 3D technique provides more reproducible measurements than the conventional 2D technique. An important point is that the 3D measurements varied less between observers, reflecting reduced operator dependency. The facts that the interobserver variability of the RT3D technique is virtually equal to the intraobserver variability and that both are <10% indicate reproducibility that is acceptable for clinical use. Also of note is the fact that although CMR imaging is commonly used as a standard reference technique for LV mass measurements, its intermeasurement and intrainmeasurement reproducibility, albeit very high, is <100%. In this regard, the RT3D echocardiographic quantification of LV mass, even with variability <10%, remains inferior to CMR, with variability values <1% reported by multiple investigators. This difference can be explained by the relatively limited ability of ultrasound imaging compared with MR to visualize the endocardial and, even more so, the epicardial boundaries.

Conclusions
Assessment of LV mass from RT3D echocardiographic data sets is feasible in consecutive patients. This technique is more accurate than conventional methods based on analysis of 2D images. It is also fast and relatively free of motion artifacts compared with previously described techniques based on 3D reconstruction from multiple planes. These findings have important clinical implications for the assessment of the severity of LV hypertrophy in patients with systemic hypertension. Also, because of the improved accuracy, reproducibility, speed of acquisition, and ease of analysis, use of this technique could potentially reduce the number of patients necessary to achieve standard levels of statistical significance and thus result in significant savings in future epidemiological studies aimed at assessing the effects of drugs on hypertensive patients. Therefore, use of this technique instead of the conventional M-mode or 2D-based techniques is recommended.

References
Fast Measurement of Left Ventricular Mass With Real-Time Three-Dimensional Echocardiography: Comparison With Magnetic Resonance Imaging
Victor Mor-Avi, Lissa Sugeng, Lynn Weinert, Peter MacEneaney, Enrico G. Caiani, Rick Koch, Ivan S. Salgo and Roberto M. Lang

_Circulation._ 2004;110:1814-1818; originally published online September 20, 2004; doi: 10.1161/01.CIR.0000142670.65971.5F

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2004 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/110/13/1814

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation_ is online at:
http://circ.ahajournals.org/subscriptions/