Anatomic Validation of Left Ventricular Mass Estimates from Clinical Two-dimensional Echocardiography: Initial Results

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SUMMARY We performed a prospective anatomic validation study to determine the accuracy of left ventricular (LV) mass estimates from clinical two-dimensional echocardiographic (2-D echo) studies. In 21 subjects, antemortem 2-D echo LV mass determinations were compared with anatomic LV weight by postmortem chamber dissection. Major cardiac diagnoses included anatomic LV aneurysm in four, status post aneurysctomy in one, transmural myocardial infarction in seven, congestive cardiomyopathy in five, rheumatic mitral disease in two, chronic severe mitral or aortic regurgitation in three, amyloid heart in two, and normal heart in three. Marked right-heart dilatation was present in 11 patients and LV thrombus in four. Regression equations derived in vitro for each 2-D echo instrument were used to correct LV mass estimates based on a short-axis, area-length method: uncorrected LV mass = 1.055 × k × 5/6 (A Lc - A Lp) + b, where A Lc = total short-axis LV image area at the high papillary muscle level, L c = endocardial LV length, k = an instrument-specific regression slope and b = an instrument-specific intercept. LV mass by 2-D echo correlated extremely well with actual LV weight (r = 0.93 slope = 0.85, SEE = 31 g, range 77-454 g). In contrast, M-mode echocardiographic LV mass estimates were less reliable (r = 0.86, SEE = 59 g) in these markedly distorted hearts. These 2-D echo LV mass results compare favorably with reported results from biplane angiography and M-mode echocardiography in more symmetric hearts. Thus, regression-corrected 2-D echo may be the method of choice for determining LV mass in man.

TWO-DIMENSIONAL echocardiography (2-D echo) is a promising method for noninvasive quantitation of left ventricular (LV) volume and myocardial mass in man.1-4 However, there is little information on the accuracy of 2-D echo images of actual cardiac targets. Moreover, validation of 2-D echo methods has relied heavily on other indirect methods, such as angiography.1-4 Reported correlations between angiography and 2-D echo have been only fair to good, but this may be due to errors in both techniques. In considering the development of methods for 2-D echo estimation of LV mass, we made the following postulates. First, short-axis imaging should usually provide optimal resolution of endocardial and epicardial boundaries because the angle of incidence of the echo beam is relatively favorable. Second, a clinically useful method must be simple to perform. Third, the relationship between 2-D echo image area and actual cardiac target area must be critically examined and quantitatively expressed. Fourth, direct comparisons of echo LV mass and postmortem LV weight would give more reliable results than angiographic comparisons. Therefore, we developed an in vitro method of imaging postmortem short-axis human heart slices to test 2-D image accuracy and used it to evaluate a simple short-axis, area-length method for determining LV mass by 2-D echo.5 From these studies, we developed regression equations to correct 2-D echo images obtained with six types of 2-D echo instrument.6

Based on our in vitro results, the present study was designed as a prospective test of the reliability of LV mass estimates derived from clinical 2-D echo images by the regression-corrected, short-axis, area-length method compared with postmortem LV weight.

Methods

From January 1, 1979, to December 31, 1981, 21 subjects who had undergone high-quality 2-D echo studies with Varian 3000R or 3400 phased-array instruments came to autopsy. The mean interval from 2-D echo to death was 21 days (range 2-76 days). Four subjects had anatomic LV aneurysms and one had undergone an aneurysctomy. Seven subjects had had transmural myocardial infarction. Five subjects had congestive cardiomyopathy, two rheumatic mitral disease, three chronic severe mitral or aortic regurgitation, two cardiac amyloidosis, and three had normal hearts. Sixteen had congestive heart failure, three mitral prostheses, one an aortic prosthesis, three clinical or angiographic evidence of severe nonrheumatic mitral regurgitation and 11 right-heart dilatation and failure. LV mural thrombus was present in four patients and occupied most of the LV cavity in one patient. In 18 hearts, LV weight was determined by the chamber dissection method of Bove and co-workers,7 which includes septal weight. Epicardial fat was removed and 3% was subtracted from LV weight to account for effects of formalin fixation.8 Three hearts were distilled at physiologic pressure, fixed, embedded in gelatin, and the LV was sliced at 5-mm intervals. Manually digitized outlines of myocardial and cavity boundaries were used in computer reconstruction of myocardial mass.9 M-mode echo data were available in 18 subjects for

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estimation of M-mode LV mass by our previously reported regression-corrected, modified cube method, which has been validated by comparison with both LV weight and angiographic LV mass for hearts without marked asymmetry.\textsuperscript{10,11}

Two-dimensional echocardiographic estimates of LV mass were based on analysis of end-diastolic (R-wave peak) stop-frame image area of short-axis views at the high papillary muscle level (fig. 1A) and LV length from apex to base in the four-chamber view (fig. 2A). After repeated real-time, slow-motion and frame-by-frame review, images were traced with fine-tip felt pens onto clear plastic superimposed on the video screen. In the short-axis view, the outer myocardial boundary included the echoes of the right side of the septum and excluded epicardial echoes (fig. 1B). The cavity boundary included all endocardial echoes and papillary muscles in myocardium. In the four-chamber view, LV cavity length was measured from the apex to the mid-mitral annulus plane, and 1 cm was added to account for myocardial thickness in estimating epicardial LV length (fig. 2B). Areas and lengths were determined on a microcomputer equipped with a high-resolution digitizer and previously validated software. For subsequent analysis, areas, lengths and M-mode echo dimensions were taken as the mean of four to 10 measurements of different cycles (mean 6.4 cycles) per subject.

The geometric analysis was adapted from that developed by Wyatt and co-workers in the dog.\textsuperscript{12} Total LV volume, including myocardial volume, was estimated as $5/6$ total LV short-axis image area ($A_s$) times the four-chamber epicardial LV length ($L_v$), or $5/6 A_s L_v$. LV cavity volume was calculated as $5/6$ cavity area ($A_c$) times LV length ($L_v$). Uncorrected LV myocardial mass was determined as total volume minus cavity volume times specific gravity, or $1.055 \times 5/6 (A_s L_v - A_c L_v)$.

Mass estimates were then corrected by previously determined in vitro regression relationships that were specific for the 2-D echo instrument used and had been developed by comparing 2-D images with calibrated photographs and the weight of LV sections.\textsuperscript{5,6} The resultant equations were: LV mass = 0.58 ($A_s L_v - A_c L_v$) + 15.8 g for 18 Varian 3000R studies, and 0.58 (0.72 $A_s L_v - 0.89 A_c L_v$) + 15.8 g for three Varian 3400 studies. Two hearts in the present series were imaged with a second Varian 3000R, and the regression correction based on the first instrument was used. To facilitate comparison of M-mode and 2-D

\begin{figure}[h]
\centering
\includegraphics[width=0.8\textwidth]{figure1.png}
\caption{(A) Two-dimensional echocardiographic short-axis end-diastolic (R-wave peak) left ventricular image at high papillary muscle level selected for analysis in a subject in the present study. (B) Same image with superimposed tracing of endocardium and epicardium.}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=0.8\textwidth]{figure2.png}
\caption{(A) Two-dimensional echocardiographic four-chamber left ventricular (LV) image selected for determination of LV length. The apex is at the top of the image and the LV is on the right. (B) Same image with LV cavity length ($L_v$) drawn from apex to mid-mitral annulus plane.}
\end{figure}
data, we used 2-D cavity and myocardial areas to calculate equivalents to the M-mode LV diameter (2\sqrt{A/\pi}) and wall thickness (\sqrt{A/\pi - \sqrt{A/\pi}}). Statistical analyses were performed by linear regression methods.13

Intraobserver reproducibility of tracing of a single image was evaluated by repeated tracing of 57 short-axis images. The correlation coefficient was 0.98, slope 0.97 and standard error 1.3 cm². The variability of image area on a series of cardiac cycles was determined by calculating the mean cycle-to-cycle percent variability of area for all 21 subjects studied. The mean percent variability was 5.5 ± 2.1%. Interobserver variability of areas of a single cardiac section with frames freely selected by two observers has been described (r = 0.97, slope = 0.99, intercept = 3.2 cm² and SEE = 4.9 cm²). Images of the first 14 hearts were reviewed and traced independently by two observers without knowledge of the LV weight, clinical information or M-mode results. The 2-D LV mass estimates produced by two different observers also correlated well (r = 0.90, slope = 0.85, intercept = 35.1 g, SEE = 24.9 g). Therefore, all analyses shown are based on tracings made by a single observer. Statistical results compared with actual weight were nearly identical when the second observer’s echo tracings were used.

**Results**

Figure 3 is a comparison of 2-D echo LV mass and anatomic LV weight. The range of anatomic LV weight is 77–454 g. The echo results were highly reliable (r = 0.93, slope 0.85, intercept = 25.9 g, SEE = 31 g). Left ventricular size and shape did not appear to alter the relationship of individual points to the regression line.

In contrast to the excellent 2-D echo results, a similar comparison of M-mode echo LV mass and anatomic LV mass, in these markedly distorted hearts (fig. 4) showed a correlation coefficient of only 0.86, a slope of 1.0 and an intercept of 79 g. The see is much higher, 59 g. M-mode estimates of mean myocardial thickness correlated poorly with the 2-D myocardial wall thickness back-calculated from myocardial area (see Methods) (r = 0.52, slope = 1.05, intercept = 0.2 cm, SEE = 0.34 cm). The LV length estimated by doubling the M-mode LV diameter (an assumption of the M-mode cube method) also correlated poorly with actual 2-D LV length (2-D LV length = 0.38 M-mode "length" + 4.49; r = 0.60, SEE = 1.53). In contrast, M-mode internal dimension (LVID) correlated well with back-calculated mean 2-D short-axis LVID from the LV cavity area (2-D = 1.01 M-mode LVID – 0.56 cm; r = 0.89, SEE = 0.77). Four hearts were subsequently divided into short-axis sections and reimaged in vitro by our previously reported method. Uncorrected in vitro area-length LV mass and uncorrected in vivo mass correlated well (r = 0.92, slope = 0.93, intercept = 80 g).

**Discussion**

Quantitative applications of two-dimensional echocardiography are limited largely by the quality of the images obtained with existing instrumentation. In attempting to develop a method for 2-D echo determination of LV mass, short-axis imaging techniques have a number of advantages. First, endocardial and epicardial definition, two variables critical to LV mass estimation, are usually superior to those obtained in other views in the same subject because the echo beam has a relatively favorable angle of incidence throughout much of the short-axis image. Second, in vitro image evaluation is readily performed with thin short-axis heart slices, as we have reported, and permits development of regression equations that may be useful for correcting systematic imaging errors in clinical images.
and for evaluating different geometric models in detail. However, short-axis images also contain less geometric information about LV shape than do long-axis or apical four-chamber or two-chamber views. Simpson’s rule approximations can be made with short-axis images only by obtaining serial images spaced along the long-axis of the ventricle. The number of such images required for optimal imaging in dogs has been shown by Eaton and co-workers to be at least six. Unfortunately, in the clinical setting, it is rarely possible to obtain so many serial short-axis images. Wyatt and co-workers showed in dogs that a simple area-length method, based on a single short-axis section at the high papillary muscle level, combined with apical LV length gives estimates of LV mass and volume nearly as accurate as those obtained with Simpson’s rule in both symmetric and asymmetric ventricles. We verified this for in vitro imaging of human hearts of normal shape and those with marked shape abnormalities. The excellent correlation between 2-D echo LV mass and postmortem LV weight in the present prospective series, which also contained many markedly distorted hearts (four with aneurysm, four with LV thrombus and 11 with marked right-heart enlargement) shows that both the regression correction and the geometric validation derived from in vitro studies have clinical applicability. Presumably, use of a short-axis image at the papillary muscle level at approximately the midpoint in LV length and reliance on end-diastolic images obtained at the time in the cardiac cycle when LV shape is least distorted in ischemic heart disease contribute to the success of this approach. The method also measures LV length directly with axial resolution. Despite the geometric limitations of short-axis imaging, the results appear to be more satisfactory than those previously obtained in man using only apical views in a study validated by biplane angiography. Nonetheless, with continued improvement in image characteristics, it will probably be possible to obtain still more reliable results using four- and two-chamber views.

Whatever views are to be used for quantitative imaging, the results obtained in both our earlier in vitro studies and in the present study suggest that overestimation of myocardial area and underestimation of LV cavity area may be consistent features of 2-D echo images, although quantitatively different for different types of 2-D instrument. The preliminary reports of Barrett and co-workers also support this view. We have also noted that the differences in regression equations obtained with different instruments of varying design require use of instrument-specific equations. Whether each instrument will require individual calibration of this type has not yet been determined, but it is encouraging that two studies in this series were accurately assessed using a regression correction derived from another instrument of the same design.

Because of the difficulty of obtaining appropriately timed 2-D echo studies and corresponding postmortem data, the number of hearts studied to date is limited. However, the regression slope, standard error and correlation coefficient have not changed appreciably since the results were analyzed for the first eight hearts. Furthermore, when in vitro and in vivo data are combined, 34 comparisons of echo results and LV weight have been made, a number similar to those available for biplane angiography. Nonetheless, our results must be confirmed by additional data obtained in our own and other laboratories before assessment of the method is complete. In that effort, it may be necessary to individually calibrate each instrument with in vitro image data until the degree of sample variation between 2-D instruments of the same design and the impact of different user techniques can be more thoroughly assessed.

The overall significance of our data is best appreciated in the context of alternative methods for estimating LV mass. The results of Kennedy et al. for biplane angiography indicate that biplane angiographic LV mass, as compared with postmortem LV weight, gave a correlation coefficient of 0.97 and a standard error of 32 g. However, large errors were noted in patients with marked right ventricular hypertrophy, who were excluded from the analysis. Patients with pericardial effusion or thickening and hypertrophic cardiomyopathy were also excluded. Furthermore, no patients with ischemic heart disease were studied and none had an LV thrombus.

Our previous M-mode echo validation study by comparison to LV weight gave statistical results very similar to those of the angiographic method. Unlike the angiographic method, the M-mode method was evaluated in 12 hearts with myocardial infarction. However, that series did not, by chance, include hearts with major geometric distortions due to LV aneurysm, mural thrombus or marked right-heart enlargement. All of these abnormalities were prevalent in the present study, in part because of a change in our institution’s patient population in the last 6 years. As our present data demonstrate, M-mode estimates of LV mass in more distorted hearts are less accurate than in the more symmetric hearts previously studied. Despite the more challenging geometry of the hearts in this series, 2-D echo gave reliable results, with a correlation coefficient and standard error comparable to those previously reported with either of the older techniques, over a smaller range of LV weights. The superiority of these results to the M-mode results in the present study probably are explained in part by the inaccuracy of the M-mode cube formula assumption of an LV length/diameter ratio for this population. A second factor appeared to be improved estimation of mean myocardial thickness by the 2-D area technique. Thus, because of its insensitivity to LV shape abnormalities, our 2-D method may improve the reliability of LV mass estimates used in clinical research and the understanding of the role of LV hypertrophy in common disorders that alter LV hemodynamic load or contractility.

We conclude that 2-D echo short-axis area-length estimates of LV mass, when corrected for the specific
image area properties of the 2-D echo instrument used, appear to provide simple, reliable estimates of in vivo LV mass despite marked abnormalities of LV shape. Further data from other laboratories will be required to determine the ultimate value of this promising method.

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