Reproducibility of Left Ventricular Mass Measurements by Two-Dimensional and M-Mode Echocardiography

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Both two-dimensional and M-mode echocardiography provide accurate estimates of left ventricular mass. However, their reproducibility in serial studies has not been compared, although this issue is critical to evaluation of regression of hypertrophy. To determine which technique provides more reproducible estimates of left ventricular mass, three serial studies were performed prospectively in each of eight normal adults over 5 months. Both two-dimensional and M-mode echocardiograms were obtained at each of these 24 studies. Measurements were performed by two independent observers who did not know patient identity. For the two-dimensional method, left ventricular mass was determined with use of a computer light-pen system and the truncated ellipsoid formula. For the M-mode method, mass was calculated from Penn convention measurements with use of the cube formula.

At study 1 the group mean left ventricular mass by two-dimensional echocardiography (115 ± 20 g) did not differ from that by M-mode study (127 ± 37 g, p = NS). However, serial estimates of left ventricular mass were more reproducible by two-dimensional echocardiography. The mean difference among the three serial two-dimensional studies in each individual was 4.8 ± 4 g ($4.2 \pm 3\%$) by the two-dimensional method, but was 18.5 ± 13 g ($14.9 \pm 10\%$) by the M-mode method (p = 0.01). Interobserver results for left ventricular mass by two-dimensional echocardiography correlated closely (r = 0.95, n = 24, p < 0.001).

The superior reproducibility of two-dimensional echocardiographic estimates of left ventricular mass in normal adults supports the use of two-dimensional echocardiography when serial studies are to be performed.

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Left ventricular mass is an important determinant of prognosis in patients with cardiovascular disease (1). Both M-mode and two-dimensional echocardiography can accurately estimate left ventricular mass in humans (2–4), and normal ranges have been determined by each method (5,6). However, the serial reproducibility of mass estimates is also critical to studies of the mechanisms controlling hypertrophy or causing its regression. To date, the reproducibility of left ventricular mass measurements by two-dimensional echocardiography has not been determined or compared with M-mode reproducibility in a single group of patients. To evaluate both questions we prospectively studied eight normal volunteers on three occasions over 5 months, performing a total of 24 two-dimensional and M-mode echocardiograms. We compared the serial reproducibility of left ventricular mass estimates by each method and determined the interobserver variability for the two-dimensional echocardiographic method.

Methods

Study subjects. Eight sedentary adult volunteers (three male, 5 female) ranging in age from 22 to 47 years (mean 29) were prospectively selected from 11 hospital employees after screening by echocardiography to assure good M-mode and two-dimensional study quality. Each subject had no history of cardiovascular disease, was normotensive, had a normal cardiac physical examination and normal electrocardiogram (ECG), took no medications during the study period and gave written informed consent. Each subject underwent repeat echocardiography at 1 and 5 months after the initial study.

Data acquisition. All two-dimensional and M-mode echocardiograms were performed in the echocardiography laboratory at the Vanderbilt University Medical Center. Echocardiograms were obtained with subjects in the left lateral decubitus position; a 2.5 or 3.5 MHz phased-array sector scanner (Hewlett-Packard 77020A) was used. Real-time two-dimensional echocardiographic images were recorded at 30 frames/s on 0.5 inch (1.27 cm) videotape with simultaneous lead ECG and phonocardiogram. Care was taken to assure that the parasternal short-axis view was aligned perpendicular to the septum, as was the M-mode cursor, and that the apical views were not foreshortened. Parallax-free measurements were made off-line using a computer light pen computational system (Clinical Database Systems, Inc.). M-mode echocardiograms were recorded on paper at 50 mm/s.

Two-dimensional echocardiographic left ventricular mass measurements. Two independent observers unaware of subject identity used the computer light pen system to perform measurements of the two-dimensional echocardiograms from freely selected video frames at the QRS onset. Each observer had practiced mass measurements on a teaching videotape from clinical studies of patients whose left ventricular mass had been determined at subsequent autopsy. The endocardial and epicardial borders were outlined from a parasternal short-axis view at the papillary muscle tips to obtain the left ventricular myocardial area and average wall thickness. Ventricular length was measured from the apical two- or four-chamber view, which maximized the distance from the apex to mid-mitral anulus.

Left ventricular (LV) mass was calculated from a formula derived by integration from the formula for a truncated ellipsoid (7):

$$LV \ Mass = 1.05$$
$$\pi \{(b + t)^2 \ [2/3 \ (a + t) + d - \frac{d^3}{3(a + t)^2}] - b^2 \ [2/3 \ a + d - \frac{d^3}{3a^2}]\}.$$

where a = the semimajor axis, b = the semiminor axis or calculated radius at the papillary muscle tips, d = the truncated semimajor axis and t = the calculated wall thickness at the papillary muscle tips. Previous studies have demonstrated a close correlation between left ventricular mass estimated in this manner and actual left ventricular weight in dogs and human hearts at necropsy (4,8).

M-mode echocardiographic mass measurements. M-mode echocardiograms were performed with two-dimensional echocardiographic guidance to obtain simultaneous images of the interventricular septum and left ventricular posterior wall at the level of the papillary muscle tips. An observer unaware of patient identity used freely selected beats from M-mode records to measure the interventricular septum (IVS), left ventricular internal dimension (LVID) and posterior wall thickness (PWT) at the peak of the R wave using the

Penn convention method (2), measuring three beats per tracing and averaging the results. These values were substituted into the formula of Devereux and Reichek (2):

$$LV \ Mass = 1.04 \ [(LVID + PWT + IVS)^3 - (LVID)^3] - 13.6 \ g.$$

Previous studies using this method have demonstrated its reproducibility and close correlation with autopsy measurements of left ventricular mass.

Statistical analysis. All data were entered into a medical data base system (CLINFO, supplied by Division of Research Resources, National Institutes of Health). For the serial studies, calculations were made of the two-dimensional and M-mode left ventricular mass values and the absolute differences in mass among the serial studies of each individual. The percent differences in these values were also tabulated. To express the variability of the two-dimensional and M-mode methods, we calculated the "mean differences" for the two-dimensional and M-mode studies. For this, we compared studies 1 and 2, 1 and 3, and 2 and 3 for each subject and calculated their "mean intraindividual differences." These were then averaged, forming a "mean difference" for the group by each method. A nonparametric test, the Wilcoxon signed rank test, was used to compare the intraindividual differences by the two echocardiographic methods. To assess interobserver correlation, linear regression analysis was performed for the 24 two-dimensional mass estimates by each observer.

Results

Comparison of methods for left ventricular mass. In study 1, mean left ventricular mass for the eight subjects was 115 ± 20 g by two-dimensional and 127 ± 37 g by M-mode study (p = NS) (Table 1). Only at study 3 was the difference between the two estimates of left ventricular mass significant (p < 0.05). The mean mass among men at study 1 was 136 ± 7 g by two-dimensional and 167 ± 19 g by M-mode study. The mean mass among women was 102 ± 10 g by two-dimensional and 104 ± 18 g by M-mode study. The mean mass was significantly greater for men than for women by both methods (p < 0.003).

There were significant differences in mean left ventricular mass at studies 1, 2 and 3 when a single method (either two-dimensional or M-mode) (Table 1) was used. However, Figure 1 and Table 2 demonstrate the greater serial reproducibility of two-dimensional compared with M-mode echocardiography. The mean difference among the serial estimates of left ventricular mass was 4.8 ± 4 g by two-dimensional and 18.5 ± 13 g by M-mode study. This corresponded to a percent difference of 4.2 ± 3% by two-dimensional echocardiography and 14.9 ± 10% by M-mode study. The mean difference was significantly less by the two-dimensional than by the M-mode method (p = 0.01).

Table 1. Serial Left Ventricular Mass Estimates by Two-Dimensional and M-Mode Echocardiography in Eight Subjects

Subject	Gender	Two-Dimensional Mass (g)			M-Mode Mass (g)		
		Study 1	Study 2	Study 3	Study 1	Study 2	Study 3
1	M	145	139	150	161	131	171
2	M	132	132	142	188	140	158
3	M	133	139	130	151	148	173
4	F	87	84	88	126	96	90
5	F	107	108	105	90	101	94
6	F	105	107	100	112	122	106
7	F	114	116	117	108	107	125
8	F	97	108	100	82	83	110
Mean		115	117	116*	127	116	128*
SD		20	19	22	37	23	34

*p < 0.05. F = female; M = male.

Interobserver variability for two-dimensional echocardiographic left ventricular mass. For the combined 24 two-dimensional studies in the eight subjects, the mean left ventricular mass determined by observer 1 was 116 ± 20 g and that determined by observer 2 was 118 ± 20 g (p = NS). The results of the two observers for the 24 studies correlated closely by linear regression (r = 0.95, p < 0.001) (Fig. 2). The mean intraindividual difference among the three serial estimates of left ventricular mass for each subject was nearly identical for observer 1 (4.6 ± 2 g, 4%) and observer 2 (4.8 ± 2 g, 4%) (p = NS).

Discussion

Previous studies. Because of its proved accuracy in symmetric left ventricles, M-mode echocardiography has been used to assess serial changes in left ventricular mass in patients whose therapy might reduce left ventricular hypertrophy (9,10) and in experimental studies of the mechanisms

controlling changes in mass (11). In these studies, the magnitude of the change in left ventricular mass has generally ranged from 10% to 19% of the baseline value. Because of these relatively small changes, it is desirable to have highly reproducible as well as accurate mass estimates for making judgments about serial changes in left ventricular mass. Devereux et al. (12) reported a mean intraindividual difference of 26 g (16%) among 53 normal adults studied twice by M-mode echocardiography over 17 months. The serial reproducibility of two-dimensional echocardiographic mass measurements, on the other hand, has not previously been examined.

Two-dimensional echocardiography provides more accurate estimates of left ventricular mass than those provided by M-mode methods in abnormal hearts (3) because this method accounts more completely for ventricular asymmetry. Working with normal human hearts at autopsy, Geiser and Bove (8) found that left ventricular mass was best estimated by the truncated ellipsoid formula, incorporating
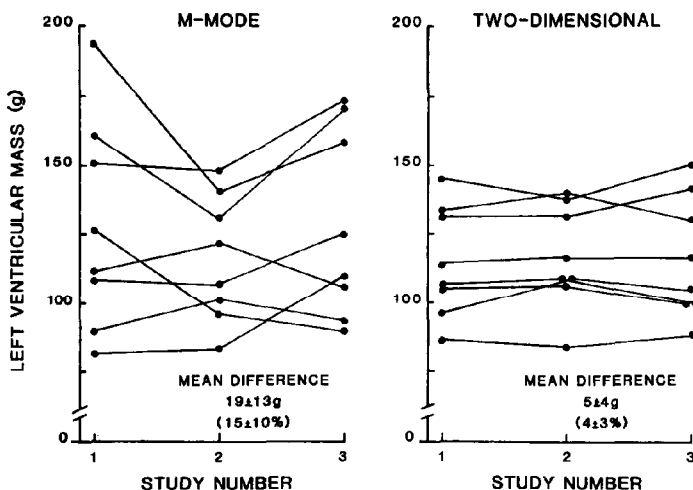

Figure 1. Serial reproducibility of left ventricular mass estimates by M-mode (left) and two-dimensional echocardiography (right) for each of the eight subjects at studies 1, 2 and 3 (p = 0.01).

Table 2. Interstudy Variability of Serial Echocardiographic Mass Estimates in Eight Subjects

Subject No.	Difference in Mass (2D) [g(%)]				Difference in Mass (M-mode) [g(%)]			
	Study 1 vs. 2	Study 1 vs. 3	Study 2 vs. 3	Study Mean	Study 1 vs. 2	Study 1 vs. 3	Study 2 vs. 3	Study Mean
1	6 (4)	5 (3)	11 (8)	7 (5)	30 (19)	10 (7)	40 (26)	27 (17)
2	0 (0)	10 (7)	10 (7)	7 (5)	48 (30)	30 (19)	18 (11)	32 (20)
3	6 (5)	3 (2)	9 (7)	6 (5)	3 (2.0)	22 (14)	25 (16)	17 (11)
4	3 (3.0)	1 (1)	4 (4)	3 (3)	30 (29)	36 (35)	6 (6)	24 (23)
5	1 (1)	2 (2)	3 (3)	2 (2)	11 (12)	4 (4)	7 (7)	7 (8)
6	2 (2)	5 (5)	7 (6)	5 (4)	10 (9)	6 (5)	16 (14)	11 (9)
7	3 (2)	4 (3)	1 (1)	2 (2)	1 (1)	17 (15)	18 (16)	12 (11)
8	11 (12)	9 (9)	3 (3)	7 (8)	1 (1)	28 (30)	27 (29)	19 (20)
Mean ± SD			4.8 ± 4 (4.2 ± 3)*				18.5 ± 13 (14.9 ± 10)*	

*p = 0.01. 2D = two-dimensional echocardiography.

direct wall thickness and chamber length measurements rather than lengths assumed from short-axis diameters as in M-mode cardiography. Two-dimensional echocardiography has provided very accurate estimates of left ventricular mass in normal dogs (7), substituting direct measurements of myocardial area (short-axis view) and chamber length (apical view) into the truncated ellipsoid formula. The method has been validated in human hearts at necropsy (3,4) and normal values for adults have been established (6).

Present study. In the present study we determined the serial and interobserver reproducibility of two-dimensional left ventricular mass estimates and then compared serial M-mode and two-dimensional reproducibility. The two-dimensional method provided more reproducible serial mass measurements than did M-mode echocardiography in this group of normal adults. In these subjects, who were selected on the basis of good quality echocardiograms, the serial

Figure 2. Two-dimensional (2D) echocardiographic left ventricular (LV) mass estimates by observer 1 correlated closely with those by observer 2 in the 24 studies.

estimates of left ventricular mass by two-dimensional echocardiography in each individual varied by only 4.8 ± 4 g (4.2 ± 3%) in contrast to the much higher value of 18.5 ± 13 g (14.9 ± 10%) among the serial M-mode estimates (p = 0.01). Because serial M-mode reproducibility in this study was quite similar to the 16% value reported by Devereux et al. (12), two-dimensional echocardiographic mass measurement clearly appears to be an improvement over the M-mode technique.

Importantly, the interobserver correlation coefficient for the two-dimensional method was high (r = 0.95, p < 0.001). Left ventricular mass by two-dimensional echocardiography was significantly greater among men than among women (136 versus 102 g, p < 0.003), as we (6) previously reported in another study of normal subjects.

Methodologic considerations. To determine the serial reproducibility of mass measurements, we studied only normal adults with no stimulus to myocardial hypertrophy or regression. We did not attempt to determine serial reproducibility among subjects with cardiac disease because changes in patients over time might be due to the underlying disease rather than to measurement variability. By directly measuring left ventricular length (apical view) and more completely sampling wall thickness (short-axis view), two-dimensional echocardiography avoids some of the geometric assumptions that cause M-mode mass measurement errors, especially in abnormal, asymmetric ventricles (13,14). However, even in normal hearts, the area and length measurements made from two-dimensional images reduce the impact of minor wall thickness measurement errors or interobserver variations. These factors also enhance the accuracy of two-dimensional mass measurements.

Limitations of the two-dimensional echocardiographic method include the need for an off-line computer analysis system with its associated increased cost and time demands. As with M-mode echocardiography, a high level of technical expertise is required to obtain the optimal gain settings and
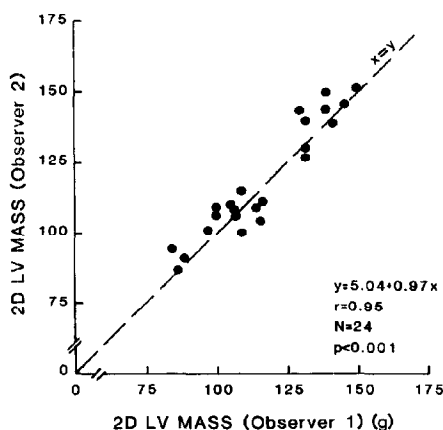
minimal lateral border dropout necessary for accurate two-dimensional measurements of myocardial area. Lateral border recognition has long been a limiting factor in the quantitation of two-dimensional echocardiograms. Poor lateral resolution led to exclusion of 2 of the 11 normal subjects screened for this study, and a third volunteer was excluded because both M-mode and two-dimensional images were technically inadequate. Although improvements in lateral border detection await advances in instrumentation and transducer design, digital storage of two-dimensional echocardiographic images may further improve the accuracy and reproducibility of research studies. Importantly, the accuracy and reproducibility of our two-dimensional echocardiographic mass measurements were enhanced by having the observers practice mass measurements on selected clinical videotapes of patients whose left ventricular mass had been determined subsequently at autopsy.

Conclusions. Two-dimensional echocardiography provides superior serial reproducibility of left ventricular mass estimates in normal adults with low interobserver variability. Although only normal subjects were studied to compare the reproducibility of two-dimensional and M-mode left ventricular mass estimates, two-dimensional echocardiography is likely to be more reproducible in abnormal hearts as well because it has been proved more accurate in asymmetric ventricles (3). Two-dimensional echocardiographic mass measurements require computer-assisted analysis, but instrumentation for such measurements is becoming generally available in both on- and off-line formats. The superior reproducibility of two-dimensional echocardiographic left ventricular mass estimates over a 5 month period supports the use of two-dimensional rather than M-mode echocardiography for serial estimates of left ventricular mass.

References

1. Casale PN, Devereux RB, Milner M, et al. Value of echocardiographic measurement of left ventricular mass in predicting cardiovascular morbid events in hypertensive men. Ann Intern Med 1986;105:173-8.

2. Devereux RB, Reichek N. Echocardiographic determination of left ventricular mass in man: anatomic validation of the method. Circulation 1977;55:613-8.

3. Reichek N, Helak J, Plappert T, Sutton M, Weber KT. Anatomic validation of left ventricular mass estimates from clinical two-dimensional echocardiography: initial results. Circulation 1983;67:348-52.

4. Byrd BF, Finkbeiner W, Bouchard A, Silverman N, Schiller NB. Factors influencing accuracy of two-dimensional echocardiographic left ventricular mass measurements (abstr). J Am Coll Cardiol 1984;3:515.

5. Devereux RB, Lutas EM, Casale PN, et al. Standardization of M-mode echocardiographic left ventricular anatomic measurements. J Am Coll Cardiol 1984;4:1222-30.

6. Byrd BF, Wahr D, Wang YS, Bouchard A, Schiller NB. Left ventricular mass and volume/mass ratio determined by two-dimensional echocardiography in normal adults. J Am Coll Cardiol 1985;6:1021-5.

7. Schiller NB, Skioldebrand CG, Schiller EJ, et al. Canine left ventricular mass estimation by two-dimensional echocardiography. Circulation 1983; 68:210-6.

8. Geiser EA, Bove KE. Calculation of left ventricular mass and relative wall thickness. Arch Pathol 1974;97:13-21.

9. Schlant RC, Felner JM, Blumenstein BA, et al. Echocardiographic documentation of regression of left ventricular hypertrophy in patients treated for essential hypertension. Eur Heart J 1982;3(suppl A):171A-5A.

10. Fouad FM, Tarazi RC, Bravo EL. Cardiac and hemodynamic effects of enalapril. J Hypertens 1983;1(suppl 1):135-40.

11. Trimarco B, Ricciardelli B, DeLuca N, et al. Participation of endogenous catecholamines in the regulation of left ventricular mass in progeny of hypertensive parents. Circulation 1985;72:38-46.

12. Devereux RB, Hammond IW, Lutas EM, Spitzer MC, Alderman MH, Laragh JH. Year-to-year variability of echocardiographic measurements in normal subjects (abstr). J Am Coll Cardiol 1984;3:516.

13. Wyatt HL, Heng MK, Meerbaum S, et al. Cross-sectional echocardiography. 1. Analysis of mathematic models for quantifying mass of the left ventricle in dogs. Circulation 1979;60:1104-13.

14. Salcedo EE, Gockowski K, Tarazi RC. Left ventricular mass and wall thickness in hypertension: comparison of M-mode and two-dimensional echocardiography in two experimental models. Am J Cardiol 1979; 44:936-40.