Echocardiographic Determination of Left Ventricular Mass in Man

Anatomic Validation of the Method

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SUMMARY An accurate echocardiographic (E) method for determination of left ventricular mass (LVM) was derived from systematic analysis of the relationship between the antemortem left ventricular echogram and postmortem anatomic LVM in 34 adults with a wide range of anatomic LVM (101-505 g). No subject had massive myocardial infarction, ventricular aneurysm, severe right ventricular volume overload or hypertrophic cardiomyopathy. The best method for LVM-E identified combined cube function geometry with a modified convention for determination of left ventricular internal dimension (LVID), posterior wall thickness (PWT), and interventricular septal thickness (IVST), which excluded the thickness of endocardial echo lines from wall thicknesses and included the thickness of left septal and posterior wall endocardial echo lines in LVID (Penn Convention, P). By this method, anatomic LVM = 1.04 ([LVIDp + PWTp + IVSTp] - [LVID,E]p) - 14 g; r = 0.96, SD = 29 g, N = 34. Standard echo measurements gave less accurate results, as did previously reported methods for LVM-E. LVM-E is an accurate, widely applicable method for the study of left ventricular hypertrophy.

LEFT VENTRICULAR HYPERTROPHY (LVH) plays a central role in chronic adaptation to pressure or volume overload of the systemic circulation. The degree of hypertrophy parallels the severity of overload\(^1\)\(^2\) and detection of extreme hypertrophy may indicate a poor prognosis.\(^3\)\(^4\) Thus, logically, serial determination of left ventricular muscle mass (LVM) should be an essential element in the study of such disorders. However, assessment of LVH in man has been limited by the lack of an accurate, well-validated, widely applicable and readily repeatable method for quantitating LVM. The biplane angiographic method of Rackley et al. is accurate by comparison with autopsy LVM, but has seen limited use because of its technical complexity and invasive methodology.\(^5\)\(^6\)

The noninvasive basis and wide applicability of echocardiography make it an appealing method for the systematic serial evaluation of LVH. Several studies have indicated a close statistical relationship between echocardiographic and angiographic estimates of LVM.\(^7\)\(^8\) However, the reliability of three-dimensional data derivations from M-mode echocardiography has recently been regarded with considerable skepticism.\(^9\)\(^10\) Moreover, the critical comparison between echocardiographic LVM and true anatomic LVM has not yet been made. Finally, existing echocardiographic studies have each evaluated a single method for LVM. None has systematically assessed the individual echocardiographic variables which determine the accuracy of such an estimate. The present study was designed to define an optimal method for echocardiographic determination of LVM and to examine its accuracy by comparison with anatomic LVM, the ultimate standard.

Methods

Patient Population

Between August 1, 1975, and June 1, 1976, the autopsy log of the Hospital of the University of Pennsylvania was examined daily and compared with the records of the Noninvasive Laboratory to identify patients who had undergone echocardiographic study within four months of autopsy. All such patients were included in the study. In addition, a weekly or biweekly canvass of the Medical Service was made to identify patients judged to have terminal disease. Using a consent procedure approved by the University of Pennsylvania Committee on Studies Involving Human Beings, research echocardiograms were obtained whenever possible on such patients. Such patients were included in the study if death occurred and an autopsy was obtained within four months.

Anatomic LVM

Following routine autopsy examination, the unfixed left ventricle was dissected by the method of Geiser and Bove\(^10\)\(^11\) and LV weight was determined. By this method, the atria are removed in the plane of the atrioventricular groove, just under the mitral and tricuspid leaflets; the great vessels are detached just under the aortic and pulmonic valves; and the free wall of the right ventricle is removed in a plane following the curve of the interventricular septum. Epicardial fat overlying the remaining cone of left ventricular myocardium (which includes the interventricular septum) is then removed. In six instances the heart had been fixed prior to dissection and the measured weight was reduced by 3% to correct for the effects of short-term formalin fixation.\(^12\)

Echocardiographic Recordings

Echocardiograms were recorded at 50 mm/sec using Smith-Kline 20 or 20A echocardiographs interfaced with
Honeywell 1856 or 1858 recorders. Patients were studied supine or in left decubitus position with transducer placement in the third to fifth intercostal space. Simultaneous visualization of interventricular septal thickness (IVST), left ventricular internal dimension (LVID) and posterior wall thickness (PWT) was sought, at or just below the tips of the mitral leaflets. Whenever possible, longitudinal scans from aorta to apex and transverse scans at the level of LVID measurement were obtained.

Echocardiographic Data Selection

All echocardiograms obtained on autopsied patients were coded and transmitted to one investigator who had no knowledge of the clinical or autopsy data. Echocardiograms which showed unambiguous high quality images of IVST, LVID and PWT with continuous interface lines were deemed technically adequate for study. Satisfactory recordings were marked by hand for semi-automated determination of IVST, LVID and PWT. Measurement points were taken at the peak of the R wave on the simultaneous electrocardiogram on an average of four cycles per recording. Two simultaneous sets of measurement points were identified. The first was selected using the standard (S) echocardiographic convention for IVST, LVID and PWT, in which the thickness of endocardial interfaces is included in IVST and PWT (fig. 1A). The second set of points was selected by an arbitrary alternative method, the Penn Convention (P). This method excludes the thickness of endocardial echoes from measurements of IVST and PWT and includes the thickness of endocardial echoes from the left side of the septum and the posterior wall endocardium in the measurement of LVID (fig. 1B). On any given recording, the Penn Convention gives larger values for LVID and smaller values for PWT and IVST than does the standard measurement convention.

Data Processing

Following manual selection of data points, recordings were calibrated for depth and measurements of PWT, IVST and LVID by both conventions performed on a Hewlett-Packard programmable calculator and digitizer, which generated the desired LVM estimates using eight different methods.

Geometric Models

Echocardiographic LVM was determined by first using LVID to estimate end-diastolic intraventricular volume (LVV). An estimate of total LV volume (LVV), which includes myocardial volume, was then derived from the sum of LVID + estimated mean myocardial thickness (MMT). LVM then equals 1.05 \times (LVV - LVV), where 1.05 = specific gravity of myocardium. LVV and LVV estimates were derived by two methods. The cube formula assumes that the left ventricle is a prolate ellipsoid with minor radii (LVID/2) that are half the major radius. Thus LVV = 4/3 \pi r_1r_2r_3 = 1.047 (LVID)\(^3\). Similarly, LVV = 1.047 (LVID + 2MMT)\(^3\) and LVM = 1.1 \times (LVV + 2MMT\(^3\) - [LVID\(^3\)]. The second method was based on a quadratic regression analysis of the relationship between LVID and angiographic LVV, reported by Ratshin et al. By this method, LVM = 1.05 (21 [(LVID + 2MMT\(^3\) - (LVID\(^3\)] + 151 [2MMT]).

Estimation of Mean Myocardial Thickness (MMT)

Use of the S and P conventions for measurement of PWT and IVST offered two general methods for MMT. In addition, MMT might be best represented by either PWT or (IVST + PWT)/2. Both of these assumptions were explored. Thus, in all, four methods for MMT were explored: MMT = PWT(S); MMT = PWT(P); MMT = (IVST + PWT)/2(S); and MMT = (IVST + PWT)/2(P). When combined with the two methods for volume estimation, a total of eight estimates of LVM were derived from each echocardiogram.

Statistical Analysis

Statistical analysis was performed using standard least squares linear regression methods and Student's t-test.

Results

Patient Population

Both autopsy and echocardiographic LVM were obtained on 34 patients. The mean interval between echocardiographic study and autopsy was 23 days (range 1–120 days) and no patient had a marked, prolonged change in left ventricular hemodynamic loading in the interval between the two. Seventeen males and 17 females were studied, with an age range from 23 to 78 years. Myocardial infarction was
detected at autopsy in 12 patients (five acute and seven old) but no patient had a discrete ventricular aneurysm. Six subjects had concentric left ventricular hypertrophy due to hypertension or aortic valve disease alone and six had concentric hypertrophy with coexistent myocardial infarction. Ten patients had normal hearts, two had congestive cardiomyopathy and one had mitral stenosis with pulmonary hypertension. Malignant disease was present in nine patients, renal failure in four, gastrointestinal hemorrhage in four and major neurologic disorders in three. LVM at autopsy ranged from 105-505 g. Echocardiographic LVVID (S) ranged from 3.3-7.5 cm, while PWT (S) ranged from .8-2.2 cm and IVST (S) from .7-2.3 cm. Asymmetric septal hypertrophy was present in two subjects.

Accuracy of Echocardiographic Estimates

All eight echocardiographic methods examined correlated strongly with anatomic LVM ($r = 0.86$ to $r = 0.96$) (table 1), but substantial differences were observed in the degree of scatter and the slope of the relationship (fig. 2).

### Impact of Geometric Formula

Cube function and quadratic regression formulae for ventricular volume yielded estimates of LVM of comparable accuracy when similar methods for determination of MMT were employed (table 1). Thus there was no advantage to use of the more complex quadratic regression instead of the cube function.

### Impact of Wall Thickness Convention

LVM estimates using conventional measurements of PWT and IVST consistently overestimated actual LVM. In contrast, estimates derived from the Penn Convention fell closer to the line of identity and consistently showed better correlation and less scatter (table 1, fig. 2).
Impact of Mean Muscle Thickness Assumption

The assumption that MMT = PWT consistently resulted in greater scatter and poorer agreement with autopsy LVM than did MMT = (PWT + IVST)/2 (table 1, fig. 3).

Optimal Estimate of LVM

The combination of the cube function, Penn Convention, and MMT = (PWT + IVST)/2 was the best method obtained for echocardiographic estimate of anatomic LVM (fig. 2B):

Anatomic LVM = 1.04 ([LVIDp + PWTp + IVSTp]^3 - [LVIDp]^3) - 13.6 g.

Effect of Time Interval between Echocardiogram and Autopsy

The echocardiographic estimate of LVM in 25 patients with an echo-autopsy interval of less than one month was no more accurate than in the nine patients with intervals of one to four months (< 1 month, r = 0.97, SD = 29.3 g; 1-4 months, r = 0.93, SD = 27.8 g).

Accuracy in Clinical Subgroups

The optimal method for echocardiographic LVM gave comparably accurate results in subgroups with myocardial infarction (r = 0.98, SD = 24.7 g, N = 12); and concentric hypertrophy (r = 0.99, SD = 19.6 g) (fig. 4). A somewhat greater degree of scatter was noted in the subgroup with normal hearts (r = 0.78, SD = 33 g), but the lower correlation coefficient reflects in part the narrow range of variation (105-215 g) in the normal group as compared to the abnormal groups (126-505 g).

Accuracy of Previously Reported Methods

When applied to our data, the method of Troy and Pombo11 showed wide scatter in hypertrophied ventricles (fig. 5A). The method of Murray et al.12 systematically underestimated LVM in all patients (fig. 5B). Bennett and Evans have used one of the methods we examined (cube function, standard measurement + MMT = PWT) to assess the accuracy of electrocardiographic and vectorcardiographic criteria for LVH.26 This method systematically overestimated LVM (fig. 5C).

Reproducibility

Reproducibility of our optimal method for echocardiographic estimation of LVM must be assessed critically in three respects: beat-to-beat variability of the estimate on a single recording, processed by a single observer; interobserver variability; and variability of repeated echocardiographic recordings on a single subject. Beat-to-beat variability, expressed as the standard deviation of beat-by-beat echo LVM estimates, ranged from 0 to 45 g, with a mean of 17.6 g. Interobserver variability was determined by having a second observer recalculate LVM in a series of 23 recordings from the present study. LVM estimates measured by the two observers were very strongly correlated, with r = 0.99 and SD = 7.3 g. Since only a single echocardiographic recording was available on each subject in this study, variation between recordings could not be assessed directly. However, the comparison between echocardiographic and anatomic LVM (r = 0.96) provides an indirect means for estimating the correlation coefficient for two successive determinations of echocardiographic LVM ($r_{E_{2}}$). An individual value for echo LVM (E) cannot correlate more closely with anatomic LVM (A) than it does with the universe mean ($M_{u}$) for all E in that subject. Thus $r_{E_{2}}$ is greater than or equal to...
r_{BA}', which is 0.96. In turn, r_{EB}' = r^2_{RM}', and must equal or exceed 0.92 (personal communication, Elliot Rubin, Ph.D.).

**Discussion**

This study demonstrates that an accurate estimate of LVM can be obtained using a simple echocardiographic method which compares favorably with biplane angiographic determinations of LVM (echocardiographic $r = 0.96$, SD = 29 g; angiographic $r = 0.97$, SD = 32 g). Given the relative ease, safety, and repeatability of the echocardiographic method, it should play a valuable role in future studies of disorders characterized by LVH. Analysis of clinical subsets in our study did not identify any group in which the method was grossly inaccurate. However, while a number of markedly dilated ventricles were included in our study, we have not yet had the opportunity to examine extensively several subgroups in which alterations of left ventricular shape could affect the accuracy of the estimate: 1) chronic severe volume overload due to aortic or mitral regurgitation, 2) massive myocardial infarction or ventricular aneurysm, 3) severe right ventricular volume loading, 4) genetic asymmetric septal hypertrophy. Moreover, only two subjects with congestive cardiomyopathy, which may produce a more globular ventricle, were included in the present study. For the present, therefore, our method should be used with caution in these subsets.

The accuracy of the echocardiographic method for LVM is at first glance surprising, since extrapolation from one-dimensional M-mode echocardiographic data to three-dimensional volume data is fraught with hazards. However, Geiser and Bove have demonstrated that anatomic LVM can be calculated precisely from autopsy measurement of PWT, IVST, LVID, apical myocardial thickness and hemimajor axis. The first three of these variables can be measured directly by echocardiography. In the absence of a direct measurement of the ventricular major axis, echocardiographic LVM is dependent on relatively simple geometric formulae, such as the cube formula, or angiographically derived regression analyses, to estimate the volume of the left ventricular myocardial shell. Our data indicate that either of these approaches permits accurate determination of LVM. Thus, estimation of LVM seems relatively insensitive to potential errors in volume formulae. One reason for this may be that the LVM determination is dependent on the difference between two volume estimates derived by the same method which incorporate the same systematic errors.

Determination of LVM also requires measurement of myocardial thickness. It has been believed heretofore that conventional echocardiographic measurements of myocardial thickness, which include the thickness of endocardial interfaces, are highly accurate, based on comparison with surgical and angiographic measurements. However, both of the latter methods are fraught with difficulties, while the limit of resolution of the echocardiographic method is on the order of 1 mm, or 10% of the thickness of a normal ventricle. Moreover, in our laboratory, enhancement of electronic gain settings increases the thickness of the interface line. In theory, the anterior edge of the line should remain fixed and accurately indicate interface location. In practice, the increase in gain displaces the anterior edge of the interface anteriorly and the posterior edge posteriorly. There is no available method for factoring the gain settings into the appraisal of an individual recording. Similarly, both septum and posterior wall are complex structures with highly variable degrees of trabeculation, superimposed on a muscular surface that curves in both the circumferential and meridional planes. Errors of both lateral resolution and interpretation are inescapable. Thus there is ample reason to doubt the absolute accuracy of echocardiographic measurements of PWT and IVST by any measurement convention.

Moreover, a complex relationship exists between true PWT and IVST and MMT, which is the mean thickness of
the hypothetical myocardial shell from which LVM is derived. Previous methods for echocardiographic estimation of LVM have assumed that conventional PWT or (IVST + PWT)/2 accurately reflect MMT. In fact, they plainly cannot, since there is no myocardium over the area of the mitral and aortic orifices, while the myocardium is thinner at the apex and much thicker at the level of the papillary muscles. These considerations have led us to examine a wide range of alternative methods for estimation of MMT. Our data indicate that the Penn Convention combined with MMT = (IVST + PWT)/2 offers the best estimate of MMT for determination of echocardiographic LVM by either the cube function or quadratic regression methods. We cannot judge whether this is due to increased accuracy of measurement of IVST and PWT, or to fortuitous compensation for many other factors outlined above, but the practical usefulness of this method for determination of LVM is not dependent on a full understanding of its biologic basis.

Earlier investigators have determined the accuracy of several methods for echocardiographic LVM using an angiographic reference standard. However, the ultimate test of the value of the method is comparison with anatomy. While reasonably good agreement between echocardiographic and angiographic LVM was demonstrated by Troy and Pombo, and Murray et al., our data indicate that their methods are less accurate when compared to anatomic rather than angiographic LVM. In contrast, the optimal method described in this study appears to be as accurate as the angiographic method itself in the patient groups studied.

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