Echocardiographic Assessment of Mitral Valve Size in Obstructive Hypertrophic Cardiomyopathy
Anatomic Validation From Mitral Valve Specimen

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Background. In patients with hypertrophic cardiomyopathy, obstruction to left ventricular outflow is produced by systolic anterior motion of the mitral valve. In many of these patients, the mitral leaflets are elongated and increased in overall size. Mitral valve size may be responsible, in part, for the presence and magnitude of the outflow gradient and the pattern of systolic anterior motion of the leaflets. It may also influence the effectiveness of ventricular septal myotomy-myectomy in relieving subaortic obstruction. Therefore, the present study was undertaken to determine whether mitral valve dimensions could be assessed in quantitative terms from the echocardiogram in patients with hypertrophic cardiomyopathy.

Methods and Results. A group of 37 patients with hypertrophic cardiomyopathy was selected for this study by virtue of having a high-quality transthoracic or intraoperative echocardiogram suitable for certain quantitative measurements from stop-frame images as well as a morphologically intact mitral valve specimen (removed during surgery). Seven measurements of mitral valve dimensions were obtained from the two-dimensional and M-mode echocardiograms. A univariate regression analysis identified the mitral valve opening area as the best single predictor of actual mitral leaflet area measured from the specimen ($r^2=.75$; $r=.87$). The linear relation between mitral valve opening area as assessed by two-dimensional echocardiography and actual mitral leaflet area measured from the mitral valve specimen accounted for approximately 75% of the variability in mitral leaflet area. With such statistical models, it was possible to reliably identify from the echocardiogram enlarged mitral valves ($>12.0 \text{ cm}^2$) in 16 of 19 patients (84%) and normal-sized valves in 15 of 18 patients (83%).

Conclusions. In a selected group of patients with obstructive hypertrophic cardiomyopathy, a model derived from a regression analysis of quantitative echocardiographic measurements permitted (with good precision) estimation of actual mitral leaflet area and consequently overall mitral valve size and the discrimination of enlarged from normal-sized mitral valves. (Circulation 1993;88:548-555)

KEY WORDS • mitral valve • cardiomyopathies • echocardiography

In patients with hypertrophic cardiomyopathy, the systolic anterior motion of the mitral valve and its contact with the ventricular septum are the principal determinants of obstruction to left ventricular outflow.1-14 Recent morphological studies of mitral valves removed at surgery or autopsy from patients with hypertrophic cardiomyopathy have shown that the majority of these valves have a variety of structural alterations, including increased leaflet area and segmental enlargement of the valve.14 Mitral valve size and leaflet length also appear, in selected patients, to be a determinant of the presence and magnitude of the subaortic gradient.13-16 The pattern of systolic anterior motion responsible for that gradient,11-13 and whether outflow obstruction is effectively relieved by ventricular septal myotomy-myectomy.17

Because of the clinical implications of mitral valve size in hypertrophic cardiomyopathy and the fact that there have been few systematic attempts at assessing mitral leaflet dimensions in patients with cardiac disease using echocardiography,15,18-21 we considered it desirable to develop a quantitative method for estimating mitral valve size from the echocardiogram prospectively during life. In the present study, the availability of both echocardiograms and mitral valve specimens from the same patients with obstructive hypertrophic cardiomyopathy afforded us the unique opportunity to validate quantitative echocardiographic measurements of mitral valve size in this disease.

Methods
Selection of Study Patients

The cardiovascular registry of the Pathology Branch from 1982 through 1989 was reviewed, and 77 mitral valve specimens that had been removed intact at surgery or autopsy from patients with obstructive hyper-
trophic cardiomyopathy were judged to be in suitable condition for morphometric study. Nine of these 77 valves were excluded because they had direct papillary muscle insertion into the anterior mitral leaflet. The remaining 68 mitral valves were free of any other intrinsic valve abnormalities, such as floppy mitral valve. Of these 68 patients, 12 were excluded because they did not have preoperative echocardiographic studies. Of the remaining 56 patients, 37 were selected for the final study group by virtue of having a preoperative transthoracic or intraoperative echocardiogram judged (by the consensus of two independent observers, H.G.K. and A.L.D.) to be of satisfactory technical quality for the present investigation (ie, they permitted selected quantitative measurements of the mitral valve to be made from stop-frame echocardiographic images with reasonable precision). In 25 of the 37 study patients, the transthoracic echocardiograms were of high technical quality and were used preferentially for analysis. In the other 12 patients, the intraoperative echocardiogram was used because the transthoracic echocardiogram was judged to be inadequate to make the measurements necessary for the present study. In the 25 patients with transthoracic echocardiographic studies, the time interval between echocardiogram and mitral valve replacement was 1 to 86 days (mean, 34 days).

Control Patients

Mitral valves from 45 consecutively studied patients with entirely normal hearts, both functionally and anatomically, were chosen as controls, solely for the purpose of determining the normal limits for mitral leaflet area measured from the surgical specimen. In each control patient, heart weight was 350 g or less in men and 300 g or less in women. The 45 controls ranged in age from 15 to 74 years (mean, 45 years); 24 were men, and 21 were women. The age and sex distributions in the controls did not significantly differ from those in the study group.

Characterization of Study Patients

The 37 study patients ranged in age from 15 to 69 years (mean, 45 ± 14); 19 were men, and 18 were women. In each patient, the diagnosis of hypertrophic cardiomyopathy was based on the presence of a hypertrophied, nondilated left ventricle in the absence of another cardiac or systemic disease capable of producing the magnitude of hypertrophy present in that patient. In addition, each patient had typical clinical features of hypertrophic cardiomyopathy and severe symptoms of cardiac dysfunction (New York Heart Association functional class III or IV). Maximal ventricular septal thickness assessed by echocardiography ranged from 17 to 30 mm (mean, 24 ± 3 mm), and left ventricular end-diastolic dimension ranged from 30 to 55 mm (mean, 41 ± 6 mm).

Each patient had undergone left-heart catheterization within 3 months of the operation. Basal left ventricular outflow gradients ranged from 0 to 165 mm Hg (average, 79 ± 42 mm Hg), including 26 with subaortic gradients of more than 50 mm Hg. Each of the 11 patients with gradients of less than 50 mm Hg under basal conditions had gradients of more than 50 mm Hg (range, 90 to 160 mm Hg; average, 110 ± 19 mm Hg) with provocative maneuvers (ie, isoproterenol infusion, Valsalva maneuver, and amyl nitrite inhalation).

Mitral Valve Morphometry

Mitral valves were fixed in 10% buffered formalin after their removal at surgery. Valves were introduced to the fixative freely, without stretching or manipulation. Tissue specimens were placed in an opened position on a cutting board and extended to their full length with the atrial aspect exposed. Quantitative morphological measurements were made directly from the mitral valve specimen of the circumference of the valve, measured along its margin of attachment; maximum length of the anterior leaflet, from annular margin to free edge; and the area of the combined anterior and posterior mitral leaflets.

To assess overall mitral leaflet area, borders of the open valve were traced onto an acetate overlay and then planimeterized using a digital tape (Micro DigiPad 1212).

Echocardiographic Techniques

Transthoracic two-dimensional echocardiograms were performed with an Advanced Technology Laboratory Mark 500 or a Hewlett-Packard Sonos 500 Instrumen, using 2.25-, 2.5-, or 3.5-MHz transducers. Two-dimensional echocardiographic images were obtained in a number of cross-sectional planes by using standard transducer positions, as previously described.

Intraoperative echocardiograms were obtained just before cardiopulmonary bypass, using a commercially available Hewlett Packard ultrasound unit with a 3.5- to 5.0-MHz transducer enclosed in a sterile sleeve. A small amount of ultrasound transmission gel was placed between the transducer head and sleeve, and the transducer was positioned directly on the surface of the right ventricle of the beating heart. Standard long-axis and short-axis planes were achieved and recorded on ½-in. videotape. M-mode echocardiograms were derived from two-dimensional images under direct anatomic visualization.

Echocardiographic Measurements

Mitral valve opening area. A continuous scan from aorta to left ventricle in the parasternal short-axis view was used to identify a representative stop-frame image at the cross-sectional level where both the anterior and the posterior mitral leaflets could be visualized and where the mitral valve opening area was greatest during diastole (usually near the tips of the leaflets). With this image, the circumferential innermost margins of the mitral valve were traced onto a plastic transparency, and the outlined area (mitral valve opening area) was then planimeterized using an Apple McIntosh SE computer. The diastolic mitral valve circumference was derived from the calculation of the opening area (Fig 1).

In addition, the maximal internal transverse and horizontal diameters of the mitral valve opening area were measured from the innermost margins of the circumference of the mitral opening area. To enhance the accuracy of these measurements, the outline of mitral valve opening area was routinely verified by reviewing the videotape in slow motion and single-frame modes against the background of the traced stop-frame.

Anterior mitral leaflet length. Length of the anterior mitral leaflet was measured from the standard paraster-
nal long-axis image (with the ultrasound beam trans-
secting the center of the left ventricular cavity) during
mid diastole and with the leaflet maximally extended, as
the distance from the junction between the anterior
leaflet and the posterior aortic wall (“hinge-point”) to
the tip of the leaflet (Fig 1). To aid in verifying the site
of these landmarks and particularly in distinguishing
mitral leaflet from chordae tendineae, the videotape
was reviewed several times in slow motion and single-
frame modes against the background of the measured
stop-frame. Anterior mitral leaflet length was measured
from the parasternal long-axis view (rather than the
apical four-chamber) because our judgment and expe-
rience indicated that the anatomic limits of the leaflet
were best perceived in that cross-sectional plane.

Left ventricular outflow tract cross-sectional area. Left
ventricular outflow tract area was measured using a
previously described method. In brief, a continuous
scan from aorta to left ventricle in the parasternal
short-axis identified a representative stop-frame image
at the level where both mitral leaflets could be visual-
ized; outflow tract area was measured at this level at the
onset of systole (ie, on the first frame showing the mitral
valve closed). From this image, the innermost margins
of the outflow tract were traced onto a plastic transpar-
cency, and the outlined area was then planimeterized (in

![Figure 1](image-url)

**Fig 1.** Representative diastolic stop-frame two-dimensional echocardiographic images illustrating the mitral valve measurements made in the study patients with hypertrophic cardiomyopathy: mitral valve opening area and circumference in the short-axis view (A, B, and C) and anterior leaflet length (broken line) in the parasternal long-axis view (D). A and B, Same stop-frame; the area and circumference of the mitral valve are demarcated only in B. C, From another patient in whom mitral valve opening is considerably less than that evident in A and B. Ant. VS indicates anterior ventricular septum; LA, left atrium; LV, left ventricle; post. VS, posterior ventricular septum; PW, posterior wall; and VS, ventricular septum.

a fashion similar to that described above for mitral valve
opening area).

**Other cardiac dimensions.** Left ventricular end-di-
stolic and end-systolic dimensions and left atrial size
were obtained from the M-mode echocardiogram ac-
cording to the criteria of the American Society of
Echocardiography. Measurement of transverse mitral
valve diameter, defined as the maximal diastolic sepa-
racion of the anterior and posterior mitral leaflets (at
the level of the leaflet tips), was also obtained from
standard M-mode echocardiographic tracings.

**Reproducibility**

Interobserver and intraobserver variability for the
measurement of mitral valve opening area was as-
sessed in all 37 patients, using the method of Bland
and Altman. To determine interobserver variability,
two observers (H.G.K. and A.L.D.) independently
measured the mitral valve opening area from the
two-dimensional videotape without prior knowledge of
the morphological data obtained from the surgical
specimens and without preselection of particular por-
tions of the videotape. To determine intraobserver
variability, one observer (H.G.K.) measured mitral
valve opening area in the same fashion on two occa-
sions (2 months apart, without preselection of portions
of the videotape).
**Statistical Analysis**

Data are expressed as mean±SD. Initially, a linear regression analysis was used to define the single echocardiographic predictor that best estimated mitral leaflet area, using actual mitral leaflet area (measured from the surgical specimen) as the dependent variable, and each of seven echocardiographic measurements as independent variables (see “Statistical Appendix”). Subsequently, a regression analysis was performed with echocardiographic measurements added singly in a stepwise fashion to determine whether the percentage of explained variability in mitral leaflet area could be increased. As a result of that analysis, the measurement of mitral valve opening area was then incorporated into regression equations that expressed the best possible echocardiographic estimation of actual mitral leaflet area. Because of the technical differences between transthoracic and intraoperative echocardiography, we independently analyzed the data in the two subgroups of patients studied by these respective techniques, thereby generating a separate regression equation for each.

Cross-validation method was used to assess the degree of error likely to occur when the regression equation for predicting mitral leaflet area from the echocardiographic measures was applied to future and similar patients with hypertrophic cardiomyopathy. Specifically, cross-validation assesses how well a calculated regression line predicts a data point that has been removed from the analysis (and therefore has not been used to fit that line). Therefore, in cross-validation (as it applies to the present analysis), a single data point consisting of mitral valve opening area and actual mitral leaflet area was deleted from the analysis. The best regression line was then fit to the remaining data to determine how reliable that equation was in predicting the omitted data point. This procedure was repeated (in turn) after reintroducing the omitted data point and eliminating another, until all 37 data points had been assessed by regression analysis.

**Results**

**Mitra Valve Morphometry**

In the 37 study patients, total mitral leaflet area ranged from 7.3 to 22.4 cm² (mean, 12.4±3.5 cm²). Of the 37 patients, 19 (51%) had increased leaflet area exceeding the 95% confidence limits for normal leaflet area (≥12.0 cm²); the remaining 18 patients had normal leaflet size (area of less than 12.0 cm²). Increased mitral leaflet area in the 19 patients was due to both increased leaflet length (2.2±0.5 versus 1.9±0.4 cm for normal-sized valves; P<.05) and increased circumference (8.9±1.4 versus 7.2±1.0 cm for normal-sized valves; P<.001).

**Echocardiographic Findings**

Mitral valve opening area measured from the echocardiogram in the overall group of 37 patients ranged from 1.6 to 6.9 cm² (mean, 3.4±1.2 cm²) and was significantly larger in the 19 patients with increased mitral leaflet area (as measured from surgical specimens) than in the 18 patients with normal-sized mitral leaflets (4.2±1.0 versus 2.6±0.8 cm²; P<.001). Also, anterior mitral leaflet length as assessed by echocardiography was longer in patients with enlarged valves (2.5±0.4 cm) than in patients with normal-sized valves (2.2±0.2 cm; P<.001).

Left ventricular outflow tract area measured from the echocardiogram in the 37 patients ranged from 0.6 to 5.0 cm² and was larger in the 19 patients with increased leaflet area (3.3±1.0 cm²) than in those 18 patients with normal leaflet area (2.0±0.6 cm²; P<.001).

Other echocardiographic dimensions were also significantly greater in patients with enlarged valves compared with those with normal-sized valves. These included circumference of the mitral valve opening area (9.7±1.4 cm in enlarged versus 8.1±1.3 cm in normal-sized valves; P<.01), horizontal diameter of the mitral valve opening area (2.7±0.5 versus 2.3±0.6 cm; P<.05), and mitral valve transverse diameter obtained from the M-mode echocardiogram (3.0±0.4 versus 2.2±0.4 cm; P<.001) and from the two-dimensional echocardiogram (2.4±0.4 versus 2.1±0.4 cm).

**Comparison of Data Obtained With Transthoracic and Intraoperative Echocardiography**

The 25 patients with transthoracic and the 12 patients with intraoperative echocardiograms were analyzed separately for the correlation between mitral valve opening area (assessed by echocardiography) and actual mitral leaflet area (measured from the surgical specimen); squared correlations were .67 (r=.82) and .86 (r=.93), respectively. Comparing the slopes of the regression lines relating mitral valve opening area with mitral leaflet area in these two subgroups showed a difference that was not statistically significant (P=.08).

**Relation Between Actual Mitral Leaflet Area and Echocardiographic Variables**

Univariate regression analysis, using actual mitral leaflet area as the dependent variable, showed mitral valve opening area to be the best single echocardiographic predictor of actual mitral leaflet area for the 37 study patients; the squared correlation (r²) for this variable was .75 (r=.87) (Table 1). Thus, approximately 75% of the variability in actual mitral leaflet area could be explained by this single variable.

Treating mitral leaflet area as the dependent variable (see “Statistical Appendix”), the other seven echocardiographic variables were added into the stepwise regression model to determine whether a further increase in the percentage of explained variability for actual leaflet area could be achieved. Variability in mitral leaflet area was increased only marginally by adding these independent variables; therefore, mitral valve opening area was chosen to be the only variable to remain in the model (Fig 2).

This analysis resulted in the following final equations. For patients with transthoracic echocardiograms,

\[ \text{MLA} = 4.64 + 2.17 \times \text{MVOA} \]

For patients with intraoperative echocardiograms,

\[ \text{MLA} = 2.19 + 3.06 \times \text{MVOA} \]

where MLA is mitral leaflet area, MVOA is mitral valve opening area, 4.64 and 2.19 reflect the intercept, and 2.17 and 3.06 are the slopes.
TABLE 1. Relation Between Actual Mitral Leaflet Area and Echocardiographic Variables in a Univariate Regression Model

<table>
<thead>
<tr>
<th>Echocardiographic variables</th>
<th>$r^2$</th>
<th>$r$</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>MVOA (cm$^2$)</td>
<td>.75</td>
<td>.87</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Circumference of MVOA (cm)</td>
<td>.58</td>
<td>.76</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Transverse diameter of MVOA (cm)*</td>
<td>.52</td>
<td>.72</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Anterior mitral leaflet length (cm)</td>
<td>.49</td>
<td>.70</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Left ventricular outflow tract area (cm$^2$)</td>
<td>.48</td>
<td>.69</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Transverse diameter of MVOA (cm)</td>
<td>.31</td>
<td>.56</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Horizontal diameter of MVOA (cm)</td>
<td>.27</td>
<td>.52</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

MVOA indicates mitral valve opening area.

*Obtained from the M-mode echocardiogram; all other variables were measured from the two-dimensional echocardiogram.

Identification of Normal or Increased Mitral Leaflet Area by Echocardiography

Using the mitral leaflet area estimated from the regression equations, echocardiography correctly predicted mitral leaflet area to be normal (<12.0 cm$^2$) in 15 of 18 patients (83%) but incorrectly overestimated leaflet area in the other three patients with normal valve size (Fig 3). Similarly, echocardiography correctly predicted mitral leaflet area to be enlarged (≥12.0 cm$^2$) in 16 of 19 patients (84%) but incorrectly underestimated leaflet area in the other three patients.

Reproducibility

Interobserver variability. The difference between the two observers for measurement of mitral valve opening area was compared with the average of the two measurements for each of the 37 patients. The mean difference between the measurements of the two observers was 0.20±0.38 cm$^2$; these differences appeared to be relatively constant across the range of values calculated for mitral valve opening area.

Intraobserver variability. The difference between the two measurements of mitral valve opening area made by the same observer was compared with the average of the two measurements for each of the 37 patients. The mean difference between the two measurements was 0.05±0.17 cm$^2$; these differences appeared to be relatively constant across the range of values calculated for mitral valve opening area.

Cross-Validation Analysis

In each of the 37 study patients, differences between the actual mitral leaflet area measured from the surgical specimen and that predicted from two-dimensional echocardiography were compared with the actual mitral leaflet area using the cross-validation method. Differences between actual and predicted mitral leaflet area were 2.0 cm$^2$ or less in 27 of the 37 patients (73%) and 2.5 cm$^2$ or less in 30 patients (81%). Also, the error in prediction proved to be relatively constant across the wide range of actual mitral leaflet areas.

Discussion

The impetus for designing the present study was our relatively recent appreciation that mitral valve structure is abnormal in many patients with hypertrophic cardiomyopathy and that such alterations may have important clinical implications. For example, in a recent morphometric study of mitral valves removed at surgery or autopsy from almost 100 patients with hypertrophic cardiomyopathy, about 60% showed an increase in leaflet area as well as a variety of patterns of valve enlargement and elongation. Indeed, increased mitral leaflet size, in association with reduced left ventricular outflow tract size and increased ventricular septal thickness, appears to be an important morphological determinant of the presence and magnitude of the subaortic gradient, the pattern of mitral valve systolic anterior...
motion,11-13,16 and the likelihood that the systolic anterior motion and outflow obstruction will be relieved by myotomy-myectomy.17 Recognition that the mitral valve is greatly increased in size may alter surgical strategy in selected patients with hypertrophic cardiomyopathy. For example, such an enlarged mitral valve may predispose to residual systolic anterior motion of the valve leaflets into an apparently adequate myotomy-myectomy trough, resulting in persistent postoperative systolic septal contact and outflow obstruction. Therefore, in such patients, more extensive muscular resection,17,31 suture plication of the mitral valve in addition to myotomy-myectomy,17 or even mitral valve replacement alone31,36 may be necessary to achieve the desired hemodynamic result. For these reasons, it was important to determine the reliability of echocardiography in the quantitative assessment of mitral valve size in patients with hypertrophic cardiomyopathy.

To date, few attempts have been made to use quantitative echocardiographic measurements in assessing mitral valve structure and motion in patients with hypertrophic cardiomyopathy15 or other cardiac diseases.18-21 One of the reasons for the lack of investigative activity in this area has been the unavailability of a gold standard (ie, mitral valve specimens) to validate the echocardiographic measurements of mitral valve dimensions. Indeed, the unique facet of the present study is the availability of suitable mitral valve specimens and echocardiographic recordings in the same patients, which permitted direct comparisons.

We incorporated morphometric and quantitative echocardiographic data from these patients into a regression analysis and formulated an equation that estimated mitral leaflet area from the echocardiographic measures with good precision. This statistical model identified mitral valve opening area as the strongest single predictor of actual mitral leaflet area. About 75% of the variability in actual mitral leaflet area was explained by this single echocardiographic measurement alone. Also, using the estimation of mitral leaflet area from our statistical model, we were able to discriminate normal-sized from enlarged mitral valves in individual patients with reasonable reliability (ie, in more than 80% of patients). It should be pointed out that the regression equations derived in this study may not apply in precise terms to all other clinical settings, due to expected variability in patient selection, instrumentation, and measurement technique. However, the results of our cross-validation statistical analysis suggests that it would not be unreasonable to apply, with acceptable error, the data from the present study patients to other

TABLE 2. Morphological and Echocardiographic Dimensions in 37 Patients With Obstructive Hypertrophic Cardiomyopathy and Normal-Sized or Enlarged Mitral Valve Leaflets

<table>
<thead>
<tr>
<th>Actual mitral leaflet area (cm²)</th>
<th>Complete study group</th>
<th>Normal-sized (&lt;12.0)</th>
<th>Enlarged (≥12.0)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients (%)</td>
<td>37</td>
<td>18 (49)</td>
<td>19 (51)</td>
<td>—</td>
</tr>
<tr>
<td>Actual mitral leaflet dimensions</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total leaflet area (cm²)</td>
<td>12.4±3.5</td>
<td>9.8±1.6</td>
<td>14.9±3.0</td>
<td>—</td>
</tr>
<tr>
<td>Leaflet circumference (cm)</td>
<td>8.1±1.5</td>
<td>7.2±1.0</td>
<td>8.9±1.4</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Anterior leaflet length (cm)</td>
<td>2.0±0.5</td>
<td>1.9±0.4</td>
<td>2.2±0.5</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Echocardiographic mitral valve dimensions</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MVOA (cm²)</td>
<td>3.4±1.2</td>
<td>2.6±0.8</td>
<td>4.2±1.0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Anterior leaflet length (cm)</td>
<td>2.4±0.4</td>
<td>2.2±0.2</td>
<td>2.5±0.4</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Circumference of MVOA (cm)</td>
<td>8.9±1.6</td>
<td>8.1±1.3</td>
<td>9.7±1.4</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Transverse diameter (cm)</td>
<td>2.3±0.5</td>
<td>2.1±0.4</td>
<td>2.4±0.4</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Transverse diameter (cm)*</td>
<td>2.6±0.6</td>
<td>2.2±0.4</td>
<td>3.0±0.4</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Horizontal diameter (cm)</td>
<td>2.5±0.6</td>
<td>2.3±0.6</td>
<td>2.7±0.5</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Left ventricular outflow tract area (cm²)</td>
<td>2.7±1.1</td>
<td>2.0±0.6</td>
<td>3.3±1.0</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

MVOA indicates mitral valve opening area.
*Obtained from the M-mode echocardiogram; all other variables were measured from the two-dimensional echocardiogram.
theoretical future and similar patients with hypertrophic cardiomyopathy.

Our data were obtained in a highly selected study population that, for the purposes of this investigation, (1) included only those patients in whom the mitral valve specimen was in suitable condition for morphometry and (2) either a throracic or intraoperative echocardiogram was available that permitted quantitative assessment of a variety of dimensions from stop-frame, two-dimensional images and the M-mode echocardiogram. Therefore, although high-precision transthoracic echocardiographic studies considered for (or included in) our study group were clinically satisfactory and of sufficient diagnostic quality, some were less than optimal for the unique design of the present study, which required quantitative measurements of several ventricular and valvular dimensions. It was for these reasons that the intraoperative echocardiogram was used in about one third of the final study group. Mitral leaflet area estimated from the intraoperative echocardiograms did not, however, differ significantly from that derived from the standard transthoracic echocardiograms in the same patients.

The results of the present investigation establish for the first time an important principle, namely, that it is possible to assess mitral valve size and dimensions from the echocardiogram with reasonable precision and also discriminate large from normal-sized valves in individual patients with hypertrophic cardiomyopathy. Such measurements may have important clinical implications by improving our understanding of the pathophysiology of outflow obstruction as well as in designing the most effective surgical strategy to relieve outflow obstruction.

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Statistical Appendix

Mitral leaflet area (MLA) is measured from the anatomic specimen with very little error, whereas mitral valve opening area (MVOA) could not be measured from the two-dimensional echocardiogram with nearly the same precision. Therefore, the most relevant regression equation would relate MVOA to MLA rather than vice versa. That is, if \( x = \text{MLA} \) and \( y = \text{MVOA} \), the most natural regression equation is:

\[
y = \alpha_0 + \alpha_1 x + \delta
\]

where \( \alpha_0 \) and \( \alpha_1 \) are the intercept and slope, respectively, and \( \delta \) is a random error. However, we wish to predict \( x = \text{MLA} \) from a given value of \( y = \text{MVOA} \), which is opposite to the way in which the Equation 1 is usually used. One way to accomplish this is to apply inverse regression. However, this method entails the concept of fiducial limits, which is not universally accepted. Nevertheless, in some instances, this technique is the only alternative. An example would be in the calibration of a measuring instrument using standard objects of known dimensions that are chosen in some systematic way and therefore cannot be regarded as a random sample. However, we believe that it is reasonable to regard the present data as a random sample of actual MLAs. Under this assumption, we are justified in inverting the regression equation so that the actual MLA is conditioned on the measured MVOA:

\[
\text{MLA} = \beta_0 + \beta_1 \text{MVOA} + e
\]

where \( \beta_0 \) and \( \beta_1 \) are the intercept and slope, respectively, and \( e \) is a random error. We can therefore regard MLA as the dependent variable in the regression analysis and use standard regression methodology.
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*Circulation*. 1993;88:548-555
doi: 10.1161/01.CIR.88.2.548
*Circulation* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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