Morphological Determinants of Echocardiographic Patterns of Mitral Valve Systolic Anterior Motion in Obstructive Hypertrophic Cardiomyopathy

Heinrich G. Klues, MD; William C. Roberts, MD; and Barry J. Maron, MD

Background. The morphological determinants of mitral valve systolic anterior motion (SAM) and obstruction to left ventricular outflow in patients within the broad clinical spectrum of hypertrophic cardiomyopathy (HCM) have not been completely understood, particularly the contribution of mitral leaflet length and size.

Methods and Results. To clarify this issue, mitral valve specimens from 43 patients with HCM and basal outflow obstruction were used to relate morphometric measurements of leaflet area to certain morphological and functional assessments of left ventricular outflow tract geometry and valvular motion obtained from echocardiograms in the same patients. Twenty-four patients (56%) had mitral valves of normal size (leaflet area <12.0 cm²) and 19 patients (44%) had enlarged and elongated valves (area ≥12.0 cm²). Compared with normal-sized mitral valves, the enlarged valves were situated more posteriorly in a larger left ventricular outflow tract (cross-sectional area, 3.3±1.0 versus 1.9±0.7 cm² for normal-sized valves; p<0.001) and also had greater systolic excursion of the anterior leaflet (16.2±4.5 versus 13.3±3.3 mm, p<0.02), usually with a distinctive sharp-angled bend and localized contact of the leaflet tip with ventricular septum ("typical" SAM); this pattern of SAM was possible because the central and distal portions of the leaflet were relatively free of fibrous thickening. In contrast, normal-sized mitral valves were situated more anteriorly in a smaller left ventricular outflow tract and frequently showed a different mechanism of SAM and subaortic obstruction with relatively limited leaflet motion, absence of a sharp bend, and septal contact involving more substantial portions of the anterior leaflet and contiguous chordae ("atypical" SAM); mitral-septal apposition was affected in large measure by posterior ventricular septal motion. This pattern of SAM was invariably associated with a more diffuse pattern of fibrous thickening.

Conclusions. Patients with obstructive HCM show patterns of mitral valve SAM that are diverse and determined largely by the interrelation of left ventricular outflow tract geometry, the size and mobility of the mitral leaflets, and the presence and distribution of fibrous thickening. (Circulation 1993;87:1570–1579)

Key Words • hypertrophic cardiomyopathy • mitral valve • systolic anterior motion • subaortic obstruction

A significant proportion of patients with hypertrophic cardiomyopathy (HCM) have obstruction to left ventricular outflow that often importantly influences clinical outcome and prognosis.1–4 Subaortic obstruction in HCM is dynamic and generally believed to be due to systolic anterior motion (SAM) of the mitral leaflets and mid-dysystolic contact with the ventricular septum.1,2,5–13

A number of morphological and hemodynamic variables have been associated with the occurrence of SAM in patients with obstructive HCM, including reduced left ventricular outflow tract size,1,4,14–16 anterior displacement of the mitral valve toward the ventricular septum,5,6,13–16 malposition of papillary muscles,17–19 and increased ejection velocity.20–23 Recent morphological studies of mitral valves from patients with HCM have shown substantial variability in structural appearance, including many with increased leaflet area and segmental elongation of one or both leaflets,24 suggesting to us that the size of the mitral leaflets may also play a potential role in producing SAM and outflow obstruction.

In the present study, the availability of both echocardiograms and mitral valve specimens from the same patients with HCM afforded the unique opportunity to compare mitral valve dimensions with echocardiographic measures of left ventricular outflow tract geometry and mitral valvular motion and to create an integrated assessment of the morphological determinants of the patterns of SAM and subaortic obstruction.

Methods

Selection of Patients

Between 1982 and 1989, 283 patients underwent operation for obstructive HCM at our institution; 210 had ventricular septal myotomy–myectomy.25,26 69 had mitral valve replacement alone, and four others had
both operations (myotomy–myectomy followed by mitral valve replacement). Mitral valve replacement was recommended when one or more of the following were identified: 1) basal ventricular septal thickness <18 mm, a circumstance in which the risk for iatrogenic ventricular septal defect or suboptimal relief of outflow obstruction is potentially increased; 2) atypical and particularly heterogeneous distribution of septal thickening; 3) previous ventricular septal myotomy–myectomy with persistent obstruction and symptoms; and 4) intrinsic abnormalities of the mitral valve, including mitral valve prolapse, rheumatic disease, healed bacterial endocarditis, or anomalous insertion of papillary muscle directly into the anterior mitral leaflet.

The files of the pathology branch from 1982 to 1989 were reviewed. Sixty-six of the 73 mitral valves previously excised at operation from patients with HCM had been removed intact and were in suitable condition for the present study. Of these 66 mitral valves, one had morphological features of mitral prolapse and was excluded, reducing the number of operative specimens to 65. Nine of these 65 valves had direct papillary muscle insertion into anterior mitral leaflet and were excluded from the present study because they have been previously described as a group and represent a unique mechanism of muscular midcavity obstruction (largely exclusive of dynamic mitral valve SAM). The remaining 56 mitral valve specimens consisted of both leaflets, the attached chordae tendineae, and in some instances, portions of the papillary muscles; each valve was without the characteristic morphological features of mitral valve prolapse.

Thirteen other valves (and patients) were excluded from the study either because SAM was absent or mild under basal conditions or the echocardiographic studies were judged to be of insufficient technical quality. The remaining 43 patients constitute the final study group, having both technically satisfactory mitral valve specimens and preoperative echocardiograms showing marked mitral valve SAM (with mitral–septal contact) under basal conditions. The magnitude of preoperative mitral regurgitation could be assessed from left ventricular angiograms in 38 patients and was judged to be mild in 11, moderate in 13, moderately severe in six, and severe in one; mitral regurgitation was absent in the other seven patients.

In each study patient, the diagnosis of HCM was based on the presence of a hypertrophied and 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 necropsy and/or clinical features of HCM. Ages ranged from 15 to 69 years (mean, 46 years); 23 were men and 20 were women. Each of the 43

| TABLE 1. Comparison of Clinical and Morphological Data Between Patients With Obstructive Hypertrophic Cardiomyopathy and Normal Control Patients |
|---------------------------------|-----------|-----------|-----|
| No. of patients                | 43        | 45        | ... |
| Age                            | 46±14     | 45±17     | NS  |
| Range (years)                  | 15–69     | 15–74     |     |
| Male:female                    | 21 (49%):22 (51%) | 24 (53%):21 (47%) | NS  |

Mitral valve measurements

| Anterior leaflet | 5.3±1.5 | 4.3±1.0 | <0.001 |
| Posterior leaflet | 2.4±1.0 | 1.7±0.5 | <0.001 |
| Total leaflets   | 11.9±3.5 | 8.7±2.0 | <0.001 |
| Circumference (cm) | 7.9±1.5 | 8.2±2.8 | NS    |
| Length (cm)      | 2.0±0.5 | 1.8±0.3 | <0.01  |
| Maximum thickness, anterior leaflet (mm) | 2.4±0.8 | 1.1±0.4 | <0.001 |

HCM, hypertrophic cardiomyopathy.

**FIGURE 1. Schematic drawing of an open normal mitral valve showing the anterior mitral valve leaflet (AML) and the posterior mitral valve leaflet (PML).** Posterior leaflet is composed of two lateral (LAT) scallops and a middle (MID) scallop; 1 represents total circumference of the valve along the annular margin; 2 and 3 represent lengths of anterior and posterior leaflets. Anatomic demarcation of the anterior from the posterior leaflet was made visually, usually by identification of the insertion of a fanlike arrangement of commissural chordae between the two. PM, papillary muscle.
patients had severe symptoms of cardiac dysfunction (New York Heart Association functional class III or IV).

Control Patients
Mitral valves from 45 consecutively studied patients with entirely normal hearts, both functionally and anatomically, were chosen as control subjects (Table 1). All 45 patients had died from noncardiac conditions. In each control patient, heart weight was ≤ 350 g in men and ≤ 300 g in women. The 45 control patients ranged in age from 15 to 74 years (mean, 45 years); 24 were men and 21 were women.

Mitral Valve Morphometry
Mitral valves were fixed in 10% buffered formalin after their removal at operation. Valves were introduced to the fixative freely without stretching or manipulation. Each specimen was placed in an open position on a cutting board and was extended to full size with the atrial aspect exposed. Usually it was necessary to affix the open valve directly to the board with pins in order to flatten the specimen. Quantitative morphological measurements were made directly from the mitral valve specimen (Figure 1): 1) circumference of the valve measured along its margin of attachment, 2) maximum...
length of anterior leaflet, from annular margin to free edge, 3) thickness of the anterior mitral leaflet, and 4) area of combined anterior and posterior mitral leaflets and the area of the anterior mitral leaflet alone.

To assess mitral leaflet area, borders of the open valves were traced on an acetate overlay and then planimeterized by using a digital tape. These measurements have been shown previously to have satisfactory reproducibility.24

Echocardiographic Techniques

Two-dimensional echocardiograms were performed with Advanced Technology Laboratory Mark 500 or Hewlett-Packard Sonos 500 instruments and 2.25- or 2.5-MHz transducers. Two-dimensional transthoracic images were obtained in standard cross-sectional planes25; 31 of the 43 study patients also had intraoperative epicardial echocardiograms (with long- and short-axis views) performed just before and after the operative procedure.26 Standard procedures in our laboratory dictated that the entire mitral valve be routinely scanned slowly in both the short-axis and long-axis views with particular attention directed toward identifying and imaging the point of maximum SAM and the greatest extent to which the anterior mitral leaflet may bend toward the ventricular septum in midsystole.

Two-dimensional echocardiographic measurements were taken preferentially from transthoracic echocardiograms in 33 patients; however, in 10 patients, the image quality was judged to be insufficient to reliably make certain quantitative measurements from stop-frame images, and the intraoperative echocardiogram was used. M-Mode echocardiograms were derived from two-dimensional images under direct anatomic visualization. In the 33 patients in whom transthoracic echocardiograms were used, the time duration between echocardiographic study and mitral valve replacement was 1–86 days (mean, 31 days).

Echocardiographic Measurements

Left ventricular outflow tract. Diastolic left ventricular outflow tract cross-sectional area was measured using a previously described method.14 A continuous scan from aorta to left ventricle in the parasternal short-axis view identified a representative stop-frame image at the cross-sectional level where both mitral leaflets could be visualized at end diastole. On this image, the innermost margins of the outflow tract were traced on a plastic transparency.
and the outlined area was planimetered. In addition, the transverse end-diastolic outflow tract dimension was measured from the M-mode echocardiogram as the maximum distance between the point of mitral valve coaptation and ventricular septal endocardium.14,15

Mitral valve geometry and motion. Position of the mitral valve in the left ventricular cavity was assessed by M-mode echocardiography at the point of valve coaptation. Mitral valve position index was calculated by dividing the distance between mitral valve and posterior free wall endocardium by the distance between mitral valve and septal endocardium.15

Systolic anterior excursion of the mitral valve was assessed quantitatively on the M-mode echocardiogram by measuring the transverse forward motion of anterior mitral leaflet from the point of coaptation (at onset of ventricular systole) to the point of initial mid-systolic contact with the ventricular septum.

Left ventricular wall. Ventricular septal and posterior free wall thicknesses at mitral valve level were measured from the M-mode echocardiogram at the peak of the R wave. Amplitude of ventricular septal excursion was obtained at the same level by calculating the difference between the maximal systolic and diastolic posterior motion of the septal endocardial border.13,35,36

Statistical Analyses
Data are expressed as mean±SD. Comparisons between groups were tested by unpaired Student's *t* test, *χ*² test, or ANOVA where appropriate.

Results

Mitral Valve Dimensions

The 43 mitral valves were segregated into two groups, based on whether or not mitral leaflet area exceeded the
95% confidence limits for normals24 (Figures 1–5 and Table 2): enlarged (>12.0 cm²; 19 patients [44%]) and normal-sized (<12.0 cm²; 24 patients [56%]). Enlarged valves ranged from 12.0 to 22.4 cm² (mean, 14.9±3.0 cm²) and normal-sized valves from 7.1 to 11.9 cm² (mean, 9.6±1.5 cm²). In enlarged valves, increased leaflet area was due to an increase in leaflet length (2.2±0.5 versus 1.8±0.3 cm for normal-sized valves, p<0.001) rather than in valve circumference (8.9±1.4 versus 8.2±0.8 cm for normal-sized valves, p>0.05).

Echocardiographic Findings

Left ventricular outflow tract. Patients with enlarged mitral valves also had greater left ventricular outflow tract cross-sectional area as assessed by echocardiography (3.3±1.0 cm²; range, 1.1–5.0 cm²) (Figures 2–4 and Table 2) than did patients with normal-sized valves (1.9±0.7 cm²; range, 0.6–3.6 cm²; p<0.001) (Figure 5 and Table 2). Therefore, for the overall group of 43 patients, a direct linear relation was evident between left ventricular outflow tract area and mitral leaflet area (Figure 6). Of the 24 patients with normal-sized valves, 16 (67%) had particularly small outflow tract areas <2.0 cm² that usually appeared elliptical in shape when viewed in short axis; conversely, only one (5%) of 19 patients with enlarged valves had an outflow area <2.0 cm². Also, the transverse end-diastolic outflow tract dimension was significantly greater in patients with enlarged mitral valves (21.7±4.1 mm) than in patients with normal-sized valves (18.1±3.3 mm, p<0.003) (Table 2). However, enlarged mitral valves showed significantly greater systolic anterior excursion of the anterior leaflet (16.2±4.5 mm) than did normal-sized valves (13.3±3.2 mm, p<0.02) (Figures 2–5 and Table 2).

In patients with normal-sized mitral valves, the position of the valve within the left ventricular cavity (as assessed by mitral valve position index) was significantly more anterior and closer to the ventricular septum than in those patients with enlarged valves (Table 2).

Morphological Determinants of Mitral Valve SAM in HCM

Mitral valve geometry and motion patterns. In most enlarged mitral valves (16 of 19, 84%), two-dimensional echocardiography showed a particular pattern of mitral valve motion—flexible and with marked systolic excursion, usually with a distinctive, sharp, right-angled bend of the anterior leaflet (about 80–90° at a point one-half the distance between its proximal and distal extent) producing localized contact of the distal and central portion of the leaflet with the ventricular septum ("typical SAM") (Figures 2–4 and Table 2). Of the 24 patients with normal-sized valves, 12 were judged to have flexible mitral valve motion, whereas the other 12 demonstrated SAM with a flattened configuration, restricted motion, and either no or relatively mild bending of the anterior mitral leaflet (usually <60°). Systolic contact with ventricular septum was not usually limited to the anterior leaflet tip but rather involved more substantial portions of the leaflet body and contiguous chordae tendineae (Figure 5) and also often appeared to be facilitated by posterior ventricular septal excision ("atypical" SAM).

Fibrous thickening and relation to pattern of mitral valve motion. Secondary fibrous thickening was present to some degree in each of the 43 mitral valves. Anterior leaflet thickening was the same in enlarged and normal-sized valves (2.4±1.8 mm).

In 15 of the 43 mitral valves (three enlarged and 12 normal-sized), the anterior leaflet was diffusely thickened and inflexible on gross examination (Figure 5C); attached chordae tendineae were also substantially thickened and often agglutinated; echocardiographic study in each of these patients showed the mitral valve to have relatively restricted mobility and little or no systolic bending (Figures 5A and 5B). In the other 28 valves (16 enlarged and 12 normal-sized), fibrous thickening was more localized, and at least the central and longitudinal portions of the anterior leaflet (including the most distal segment) were spared from fibrosis (Figures 2D, 3C, and 4B) and judged to be flexible on gross examination; attached chordae tendineae were normal or only mildly thickened. Echocardiographic study in each of these patients showed mitral valve motion to be more flexible with substantial excursion, an acute right-angled bend, and localized systolic septal contact (Figures 2A–C, 3A–B, and 4A).

Demographic Findings

Seventeen (71%) of the 24 patients with normal-sized valves but only five (26%) of the 19 patients with enlarged valves were women (p<0.004). Patients with enlarged and normal-sized mitral valves were similar in respect to age (44±13 versus 47±14 years) (Table 3).

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Hemodynamic Findings

All 43 patients underwent cardiac catheterization (Table 3). Basal peak left ventricular outflow pressure gradients were 30–165 mm Hg (average, 82 mm Hg). Thirty-four patients had gradients >50 mm Hg. In the nine other patients with basal gradients <50 mm Hg, gradients of 60–130 mm Hg were elicited by provocative maneuvers. Patients with enlarged and normal-sized mitral valves were similar in respect to magnitude of the subaortic gradient and end-diastolic pressure and the presence or degree of mitral regurgitation (Table 3). Mitral stenosis was excluded in each patient by the
absence of a diastolic gradient between simultaneously recorded left ventricular end-diastolic and pulmonary capillary wedge pressures.

Discussion

The occurrence of dynamic obstruction to left ventricular outflow in many patients with HCM has been recognized since the earliest descriptions of the disease over 30 years ago, and its importance in the genesis of symptoms and disease progression have been emphasized repeatedly. Mechanisms by which subaortic gradients are produced in patients with HCM have been scrutinized, and numerous studies have focused on defining the contributions of several morphological and hemodynamic factors, including reduced diastolic outflow tract size, substantial hypertrophy of the basal anterior ventricular septum, anterior displacement of mitral valve and papillary muscles within the ventricular cavity, and hyperdynamic left ventricular ejection producing a high-velocity jet streaming through a narrowed outflow tract and pulling the mitral leaflets toward the septum (Venturi effect), or, alternatively, primary geometric abnormalities of the papillary muscle–mitral valve apparatus creating altered distribution of tension to the mitral leaflets.

Isolated observations in selected patients with HCM have described structural abnormalities of the mitral valve that appear to be congenital and are associated with SAM and outflow obstruction; some investigators have identified increased anterior mitral leaflet length in patients with HCM, particularly those with outflow obstruction. Nevertheless, the contribution of mitral valve size to outflow obstruction in patients with HCM has been largely ignored. This has occurred because: 1) mitral valve dimensions are often difficult to assess reliably from the echocardiogram, and 2) mitral valve specimens from such patients have rarely been available for study (and for validation of the echocardiographic measurements), since septal myotomy–myectomy rather than mitral valve replacement has traditionally been the operation of choice for patients with outflow obstruction.

However, in the present integrated echocardiographic and pathological investigation, we were able to study a sizeable group of mitral valve specimens from patients with HCM who had undergone mitral valve replacement to relieve marked symptoms and obstruction to left ventricular outflow. Consequently, it was possible to compare the morphometric measurements made in those operatively removed valves with an assessment of left ventricular outflow tract geometry and valve motion obtained from the echocardiograms previously recorded in the same patients. This unique circumstance permitted us to focus on the significance of mitral valve structure in determining different patterns of SAM (and subaortic obstruction). Hence, we have segregated patients in this study with regard to their total mitral leaflet area. This measurement, made directly from the valve specimen itself, has been shown previously to be highly reproducible, and the subgrouping of patients in this fashion was based on the following criteria: (1) normal leaflet area, (2) leaflet area increased by more than 50%, (3) leaflet area increased by less than 50% but with SAM, and (4) leaflet area increased by less than 50% without SAM.

This approach permitted us to define the role of each valve morphology in the causation of SAM, with SAM defined as an anterior mitral leaflet excursion equal to 6 cm per second or greater. The patients were divided into two groups: those with SAM (n = 48) and those without SAM (n = 24). The groups were matched for age, sex, and extent of hypertrophy. The mitral leaflet area was determined by planimetry, and the leaflet excursion was measured by planimetry to the leading edge of the anterior leaflet. The values were compared using a Student t-test for unpaired data.

TABLE 2. Comparison of Echocardiographic Findings in Patients With Obstructive Hypertrophic Cardiomyopathy and Normal-Sized or Enlarged Mitral Valves

<table>
<thead>
<tr>
<th>Mitral leaflet area</th>
<th>Normal (&lt;12.0 cm²)</th>
<th>Enlarged (≥12.0 cm²)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients (%)</td>
<td>24 (56%)</td>
<td>19 (44%)</td>
<td></td>
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<tr>
<td>LV wall thickness (mm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior ventricular septum</td>
<td>18.3±3.3</td>
<td>18.8±4.0</td>
<td>NS</td>
</tr>
<tr>
<td>Posterior free wall</td>
<td>13.4±4.5</td>
<td>13.8±5.1</td>
<td>NS</td>
</tr>
<tr>
<td>Amplitude posterior septal excursion (mm)</td>
<td>4.9±2.4</td>
<td>5.6±2.1</td>
<td>NS</td>
</tr>
<tr>
<td>LV outflow tract</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cross-sectional area (cm²)</td>
<td>1.9±0.7</td>
<td>3.3±1.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Transverse dimension (mm)</td>
<td>18.1±3.3</td>
<td>21.7±4.1</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Mitral valve geometry/motion</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Position index</td>
<td>1.4±0.4</td>
<td>1.1±0.3</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Systolic anterior excursion (mm)</td>
<td>13.3±3.3</td>
<td>16.2±4.5</td>
<td>&lt;0.02</td>
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<tr>
<td>Mitral annular calcium</td>
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<tr>
<td>None/mild</td>
<td>14 (58%)</td>
<td>18 (95%)</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>Moderate/severe</td>
<td>10 (42%)</td>
<td>1 (5%)</td>
<td></td>
</tr>
<tr>
<td>Patterns of SAM</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>“Typical”</td>
<td>12 (50%)</td>
<td>16 (84%)</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>“Atypical”</td>
<td>12 (50%)</td>
<td>3 (16%)</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>LV cavity dimensions (mm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>End diastole</td>
<td>37±6</td>
<td>42±5</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>End systole</td>
<td>22±4</td>
<td>24±5</td>
<td>NS</td>
</tr>
<tr>
<td>Left atrial dimension (mm)</td>
<td>44±7</td>
<td>53±6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Aortic root dimension (mm)</td>
<td>30±5</td>
<td>33±3</td>
<td>NS</td>
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LV, left ventricle; SAM, systolic anterior motion of the mitral valve.
the 95th percentile cutoff for leaflet area derived from a group of normal valves.\textsuperscript{24} Using this aforementioned approach, we identified elongated and enlarged mitral leaflets (area \( \geq 12.0 \, \text{cm}^2 \)) in about 45\% of our patients. When subjected to our integrated echocardiographic and morphological analysis, these valves were shown to be situated more posteriorly in a larger left ventricular outflow tract compared with mitral valves of normal size; this circumstance appeared to permit more extensive systolic anterior excursion and usually a distinctive sharp-angled bend of the anterior leaflet and localized mitral valve–septal contact that we have termed “typical” SAM. Hence, in these particular patients, mitral valve size and length per se appeared to represent an important determinant of outflow obstruction.

In contrast, about 55\% of our patients had normal-sized mitral valves (leaflet area <12.0 \( \text{cm}^2 \)). These valves were situated within a much smaller (and often elliptically shaped) left ventricular outflow tract and consequently were displaced more anteriorly toward the ventricular septum; frequently, the presence of mitral annular calcification posteriorly appeared to contribute to the exaggerated anterior position of the mitral valve.\textsuperscript{13} While such normal-sized mitral valves often produced SAM characterized by flexible anterior leaflet motion and a sharp-angled bend, in many other patients with normal-sized valves the pattern of SAM was “atypical,” with more restricted systolic valve excursion in which substantial portions of the anterior leaflet body (as well as the distal tip and contiguous chordae) contacted the septum. In the latter patient subgroup, systolic posterior ventricular septal motion also appeared to contribute importantly to resultant mitral–septal contact.\textsuperscript{13}

The fact that the pattern of SAM differed among patients with normal-sized mitral valves only serves to emphasize that SAM is not determined solely by anterior mitral leaflet length but rather on the interplay of a number of morphological variables related to left ventricular outflow tract geometry, septal motion, the relative position of the mitral apparatus within the left ventricular cavity, and particularly the extent and distribution of fibrous anterior mitral leaflet thickening. Flexible systolic motion of the anterior leaflet in patients with “typical” SAM (regardless of whether the mitral valve was enlarged or normal-sized) was possible because the central portion of the anterior leaflet was largely spared from fibrosis. In contrast, more restricted valvular motion (“atypical” SAM) appears to be a direct consequence of a more diffuse pattern of anterior leaflet thickening. Of note, basal anterior ventricular septal thickness was not shown to be a particularly important independent determinant of the pattern of SAM in our study patients, a finding consistent with prior echocardiographic observations in patients with HCM and marked left ventricular hypertrophy.\textsuperscript{51} The observations in the present study do not obviate other previously described determinants of outflow obstruction\textsuperscript{1–6,9,11,13–17,20–22,41–46} but rather expand and amplify our concepts of the mechanisms of the gradient in this disease. For example, our data do not exclude the potential role played by the anterior position of the papillary muscles, which in large measure determine the relative position of the mitral valve apparatus within the left ventricular cavity.

Our normal values for anterior leaflet length are somewhat less than those previously reported in other necropsy or echocardiographic studies.\textsuperscript{17,43,44,47,48} For example, our normal average value for anterior leaflet length was 1.8 ± 0.3 mm, whereas in other studies published in the literature, average length was 2.3 ± 0.2 mm. We believe that these discrepancies can be explained largely on differences in scientific methodology. In the present study, measurements of anterior leaflet length were made from the mitral valve specimen after its excision from the heart at the time of mitral valve replacement. It was not possible for the surgeon to remove the entire mitral valve out of the necessity to facilitate securing the prosthetic valve in place; there-

![Graph](https://via.placeholder.com/150)

**Figure 6.** Scatterplot shows relation between left ventricular outflow tract (LVOT) cross-sectional area (obtained from two-dimensional echocardiogram) and mitral leaflet area (obtained directly from mitral valve specimen) in 43 patients with obstructive hypertrophic cardiomyopathy.

**Table 3.** Clinical and Hemodynamic Data in Patients With Obstructive Hypertrophic Cardiomyopathy and Normal-Sized or Enlarged Mitral Valves

<table>
<thead>
<tr>
<th>Mitral leaflet area</th>
<th>Normal ((&lt;12.0 , \text{cm}^2))</th>
<th>Enlarged ((\geq 12.0 , \text{cm}^2))</th>
<th>(p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>24 (56%)</td>
<td>19 (44%)</td>
<td>...</td>
</tr>
<tr>
<td>Age</td>
<td>47±14</td>
<td>44±13</td>
<td>NS</td>
</tr>
<tr>
<td>Range</td>
<td>15–69</td>
<td>16–65</td>
<td></td>
</tr>
<tr>
<td>Male:female (%)</td>
<td>7:17</td>
<td>15:4</td>
<td>&lt;0.002</td>
</tr>
<tr>
<td>Functional class (NYHA)</td>
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<td></td>
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</tr>
<tr>
<td>I/II</td>
<td>0</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>III</td>
<td>19 (79%)</td>
<td>19 (100%)</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>5 (21%)</td>
<td>0</td>
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<tr>
<td>LV–to–systemic artery peak systolic gradient (mm Hg)</td>
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<tr>
<td>Basal</td>
<td>85±43</td>
<td>79±32</td>
<td>NS</td>
</tr>
<tr>
<td>Provoked</td>
<td>121±23</td>
<td>110±20</td>
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<tr>
<td>Mitral regurgitation</td>
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<tr>
<td>Mild</td>
<td>4/24</td>
<td>4/19</td>
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<tr>
<td>Moderate</td>
<td>8/24</td>
<td>7/19</td>
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</tr>
<tr>
<td>Severe</td>
<td>5/24</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>LVEDP (mm Hg)</td>
<td>17±6</td>
<td>17±6</td>
<td>NS</td>
</tr>
</tbody>
</table>

NYHA, New York Heart Association; LV, left ventricle; LVEDP, left ventricular end-diastolic pressure.
fore, a 2–3-mm circumferential margin of leaflet tissue along the annulus remained after valve excision. In contrast, in the aforementioned previous necropsy studies, mitral valve measurements were obtained from a completely intact specimen.

The present study was unavoidably limited to patients with the obstructive form of HCM. Patients without outflow obstruction do not undergo mitral valve replacement and therefore their valve specimens have been generally unavailable for detailed study. Consequently, our study cannot address the significance of mitral valve size in determining the presence or absence of SAM (and obstruction to left ventricular outflow). However, of note, a previous morphometric analysis of almost 100 mitral valves from patients with HCM24 showed that valves from patients without obstruction were significantly larger with regard to leaflet length, circumference, and overall area than those from patients with obstruction.

Acknowledgment

We wish to recognize the expert photographic assistance of Michael Spencer.

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_Circulation._ 1993;87:1570-1579
doi: 10.1161/01.CIR.87.5.1570

_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

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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