Significance of Left Ventricular Outflow Tract Cross-sectional Area in Hypertrophic Cardiomyopathy: A Two-dimensional Echocardiographic Assessment

PAOLO SPIRITO, M.D., AND BARRY J. MARON, M.D.

SUMMARY The morphologic determinants of subaortic obstruction in patients with hypertrophic cardiomyopathy are not completely understood. To define the relation between left ventricular outflow tract orifice size and presence or absence of subaortic obstruction, we studied 65 patients with hypertrophic cardiomyopathy and 16 normal controls by quantitative two-dimensional echocardiography. Left ventricular outflow tract area was measured at the onset of systole in the short-axis view in the stop-frame mode.

Left ventricular outflow tract area was significantly smaller in patients with hypertrophic cardiomyopathy and subaortic obstruction (2.6 ± 0.7 cm²) than in patients without obstruction (5.9 ± 1.6 cm², p < 0.001). Twenty of 21 patients with obstruction had a left ventricular outflow tract area smaller than 4.0 cm², whereas 28 of 30 patients without obstruction had a left ventricular outflow tract area of 4.0 cm² or greater. The outflow tract area in patients with provokable obstruction (4.6 ± 1.6 cm²) was intermediate between the areas of patients with and without obstruction. Left ventricular outflow tract area was significantly smaller in patients with hypertrophic cardiomyopathy (4.6 ± 2.0 cm²) than in normal subjects (10.4 ± 1.2 cm², p < 0.001).

We conclude that the cross-sectional outflow tract area is closely related to the presence or absence of subaortic obstruction in patients with hypertrophic cardiomyopathy. Hence, the size of the outflow tract at the level of the mitral valve appears to be of major pathophysiologic significance in producing obstruction in these patients.

HYPERTROPHIC CARDIOMYOPATHY (HCM) has varied clinical and morphologic expressions. Obstruction to left ventricular outflow may be present under basal conditions or with provocative interventions, or may be absent.1-6 The mechanism by which subaortic obstruction occurs in HCM is not definitively known, but substantial data support the view that obstruction is produced by systolic anterior motion of the mitral valve.7-13 The factors responsible for this particular mitral valvular motion are not entirely understood. Some investigators have suggested that hydrodynamic forces generated by a high-velocity blood flow during ejection into a narrowed left ventricular outflow tract cause the mitral valve leaflets to move anteriorly and touch the ventricular septum.14, 15

Wide-angle, two-dimensional echocardiography permits accurate visualization of the anatomic configuratio

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mm Hg with provocation, such as Valsalva maneuver, i.v. isoproterenol or amyl nitrite inhalation (14 patients); or nonobstructive — gradient of zero or less than 30 mm Hg under basal conditions and less than 30 mm Hg with provocation (30 patients). These definitions ensured that each hemodynamic subgroup consisted of patients in whom the magnitude of subaortic obstruction was distinctly different from that in patients in the other subgroups. No patient in our study had apical HCM.16,17 (left ventricular hypertrophy confined to the apical half of the left ventricle).

The diagnosis of HCM was established by M-mode and two-dimensional echocardiographic demonstration of a hypertrophied, nondilated left ventricle in the absence of another cardiac or systemic disease that could produce left ventricular hypertrophy.18 One patient with associated mild aortic regurgitation was included because the valvular insufficiency was not hemodynamically significant.

Characterization of Patients

The 65 patients with HCM were 5–69 years old (mean 38 years). Four patients were younger than 15 years of age and five patients were older than 60 years of age; 40 patients (62%) were male. Six patients were asymptomatic, 29 had mild functional limitation (New York Heart Association functional class II) and 30 had moderate-to-severe functional limitation (classes III and IV).

Sixteen asymptomatic subjects without evidence of cardiovascular disease served as controls. The controls were 22–52 years old (mean 26 years) and 10 were male.

M-mode Echocardiography

M-mode echocardiograms were performed using a 2.25-MHz, 1.25-cm-diameter, unfocused Aerotech transducer and a Hoffrel 201 ultrasound receiver interfaced with a Honeywell 1856 strip-chart recorder or an Irex System II ultrasound unit that had either a 2.25-MHz or 3.5-MHz, 1.3-cm-diameter transducer. The methods for imaging the ventricular septum and posterior left ventricular free wall have been described.19 The ventricular septal thickness was measured just before atrial systole at two levels: with the ultrasound beam directed through the mitral valve leaflets and also just distal to the mitral leaflets. The thickness of the posterior left ventricular free wall was measured during the same phase of the cardiac cycle, with the ultrasound beam passing just distal to the mitral leaflets.

The position of the mitral valve in the left ventricular cavity was assessed at the point of valve leaflet closure. The mitral valve position index was calculated by dividing the distance between mitral valve and posterior left ventricular free wall endocardium by the distance between mitral valve and ventricular septal endocardium.15

Systolic anterior motion of the mitral valve was evaluated semiquantitatively using a modification of the classification proposed by Gilbert et al.20 Systolic anterior motion was defined as mild if the minimal mitral-septal distance was greater than 10 mm, moder-
tricular septum, i.e., the posterior segment of the septum or anterolateral free wall or both.

In addition, the distribution of ventricular septal hypertrophy in the cephalad-caudal plane (long-axis view) was qualitatively assessed in each patient. The ventricular septum was divided into two segments: the cephalad portion, which extended from the cardiac base to the distal margins of the mitral leaflets, and the caudal portion, which included the portion of the left ventricle imaged below the mitral leaflets. The relative magnitude of septal hypertrophy in these two segments was compared by reviewing the two-dimensional echocardiogram in slow-motion and stop-frame modes. When possible, the M-mode echocardiogram was used to verify the thickness of the cephalad and caudal portions of the anterior ventricular septum quantitatively.

Assessment of Left Ventricular Outflow Tract

Cross-sectional Area

After a thorough examination of the continuous aorta-to-left ventricle short-axis scan in each patient, a representative stop-frame image was selected at the first level where both mitral valve leaflets could be visualized at onset of ventricular systole (judged as the first frame during the cardiac cycle in which the mitral valve appeared closed). This cross-sectional plane was selected because in patients with HCM it is the level at which the mitral valve approaches or contacts the ventricular septum during systole and is presumably the site of obstruction to left ventricular outflow.7-15 Although this cross-sectional level may be most appropriate for assessing left ventricular outflow tract dimension in patients with HCM, it may not be universally applicable to the assessment of outflow tract size in patients with other cardiac diseases associated with a narrowed outflow tract. However, for the purposes of this study, we refer to the portion of left ventricular cavity at this cross-sectional level, which is bordered by the ventricular septum anteriorly and medially, the anterolateral free wall laterally and the mitral valve posteriorly (fig. 1) as the left ventricular outflow tract.

On the stop-frame image selected for analysis, the innermost margins of the left ventricular outflow tract were traced onto a plastic transparency. To assure the accuracy of this measurement, the outline of the outflow tract was routinely verified by reviewing the pertinent portions of the videotape in slow motion or single-frame mode against the background of the traced stop frame. The area of the outlined silhouette of left ventricular outflow tract was then quantitated with a video planimetry system.16 The left ventricular outflow tract was measured without knowledge of the hemodynamic classification of the patient.

Inter- and intraobserver reproducibility of the left ventricular outflow tract measurement was assessed by two investigators who were unaware of the identity of the patient. To assess interobserver variability, each observer independently measured the outflow tract area in 24 study patients, including nine with obstructive HCM, eight with nonobstructive HCM and seven control subjects. In addition, outflow tract area was measured by one observer in the same 24 patients on two occasions (2 months apart) to assess intraobserver variability.

Statistical Analysis

Differences between groups of patients were analyzed by the unpaired t test and the chi-square test. Data were expressed as the mean ± SD. Reproducibility of the left ventricular outflow tract area measurements was expressed in terms of a linear regression correlation coefficient and standard error of the estimate.

Results

M-mode Echocardiographic Findings

Ventricular Wall Thicknesses

Ventricular septal thickness measured at the level of the mitral valve leaflets was significantly greater in patients with obstructive HCM (21 ± 5 mm) than in patients with the nonobstructive form of the disease (17 ± 5 mm, p < 0.01) (table 1). Septal thickness in patients with provocative obstruction (19 ± 4 mm) did not differ significantly from that in patients in the other two groups.

Patients without obstruction demonstrated more substantial septal thickening distal to the mitral valve (21 ± 5 mm) than in the cephalad portion of the septum at the level of the mitral valve leaflets (17 ± 5 mm, p < 0.01). In contrast, patients with obstruction at rest or with provocation showed a similar magnitude of septal thickening at the level of the mitral valve and distal to the valve (table 1).

Mitral Valve Position

The mean ventricular septal-to-mitral valve distance was identical in the obstructive and provocative groups (22 ± 4 mm), but significantly greater in patients with nonobstructive HCM (28 ± 6 mm, p < 0.001) (table 1, fig. 2). Furthermore, the mitral valve position index confirmed that the mitral valve was situated more anteriorly within the left ventricular cavity in patients with obstruction (0.85 ± 0.3) than in patients without
obstruction (0.66 ± 0.3, p < 0.05). Patients with provocative obstruction were intermediate between these two subgroups (0.82 ± 0.2), but did not differ significantly from either.

**Mitral Valvular Motion**

Each of the 21 patients with obstructive HCM showed systolic anterior motion of the mitral valve. In 18 of these 21 patients the magnitude and duration of systolic anterior motion was marked and consistent with obstruction to left ventricular outflow under basal conditions. Only three of the 30 patients with nonobstructive HCM showed systolic anterior motion of the mitral valve, which was mild and not consistent with subaortic obstruction in each case. Six of the 14 patients with only provocable obstruction had either no or mild systolic anterior motion at rest and eight had either moderate or marked systolic anterior motion (table 1).

**Cross-sectional Area of the Left Ventricular Outflow Tract**

The left ventricular outflow tract area was significantly smaller in patients with obstructive HCM (2.6 ± 0.7 cm²) than in patients with nonobstructive HCM (5.9 ± 1.6 cm², p < 0.001) (figs 3 and 4); the outflow tract area in patients with provocative obstruction was intermediate in size between the other two subgroups (4.6 ± 1.6 cm², p < 0.05 vs nonobstructive and p < 0.001 vs obstructive). Twenty of the 21 patients with obstruction had an outflow tract area of less than 4.0 cm², whereas 28 of the 30 patients without obstruction had an outflow area of 4.0 cm² or greater (fig. 4). The distribution of left ventricular outflow tract areas in these three hemodynamic subgroups was not altered significantly when the calculated values were normalized for body surface area (fig. 5). This two-dimensional echocardiographic measurement of the outflow tract size allowed a better separation of the obstructive from the nonobstructive patients than did the M-mode echocardiographic assessment of the linear dimension of the outflow tract (i.e., the distance from the ventricular septum to the mitral valve) (figs. 2 and 4).

The left ventricular outflow tract area was significantly greater in the 16 control subjects (10.4 ± 2.0 cm²) than in the 65 patients with HCM (4.6 ± 2.0 cm², p < 0.001). Each of the controls had an outflow tract area of 9.0 cm² or greater, whereas 63 of 65 patients with HCM had an outflow tract area smaller than 9.0 cm² (figs. 3 and 4); the two patients with outflow tract areas greater than 9.0 cm² (9.3 cm² and 10.5 cm²) had nonobstructive HCM. Thus, an outflow tract area of 9.0 cm² appeared to separate patients with HCM from subjects without heart disease. When the left ventricular outflow tract area was normalized for body surface area, 64 of the 65 patients with HCM had a value smaller than the controls (fig. 5).

**Reproducibility Analysis**

Interobserver variability in the measurement of left ventricular outflow tract area was small. The equation of the regression line was y = 0.07 + 1.07x; see =
Distribution of Left Ventricular Hypertrophy

Thirty-six of 65 patients (55%) showed an extensive distribution of hypertrophy involving substantial portions of both the ventricular septum and left ventricular free wall (type III). The prevalence of morphologic type III was highest in patients with basal subaortic obstruction (16 of 21, 76%) and lowest in patients without obstruction (13 of 30, 42%) (table 2). Other morphologic types showed no obvious predilection for a particular hemodynamic state.

Distribution of Ventricular Septal Hypertrophy

Distribution of ventricular septal hypertrophy in the cephalad-caudal plane (long-axis view) differed considerably in patients with the obstructive and nonobstructive forms of HCM (table 3, figs. 7 and 8). The magnitude of hypertrophy was substantially greater in the caudal portion of the septum than in the cephalad portion in 16 of the 30 patients (53%) with nonobstructive HCM. In contrast, this pattern of ventricular septal hypertrophy was present in only three of the 35 patients (9%) with obstruction at rest or with provocation ($p < 0.01$). In none of the patients with nonobstructive HCM did hypertrophy in the cephalad septum exceed that in the caudal septum, and in 14 patients (47%)

0.995, $r = 0.95$). Intraobserver variability was similar for this measurement ($y = 0.39 + 1.02x$; $y = 0.729, r = 0.97$) (fig. 6).

**Figure 4.** Left ventricular outflow tract (LVOT) area, assessed by two-dimensional echocardiography in 65 patients with hypertrophic cardiomyopathy and in 16 normal subjects. The patients with hypertrophic cardiomyopathy are segregated into three groups (obstructive, provocable, nonobstructive) based on the magnitude of the subaortic gradient. Mean values are denoted by 0.

**Figure 3.** Stop frames of two-dimensional echocardiograms (obtained in short-axis view at the level of the mitral valve at onset of systole) from patients with obstructive hypertrophic cardiomyopathy (HCM) (A) and nonobstructive HCM (B) and from a normal subject (C). Broken line denotes margins of left ventricular outflow tract (LVOT). Outflow tract area in the patient with obstructive HCM is significantly smaller than that in the patient without obstruction. The outflow tract area in the normal subject is larger than that in the patients with HCM. Calibration dots are 1 cm apart. ALFW = anterolateral free wall; FW = free wall; MV = mitral valve; VS = ventricular septum.
LVOT AREA IN HCM: Spirito and Maron

FIGURE 5. Left ventricular outflow tract (LVOT) area, assessed by two-dimensional echocardiography, and normalized for body surface area (BSA) in 65 patients with hypertrophic cardiomyopathy and in 16 normal subjects. Distribution of LVOT areas in the three hemodynamic subgroups and in the normal subjects does not differ significantly from that depicted in figure 4, where outflow tract areas were not normalized for body surface area.

septal hypertrophy was relatively uniform throughout. In 19 of the 21 patients (90%) with obstructive HCM, the magnitude of hypertrophy in the cephalad portion of the ventricular septum either exceeded (four patients) or was approximately equal to that in the caudal portion of the septum (15 patients) (figs. 7 and 8). In patients with provokable obstruction, the distribution of ventricular septal hypertrophy was most similar to that of patients with obstruction (table 3).

Discussion

The present study of patients with HCM demonstrates a relation between the presence or absence of subaortic obstruction and the cross-sectional area of the left ventricular outflow tract (at onset of systole), as assessed quantitatively by two-dimensional echocardiography, and confirms the hypothesis\(^{14, 15}\) that the size of the outflow tract is of major pathophysiologic significance in producing subaortic obstruction. Left ventricular outflow tract area was significantly smaller in our patients with subaortic obstruction than in patients with the nonobstructive form of the disease. Specifically, 95% of patients with subaortic obstruction had a left ventricular outflow tract area less than 4.0 cm\(^2\), while 93% of patients without obstruction had an outflow tract area of at least 4.0 cm\(^2\). In the patients with outflow obstruction only during provocation, the size of the left ventricular outflow tract was intermedi-

Table 2. Distribution of Left Ventricular Hypertrophy in 65 Patients with Hypertrophic Cardiomyopathy

<table>
<thead>
<tr>
<th>Morphologic type (2-D echo)</th>
<th>Obstructive (n = 21)</th>
<th>Provocable (n = 14)</th>
<th>Nonobstructive (n = 30)</th>
<th>Total (n = 65)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>1 (5%)</td>
<td>1 (7%)</td>
<td>3 (10%)</td>
<td>5 (7%)</td>
</tr>
<tr>
<td>II</td>
<td>4 (19%)</td>
<td>5 (36%)</td>
<td>12 (38%)</td>
<td>21 (32%)</td>
</tr>
<tr>
<td>III</td>
<td>16 (76%)</td>
<td>7 (50%)</td>
<td>13 (42%)</td>
<td>36 (55%)</td>
</tr>
<tr>
<td>IV</td>
<td>0</td>
<td>1 (7%)</td>
<td>3 (10%)</td>
<td>4 (6%)</td>
</tr>
</tbody>
</table>

Figure 6. Interobserver (top) and intraobserver (bottom) agreement for measurement of left ventricular outflow tract (LVOT) area. \(n = \) number of patients.
ate between those of patients with obstruction at rest and patients with nonobstructive HCM. The reasons for these differences in left ventricular outflow tract size may be better understood by considering the variability in outflow tract morphology in the three subgroups of patients with HCM (fig. 8).

In patients with subaortic obstruction at rest, the maximal thickening of the ventricular septum was usually located at the level of the mitral valve and outflow tract. These patients also often showed marked anterior displacement of the mitral valve in the left ventricular cavity, and often substantial hypertrophy of the anterolateral free wall. In fact, 70% of the patients with obstruction at rest showed marked ventricular septal thickening greater than 18 mm, cephalad septal hypertrophy greater than or equal to caudal septal hypertrophy and reduced septal-mitral valve distance (< 26 mm). The abnormalities of these structures that constitute the borders of the left ventricular outflow tract seemed to contribute to a reduction in outflow tract area. In patients with provokable subaortic obstruction, the morphologic features of the left ventricular outflow tract most closely resembled those of patients with obstruction at rest.

In contrast, in patients without subaortic obstruction, these structures were less altered and the outflow tract was larger. Maximal ventricular septal hypertrophy was frequently located distal to the mitral valve and the outflow tract. Furthermore, the mitral valve was more posterior in the left ventricular cavity and the anterolateral free wall was often uninvolved in the hypertrophic process. Seventy percent of the patients with nonobstructive HCM showed relatively mild ventricular septal thickening (≤ 18 mm), caudal septal hypertrophy greater or equal to cephalad septal hypertrophy and a septal-mitral valve distance of 26 mm or greater.

Numerous authors have suggested that in most patients with HCM, subaortic obstruction is produced by anterior motion of the mitral valve leaflets (and possibly the attached chordae tendineae) into the left ventricular outflow tract during systole. Of the mechanisms proposed to explain how systolic anterior motion of the mitral valve occurs, perhaps the most plausible is that the mitral leaflets are pulled forward by the high-velocity blood flow generated during ejection in a small left ventricular cavity (i.e., the Venturi effect). In our study, we found an important association between systolic anterior motion of the mitral valve and the two-dimensional echocardiographic cross-sectional area of the left ventricular outflow tract. Marked systolic anterior motion of the mitral valve was present in 85% of the patients with subaortic obstruction and a small outflow tract area (< 4 cm²). In contrast, about 90% of the patients without obstruction and with a large outflow tract area (≥ 4 cm²) showed no mitral systolic anterior motion. Hence, our findings support the hypothesis that the size of the left ventricular cavity in the region of the mitral leaflets is a major determinant of systolic anterior motion of the

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**TABLE 3. Distribution of Ventricular Septal Hypertrophy (Cephalad-Caudal Plane) in 65 Patients with Hypertrophic Cardiomyopathy**

<table>
<thead>
<tr>
<th>Distribution of septal hypertrophy</th>
<th>Obstructive (n = 21)</th>
<th>Provocable (n = 14)</th>
<th>Nonobstructive (n = 30)</th>
<th>Total (n = 65)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cephalad = caudal</td>
<td>15 (71%)</td>
<td>8 (57%)</td>
<td>14 (47%)</td>
<td>37 (57%)</td>
</tr>
<tr>
<td>Cephalad &gt; caudal</td>
<td>4 (19%)</td>
<td>5 (36%)</td>
<td>0</td>
<td>9 (14%)</td>
</tr>
<tr>
<td>Cephalad &lt; caudal</td>
<td>2 (10%)</td>
<td>1 (7%)</td>
<td>16 (53%)*</td>
<td>19 (29%)</td>
</tr>
</tbody>
</table>

*p < 0.01 vs combined values for patients with obstruction at rest and patients with provokable obstruction.
Figure 8. Morphology of the left ventricle, as assessed by two-dimensional echocardiography, that is characteristic of patients in each of the three hemodynamic subgroups of hypertrophic cardiomyopathy (HCM) and in subjects with normal hearts. The left ventricle is viewed in short-axis plane at the mitral valve (MV) level (left) and in long-axis (right). (left) The left ventricular outflow tract (LVOT) area in the normal subject is larger than that in each of the patients with HCM. The outflow area decreases progressively in the three subgroups of patients (from nonobstructive to provokable to obstructive), in relation to the increasing amount of hypertrophy at the level of the mitral valve and to the more anterior position of the valve in the left ventricular cavity. (right) The distribution of septal hypertrophy in the cephalad-caudad axis also influences the size of the outflow tract. In patients with obstruction at rest or with provocation, hypertrophy is particularly prominent in the cephalad portion of the septum; patients without obstruction commonly show more substantial septal hypertrophy caudal to the mitral valve. AML = anterior mitral leaflet; FW = free wall; Ao = aorta; VS = ventricular septum.

mitral valve in patients with HCM. These data are also consistent with the concept that subaortic obstruction is localized at the level of the mitral valve in most patients with obstructive HCM.

Technical considerations can limit the application of two-dimensional echocardiography to the quantitative assessment of left ventricular structure. However, quantitative two-dimensional echocardiographic measurements of left ventricular outflow tract area performed in the present study proved to be reliable with relatively small interobserver and intraobserver variability. We believe that the left ventricular outflow tract is particularly favorable to quantitative examination by two-dimensional echocardiography. This region of the left ventricle (when imaged in the short-axis plane) appears in the center of the sector where errors related to lateral beam resolution are minimized. Furthermore, in our experience, the margins of the left ventricular outflow tract (i.e., the mitral valve and the endocardium of septum and anterolateral free wall) are generally well imaged in patients with HCM.

Echocardiography has proved reliable for the identification of increased left ventricular mass and the asymmetric pattern of hypertrophy that are characteristic morphologic features of HCM. However, in some patients it is difficult to make a definitive diagnosis of HCM because the ventricular wall thickness cannot be precisely determined or the ratio of septal to posterior wall thickness is borderline and inconclusive. Therefore, recognition of other structural features of HCM identifiable by echocardiography would be diagnostically useful. The left ventricular outflow tract area appeared to distinguish patients with HCM from normal subjects without heart disease. None of our normal controls had a left ventricular outflow tract area smaller than 9 cm², while only 3% of the patients with HCM showed an outflow tract area greater than 9 cm². However, our control population was small, and although the statistical significance of the group data was high, some intergroup overlap was present. Hence, this observation cannot be considered definitive and requires validation in a larger, prospectively selected group of patients.

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