Left Ventricular Outflow Tract Obstruction Due to Systolic Anterior Motion of the Anterior Mitral Leaflet in Patients with Concentric Left Ventricular Hypertrophy

BARRY J. MARON, M.D., JOHN S. GOTTDIENER, M.D., WILLIAM C. ROBERTS, M.D., WALTER L. HENRY, M.D., DANIEL D. SAVAGE, M.D., AND STEPHEN E. EPSTEIN, M.D.

SUMMARY Patients with hypertrophic cardiomyopathy (i.e., asymmetric septal hypertrophy) may show obstruction to left ventricular outflow under basal conditions or with provocative maneuvers. The presence of dynamic left ventricular outflow tract obstruction in patients with concentric ventricular wall thickening (but without abnormalities of the aortic valve) has been less well appreciated. Clinical and morphologic features of five patients with nondilated left ventricles and with left ventricular outflow obstruction are presented. In each patient peak systolic pressure gradients between left ventricle and systemic artery were measured at cardiac catheterization and ranged from 60–140 mm Hg under basal conditions or with provocation. Each patient had echocardiographically documented systolic anterior motion of the anterior mitral leaflet, which was apparently responsible for the outflow obstruction, and concentric left ventricular wall thickening (septal-free wall thickness ratio of <1.3). Two of the five patients had evidence of genetically transmitted hypertrophic cardiomyopathy, as evidenced by disorganized muscle cells in the ventricular septum or asymmetric septal hypertrophy in first degree relatives. Hence, left ventricular outflow tract obstruction associated with systolic anterior motion of the anterior mitral leaflet may occur in some patients with concentric left ventricular hypertrophy who do not have typical hypertrophic cardiomyopathy.

Echocardiograms were performed in each patient and in 19 first degree relatives of two patients (R.B. and L.B.). Echocardiograms were obtained with a 2.25 MHz, 1.2 cm diameter Aerotech transducer connected to either a modified Ekoline-20A or a Hoffrel 201 ultrasound unit employing methods previously described. The ultrasound signal was connected via a custom built video amplifier to a Honeywell 1856-Viscororder and recorded continuously on light sensitive paper. Thickness of the ventricular septum was measured below the distal margins of the mitral valve leaflets just prior to atrial systole; postero basal left ventricular wall thickness was measured at the level of the distal margins of the mitral valve leaflets during the same phase of the cardiac cycle.

Results

Clinical and Hemodynamic Data

The clinical and hemodynamic findings in the five patients are summarized in table 1. At cardiac catheterization patients B.Z., R.B., and H.W. had no obstruction to left ventricular outflow under basal conditions, but showed marked outflow gradients with provocation (i.e., Valsalva maneuver, isoproterenol or amyl nitrate administration, fig. 1). With provocation, B.Z. developed a maximum outflow gradient of 120 mm Hg, R.B. a gradient of 100 mm Hg, and H.W. a gradient of 60 mm Hg. These same maneuvers were repeated on a different day (but without cardiac catheterization) and each patient also showed SAM by echocardiography (figs. 2 and 3). Patient B.Z. also demonstrated narrowing of the pulse pressure of the beat following a premature ventricular contraction and obliteration of the left ventricular apex in end systole as shown by left ventricular cineangiogram, findings usually considered to be typical of hypertrophic cardiomyopathy. In patients R.B. and H.W. the pulse pressure response in the postectopic beat was normal; cavity obliteration in end systole was not present on left ventricular cineangiogram in either patient. The peripheral arterial pulse pressure in H.W., however,
TABLE 1. Clinical and Hemodynamic Data

<table>
<thead>
<tr>
<th>Pt</th>
<th>Age/Sex</th>
<th>FC</th>
<th>Systolic murmur (basal conditions)</th>
<th>Symptoms</th>
<th>Brachial BP (mm Hg)</th>
<th>Associated cardiac abnormalities</th>
<th>ECG</th>
<th>Basal</th>
<th>Valsalva</th>
<th>Isoproterenol</th>
</tr>
</thead>
<tbody>
<tr>
<td>B.Z.</td>
<td>64F</td>
<td>IV</td>
<td>Grade 1/6</td>
<td>L-dyspnea; fatigue; atypical chest pain</td>
<td>135/80</td>
<td>Paroxysmal AF</td>
<td>LVH with strain; diffuse ST-T changes</td>
<td>0</td>
<td>10</td>
<td>30</td>
</tr>
<tr>
<td>R.B.</td>
<td>47M</td>
<td>II</td>
<td>Grade 1/6</td>
<td>Atypical chest pain evolving into presyncope and syncope</td>
<td>130/80</td>
<td>None</td>
<td>Normal</td>
<td>0</td>
<td>55</td>
<td>100†</td>
</tr>
<tr>
<td>L.B.</td>
<td>57M</td>
<td>III</td>
<td>Grade 4/6</td>
<td>Presyncope; atypical chest pain</td>
<td>150/70‡</td>
<td>None</td>
<td>LVH with strain</td>
<td>140</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>M.N.</td>
<td>56F</td>
<td>III</td>
<td>Grade 4/6</td>
<td>Syncope; presyncope; dyspnea; fatigue; angina; palpitations</td>
<td>140/100α</td>
<td>None</td>
<td>LVH with strain</td>
<td>0-40</td>
<td>75</td>
<td>80</td>
</tr>
<tr>
<td>H.W.</td>
<td>33M</td>
<td>IV</td>
<td>Grade 4/6</td>
<td>Syncope; angina; dyspnea; fatigue</td>
<td>105/70</td>
<td>Paroxysmal AF</td>
<td>LVH with strain</td>
<td>0</td>
<td>15</td>
<td>60</td>
</tr>
</tbody>
</table>

*Heart rate increased to 135/min over control heart rate of 55/min.
**Heart rate increased to 100/min over control heart rate of 85/min.
†Comparison of the arterial pulse pressure of the beat following a premature ventricular contraction to that of a control beat.§Six-year history of severe systemic hypertension, treated with guanethidine.
¶This catheterization was performed while the patient had residual β-blockade effect from taking propranolol; a catheterization performed four months earlier while the patient was not taking propranolol showed a 65 mm Hg left ventricular outflow gradient under basal conditions and a 140 mm Hg gradient with Valsalva maneuver.

FIGURE 1. Simultaneous left ventricular (LV) and left brachial artery (LBA) pressure recordings in patient R.B. under basal conditions and during isoproterenol administration.

showed the spike and dome contour typical of patients with obstructive hypertrophic cardiomyopathy.

The other two patients (L.B. and M.N.) showed left ventricular outflow obstruction under basal conditions at cardiac catheterization. L.B. had a 140 mm Hg gradient and M.N. had a gradient of up to 40 mm Hg (although at times no gradient was measured). In patient M.N. the gradient increased to 80 mm Hg with provocation. L.B. and M.N. both showed marked SAM on echocardiographic study under basal conditions. Both patients also demonstrated other...
Table 1. Continued

<table>
<thead>
<tr>
<th>Peak systolic LVOT gradient (mm Hg)</th>
<th>PVC response</th>
<th>LVEDP (mm Hg)</th>
<th>RV S/D (L/min/m²)</th>
<th>CI (¥/min/m²)</th>
<th>LV angio</th>
<th>Operation</th>
<th>Phonocardiogram</th>
<th>T-time (Normal = 0.02-0.05 sec)</th>
<th>LVET (Normal = 0.26-0.35 sec)</th>
<th>S₁ S₂ S₃</th>
</tr>
</thead>
<tbody>
<tr>
<td>120*</td>
<td>+</td>
<td>12</td>
<td>24/-</td>
<td>2.5</td>
<td>Obiteration LV spex in end-systole (EF = 0.88)</td>
<td>LVM-M</td>
<td>0.03</td>
<td>0.32</td>
<td>present</td>
<td>absent</td>
</tr>
<tr>
<td>-</td>
<td>0</td>
<td>6</td>
<td>20/2</td>
<td>2.7</td>
<td>Elongated, “banana” configuration; septal configuration by biventricular angiocardiogram typical of concentric hypertrophy (EF = 0.80)</td>
<td>none</td>
<td>0.02</td>
<td>0.28</td>
<td>absent</td>
<td>present</td>
</tr>
<tr>
<td>-</td>
<td>+</td>
<td>23</td>
<td>25/5</td>
<td>-</td>
<td>Vigorously contracting LV</td>
<td>LVM-M</td>
<td>0.04</td>
<td>0.41</td>
<td>absent</td>
<td>present</td>
</tr>
<tr>
<td>-</td>
<td>+</td>
<td>12</td>
<td>40/3</td>
<td>2.9</td>
<td>Vigorously contracting LV (EF = 0.90)</td>
<td>LVM-M</td>
<td>0.03</td>
<td>0.36</td>
<td>absent</td>
<td>present</td>
</tr>
<tr>
<td>-</td>
<td>0</td>
<td>18</td>
<td>32/5</td>
<td>1.9</td>
<td>Vigorously contracting LV (EF = 0.75)</td>
<td>LVM-M</td>
<td>0.03</td>
<td>0.30</td>
<td>absent</td>
<td>present</td>
</tr>
</tbody>
</table>

![Table 1 Image](image_url)

- History of intermittent hypertension since childhood; controlled with diuretic therapy over the past nine years.
- Arterial pulse pressure of the postectopic beat did not exceed the pulse pressure of a control beat, typical of patients with hypertrophic cardiomyopathy.
- Cardiac index; ECG = electrocardiogram; EF = ejection fraction; FC = functional class (New York Heart Association); LV = left ventricle; LVEDP = left ventricular end-diastolic pressure; LVET = left ventricular ejection time corrected for heart rate; LVM = left ventricular hypertrophy; LVOT = left ventricular outflow tract; MC = mitral commissurotomy; MVA = mitral valve area; RV = right ventricle; S/D = systolic/diastolic pressure; Pt = patient.

Clinical features that occur in patients with hypertrophic cardiomyopathy. First, narrowing of the pulse pressure of the postectopic beat was present. Second, the peripheral arterial pulse pressure showed a spike and dome contour (fig. 4); apical cardiogram showed a typical triple apical impulse only in L.B.

In each of the five patients the alterations that occurred in the intensity of the heart murmur with various maneuvers

![Echocardiogram Image](image_url)

**Figure 3.** Echocardiogram recorded in patient B.Z. under basal conditions and with the administration of isoproterenol. Arrows signify the anterior mitral leaflet. Note that systolic anterior motion of the anterior mitral leaflet is present only with isoproterenol. VS = ventricular septum; MV = mitral valve.

**Figure 2.** Echocardiogram recorded in patient R.B. under basal conditions and with administration of amyl nitrite. Note that systolic anterior motion of the anterior mitral leaflet (SAM) is present only with amyl nitrite. IVS = ventricular septum; MV = mitral valve.
were similar to those typically found in patients with obstructive hypertrophic cardiomyopathy. The murmur increased with Valsalva maneuver or administration of amyl nitrite (fig. 5) and usually diminished with squatting or handgrip.

Two patients had systemic hypertension. Patient L.B. had a six-year history of hypertension requiring treatment with guanethidine; patient M.N. had a history of intermittent hypertension since childhood.

Four patients (B.Z., M.N., L.B., and H.W.) underwent left ventricular myotomy-myectomy. Patients B.Z. and M.N. both died within four days following operation, principally due to ventricular septal infarction and rupture. Patient H.W. appeared to derive no benefit from left ventricular myotomy-myectomy and remained severely symptomatic two months following operation. Patient L.B. experienced an uneventful postoperative course; SAM was absent on the first postoperative day and for the remainder of the postoperative period. This patient has only recently undergone operation and, therefore, routine postoperative cardiac catheterization has not been performed.

Echocardiographic and Necropsy Findings

The echocardiographic and necropsy findings in the five patients are summarized in table 2. Ventricular septal and posterobasal left ventricular wall thicknesses documented by echocardiography were mildly to moderately increased (14 to 20 mm). Each patient had normal or small end-diastolic left ventricular dimensions by echocardiography.

The left ventricle was concentrically thickened (septal-free wall thickness ratio of < 1.3) in each of the five patients. Concentric thickening was documented in B.Z. and M.N. by echocardiography and at necropsy, and in R.B. (fig. 6), L.B. and H.W. by echocardiography alone. In addition, ventricular septal configuration defined by biventricular cineangiography in R.B. was typical of patients with concentric ventricular wall thickening (i.e., the right and left ventricular surfaces of the septum were parallel) (fig. 7).

There was also no evidence of genetic transmission of hypertrophic cardiomyopathy in three of the five patients (B.Z., L.B., or R.B.). In B.Z. and L.B. disorganized cardiac muscle cells which are, in our experience, characteristic of patients with genetically transmitted hypertrophic cardiomyopathy, were absent from ventricular septal tissue obtained at operation or at necropsy. Furthermore, patient B.Z. did not have either an endocardial contact plaque on the ventricular septum or a thickened anterior mitral leaflet, a combination of abnormalities often found at necropsy in patients with genetically transmitted hypertrophic cardiomyopathy. Echocardiograms in nine first degree relatives of both patients L.B. and R.B. showed normal septal-free wall ratios. One other relative of L.B. (a 60-year-old brother with...
This study demonstrates that left ventricular outflow tract obstruction due to SAM may occur in patients with concentric LV hypertrophy. In this regard, the spectrum of hypertrophic cardiomyopathy includes not only aortic valve abnormalities, but also mitral valve abnormalities. The question naturally arises as to whether the cardiac disease spectrum of hypertrophic cardiomyopathy, as characterized by these patients, with genetic transmission in the family, is not diagnostic of mitral valve prolapse. A recent study of 100 consecutive patients with hypertrophic cardiomyopathy demonstrated no significant differences in the prevalence of mitral valve prolapse compared to the general population.

**Discussion**

The fact that mitral valve prolapse is present in a significant proportion of patients with hypertrophic cardiomyopathy suggests that it may be a common finding in this condition. It is important to consider the presence of mitral valve prolapse in patients with hypertrophic cardiomyopathy, as it may affect the management of the disease.

**Table 2. Echocardiographic and Necropsy Data**

<table>
<thead>
<tr>
<th>Patient</th>
<th>LVID (normal = 40-52 mm)</th>
<th>LA (normal = 19-40 mm)</th>
<th>% Systolic thickening of myocardium</th>
<th>Heart wt. (g)</th>
<th>VS/PW</th>
<th>PW (mm)</th>
<th>VS/PW</th>
<th>Circumstances of death</th>
</tr>
</thead>
<tbody>
<tr>
<td>B.Z.</td>
<td>48</td>
<td>48</td>
<td>1.0</td>
<td>5</td>
<td>22</td>
<td>22</td>
<td>1.0</td>
<td>Postop 4 days (traumatic VSD from LVM-M)</td>
</tr>
<tr>
<td>R.B.</td>
<td>38</td>
<td>43</td>
<td>0.8</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L.B.</td>
<td>44</td>
<td>54</td>
<td>0.7</td>
<td>15</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M.N.</td>
<td>33*</td>
<td>38</td>
<td>0.9</td>
<td>315</td>
<td>15</td>
<td>15</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>H.W.</td>
<td>44</td>
<td>64</td>
<td>1.0</td>
<td>17</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*At necropsy this patient had a small right ventricular cavity (about 50% of normal) and a markedly dilated right atrium (about three times normal); tricuspid valve was normal.

**Notes:**
- LVID = left ventricular internal dimension; LA = left atrial dimension; % Systolic thickening of myocardium = thickness of myocardium at systole/thickness of myocardium at diastole; Heart wt. = heart weight; VS/PW = ventricular septal wall thickness.
- Postop = postoperative.
- VSD = ventricular septal defect.
- LVM-M = left ventricular myectomy.
patients with concentric hypertrophy do not appear to be part of the disease spectrum of familial hypertrophic cardiomyopathy, even though they demonstrate subaortic obstruction due to SAM.

In contrast, patients M.N. and H.W., who also had concentric hypertrophy, both had unequivocal family histories of hypertrophic cardiomyopathy (with ASH documented in family members). Patient M.N. also had severe disorganization of cardiac muscle cells in her ventricular septum. These findings indicate that members of families with hypertrophic cardiomyopathy occasionally may demonstrate left ventricular outflow obstruction associated with concentric hypertrophy.

Rossen et al.\textsuperscript{18} described a patient with concentric ventricular wall thickening and systolic anterior motion of the anterior mitral leaflet in whom there was no outflow gradient under basal conditions at cardiac catheterization. This patient, like our patients M.N. and H.W., had a family history of hypertrophic cardiomyopathy. Other investigators also have described patients with SAM who at cardiac catheterization demonstrated left ventricular outflow obstruction in the absence of cardiac hypertrophy.\textsuperscript{19} The contribution of systemic hypertension in two of our five patients to the present findings is unclear. It is possible that some patients with hypertension develop secondary left ventricular hypertrophy that, in association with other as yet undefined factors, leads to SAM. Systolic anterior motion, however, was observed in only two of almost 300 patients with stable systemic hypertension evaluated recently in an echocardiographic study (unpublished observations). Also deserving of consideration is the possibility that some of our patients actually demonstrated ASH (with SAM) at an earlier point in the natural history of their disease. However, as a result of their chronic left ventricular hypertension, posterior wall thickening may have occurred subsequently and resulted in "concentric hypertrophy."
Left ventricular myotomy-myectomy produced septal rupture and eventual death in patients B.Z. and M.N., in whom the septum was 18 mm and 16 mm in thickness, respectively. These results are based on too few experiences to warrant definitive conclusions. They do suggest, however, that the operation conventionally performed in patients with hypertrophic cardiomyopathy to eliminate left ventricular outflow tract obstruction may be associated with high risk in patients with only mild thickening of the ventricular septum.

Lastly, the possibility must be raised that the pressure gradients measured at cardiac catheterization in our patients were due to catheter entrapment in a hypertrophied heart, rather than to true outflow obstruction. However, during hemodynamic measurements in our patients, blood could be withdrawn and contrast ejected through the catheter (of which the tip was free in the left ventricular cavity) during the entire cardiac cycle. Also, the left ventricular pressure contour was not damped or distorted, suggesting that the catheter was not recording intramural pressures. Furthermore, only one of our patients demonstrated under basal conditions typical obliteration of the left ventricular apex during end systole, angiographically. It is possible that cavity obliteration could have occurred during provocative interventions and could have been responsible for recorded outflow gradients in four of our five patients who showed pressure gradients with provocation (B.Z., R.B., M.N., and H.W.). However, several findings support strongly the presence of true obstruction to left ventricular outflow. First, in each of these patients marked SAM was demonstrated by echocardiography (under basal conditions in M.N. and H.W. and with provocation in B.Z. and R.B.). In our experience, such a finding is highly correlated with obstruction. Second, in three patients (M.N., L.B., and H.W.) a spike and dome configuration was observed in the external carotid pulse tracing, a phenomenon present almost always with obstruction to left ventricular outflow.

In summary, it appears that SAM can occur in patients who have concentric hypertrophy not related to familial hypertrophic cardiomyopathy, and that patients with familial hypertrophic cardiomyopathy can occasionally have, on echocardiographic study, concentric hypertrophy. It should be emphasized that these findings are probably relatively uncommon and therefore modify, but do not negate, the commonly held concepts that: 1) patients with SAM usually have hypertrophic cardiomyopathy and 2) it is the rare patient with hypertrophic cardiomyopathy who does not have ASH on echocardiographic study.

References


Left ventricular outflow tract obstruction due to systolic anterior motion of the anterior mitral leaflet in patients with concentric left ventricular hypertrophy.
B J Maron, J S Gottdiener, W C Roberts, W L Henry, D D Savage and S E Epstein

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