Regional Myocardial Function in Idiopathic Hypertrophic Subaortic Stenosis

An Echocardiographic Study

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SUMMARY
To assess regional contractility in idiopathic hypertrophic subaortic stenosis (IHSS), a primary myopathic disorder with documented hyperdynamic ventricular contractions, systolic wall thickening and velocity of contraction of the septum and left ventricular posterior wall were measured in echocardiograms from 16 patients with IHSS and 16 normal subjects. The average thickening of the normal septum and posterior wall was 75.9 ± 8.8% and 84.8 ± 6.3%, respectively. The posterior wall in IHSS thickened by 75.1 ± 6.8%. None of these values differed significantly. However, the increase in thickness of the IHSS septum averaged 22.5 ± 2.4%, significantly less than that of either the IHSS posterior wall or the normal septum. Velocity measurements confirmed the impression of diminished septal function. The mean velocity of normal septal contraction averaged 37.0 ± 2.3 mm/sec, normal posterior wall 42.3 ± 2.0 mm/sec and IHSS posterior wall 55.7 ± 3.5 mm/sec, whereas the septum in IHSS contracted at the rate of 26.0 ± 2.5 mm/sec. Thus, the IHSS septum contracted significantly more slowly than the normal septum or IHSS posterior wall. However, the posterior wall velocity in IHSS was significantly more rapid than that measured in normal ventricles — perhaps to compensate for the septum. Normalization of all velocities for left ventricular end-diastolic internal diameter did not alter the significance of the results. Consideration of IHSS as an asymmetric myopathy based on prior observations of predominantly septal hypertrophy and distorted septal cellular architecture is now supported by the above evidence of functional left ventricular asymmetry. Although the total left ventricular function in IHSS may be hyperdynamic, regional function is not uniform. The septum appears to be hypodynamic, while the contractile capacity of the posterior wall is increased.

EXPERIMENTAL AND CLINICAL cardiomyopathies are characteristically associated with progressive cardiac failure and death. Cardiac function is often impaired long before clinical symptoms occur. In congestive cardiomyopathy hemodynamic and angiographic evaluations reveal elevated end-diastolic pressures, abnormal ventricular function curves, and diffuse hypokinetic contraction patterns. However, idiopathic hypertrophic subaortic stenosis (IHSS), a primary cardiac myopathic disorder, is paradoxically associated with normal myocardial contractility. The left ventricle in this entity is hyperdynamic and angiographic ejection fractions are frequently in excess of 0.70. Histologic studies of the myocardial cells in IHSS have shown them to be multinucleated, bizarre, and misaligned, thus confirming that this is a myopathic disease. These abnormalities are restricted most often to the interventricular septum. Furthermore, disproportionate thickening of the septum compared to the free walls of the left ventricle has been documented by angiography, echocardiography, and direct measurements at the time of cardiac surgery or necropsy. This evidence of histologic and anatomic asymmetry suggests that there also might be a functional ventricular asymmetry.

To investigate whether the interventricular septum and free posterior left ventricular wall are functionally equivalent and whether any observed asymmetry might account for the excellent mechanical function of this myopathic ventricle, echocardiographic examination of patients with IHSS was performed. This study supports the concept that the septum has diminished contractile capacity.

Methods
Sixteen patients with IHSS documented by cardiac catheterization were selected for further evaluation. Each patient had diagnostic echocardiographic systolic anterior movement of the anterior mitral leaflet. None had other conditions which might alter echocardiographic systolic anterior movement of the anterior mitral leaflet. Eight of the patients were male and eight were female, ranging in age from 15 to 69 years (average 38.6 years). Seven had no resting gradients, but developed left ventricular outflow tract obstruction during isoproterenol infusion. Two patients had gradients exceeding 100 mm Hg in the basal...
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state. At the time of the echocardiographic study, eight patients were being treated with propranolol, but three were taking less than 80 mg/day. Serial echocardiograms were recorded in two patients as the daily dose of propranolol was progressively increased — in one from 0 to 240 and in the other from 160 to 400 mg. In neither patient did the measured echocardiographic parameters change. Furthermore, there was no significant difference between the measurements in the treated and untreated groups, and therefore results from all patients have been combined.

The sixteen subjects who served as controls were referred for evaluation of functional murmurs or atypical chest pain. There were five males and eleven females with ages ranging from 4 to 72 years (average 26.8 years). Clinical phonocardiographic and echocardiographic examinations revealed no evidence of cardiac disease. Additionally, cardiac catheterization data in three were normal.

All echocardiographic studies were done in the supine or left lateral recumbent position with the transducer in the third or fourth left intercostal space. A commercially available echocardiograph (Hoffrel Ultrasonoscope, model 101) with either a 2.25 MHz transducer focused at 7.5 cm or a 2 MHz unfocused transducer was used. The resulting image was displayed and recorded with a simultaneous electrocardiogram (ECG) on a Cambridge multichannel processing recorder.

Ventricular dimensions and wall motion were evaluated at the level of the chordae tendineae. The mitral leaflets were identified and the transducer was then rotated toward the apex of the left ventricle until the appropriate location was found. The near and far gains were then adjusted so that both sides of the septum as well as the full thickness of the posterior wall were seen. Tracings were not analyzed if there was any doubt concerning the location of the right septal border. Echocardiograms in which the ultrasound beam was considered to be tangential to the ventricular surfaces were excluded. Thus, in accordance with previously published criteria, echocardiograms were discarded unless the degree of systolic thickening of the posterior wall exceeded 50% of the proportional change in left ventricular internal diameter during systole. More complex transducer positioning maneuvers in some patients, as suggested by Henry et al., did not appear to substantially alter the results.

Echocardiograms were analyzed independently by the same two observers. In all cases measurements agreed to within 5%.

Septal and posterior left ventricular wall thicknesses (T) at the peak of the R wave of the ECG were considered to represent end-diastolic (dias) measurements (fig. 1). Maximal thickness of the septum and posterior wall during systole (sys) was also determined. Maximal wall thicknesses were not always seen at identical points in the cardiac cycle. The percent thickening (ΔT) of each wall was then calculated as

\[ \frac{T_{sys} - T_{dias}}{T_{dias}} \times 100.\]

The mean velocity of motion of the posterior wall was measured by noting the timed displacement of a line drawn through the most posterior point of the left ventricular endocardiial tracing immediately preceding ventricular contraction and the most anterior point in systole (fig. 2). Similar points at the beginning and peak of the septal systolic excursion were selected to measure mean septal velocity. If the septal excursion reached a plateau during systole, the earliest point of maximal posterior displacement was used to calculate the wall velocity, thus maximizing this measurement. The velocity of wall motion was also corrected for differing ventricular volumes by dividing wall velocity by the measured end-diastolic diameter. The mean velocity of circumferential fiber shortening was calculated as previously described.

All results are expressed as means ± se. Student’s t-test for independent observations was used to determine the significance of differences.

Results

Wall Thickening

Septal thickness at end-diastole ranged from 12 to

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**Figure 1**

Systolic thickening of septum and posterior wall in a normal subject (left) and a patient with idiopathic hypertrophic subaortic stenosis (IHSS) (right). Whereas thickening of the walls is equal in the former, the septum in the IHSS patient thickens one-fourth as much as the posterior wall.
29 mm in patients with IHSS. This contrasts with the posterior wall thickness of 6-17 mm. Fourteen patients had a septum to posterior wall thickness ratio of 1.3 or greater. However, two patients had ratios in the normal range. In one 15-year-old girl the ratio was 1.1, while the ratio was 1.0 in a 69-year-old woman.

In normal subjects the septum measured from 5 to 11 mm at end-diastole, while the posterior wall thickness ranged from 5 to 10 mm. The thickness ratio never exceeded 1.1.

The degree of systolic wall thickening was assessed in all patients (table 1, fig. 3). The increase in posterior wall thickness averaged 75% in IHSS ventricles and 85% in normal hearts. This difference is not significant. The normal septums also thickened by 76%. Thus, in the normal ventricle the septum and posterior wall thickened equally during systole. The IHSS septum, however, was distinctly abnormal. The degree of systolic thickening averaged 22%, significantly less than that for posterior walls in the same ventricles (P < 0.001) or septums in normal hearts (P < 0.001). The range was quite narrow for
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Table 1

Comparison of Normal and IHSS Left Ventricles

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>IHSS</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVID, diastole (cm)</td>
<td>4.5 ± 0.2*</td>
<td>4.0 ± 0.1†</td>
</tr>
<tr>
<td>LVID, systole (cm)</td>
<td>2.7 ± 0.1</td>
<td>2.0 ± 0.1†</td>
</tr>
<tr>
<td>Tsep diastole (mm)</td>
<td>8.1 ± 0.4</td>
<td>18.7 ± 1.3†</td>
</tr>
<tr>
<td>Tsep systole (mm)</td>
<td>13.9 ± 0.6</td>
<td>22.9 ± 1.4†</td>
</tr>
<tr>
<td>∆Tsep (%)</td>
<td>75.9 ± 8.8</td>
<td>22.3 ± 2.4†</td>
</tr>
<tr>
<td>Tpw diastole (mm)</td>
<td>7.8 ± 0.4</td>
<td>11.8 ± 0.6</td>
</tr>
<tr>
<td>Tpw systole (mm)</td>
<td>14.1 ± 0.6</td>
<td>20.0 ± 1.2†</td>
</tr>
<tr>
<td>∆Tpw (%)</td>
<td>84.8 ± 6.3**</td>
<td>75.1 ± 6.8††</td>
</tr>
<tr>
<td>∆Tsep/∆Tpw</td>
<td>0.92 ± 0.10</td>
<td>0.33 ± 0.04§</td>
</tr>
<tr>
<td>Tsep dias/Tpw dias</td>
<td>1.0 ± 0.0</td>
<td>1.7 ± 0.1†</td>
</tr>
<tr>
<td>Velocitysep (mm/sec)</td>
<td>37.0 ± 2.3</td>
<td>260 ± 2.5§</td>
</tr>
<tr>
<td>Velocitypw (mm/sec)</td>
<td>42.3 ± 2.0††</td>
<td>357 ± 3.5‡‡</td>
</tr>
<tr>
<td>Velocitysep/velocitypw</td>
<td>0.84 ± 0.06</td>
<td>0.66 ± 0.06†</td>
</tr>
<tr>
<td>Norm Vsep (sec⁻¹)</td>
<td>0.97 ± 0.06††</td>
<td>1.41 ± 0.08‡‡</td>
</tr>
<tr>
<td>Vcf (circ/sec)</td>
<td>1.24 ± 0.07</td>
<td>1.62 ± 0.09§</td>
</tr>
</tbody>
</table>

*Mean ± SEM.
Statistical significance of difference between normal and IHSS: *P < 0.05; †P < 0.005; ‡P < 0.001.

The data on wall velocities are graphically depicted in figure 5 and the averages tabulated in table 1. The velocity measurements again confirm the similarities between the normal posterior wall and septum. The posterior wall velocity averaged 42 mm/sec, whereas the septum moved at a rate of 37 mm/sec. The septal and posterior wall velocities in the IHSS hearts, however, were significantly different (P < 0.001), averaging 26 and 56 mm/sec, respectively. The IHSS septal velocity was significantly less than that of the normal septum (P < 0.005) while the posterior wall moved more rapidly in the IHSS than the normal ventricle (P < 0.005). The significance of these results is unchanged when the wall velocities are normalized for ventricular size. Despite these significant differences, considerable overlap between the normal and IHSS patients exists.

The observed variations between the IHSS and normal patients are perhaps made more evident when the ratio of septal velocity to posterior wall velocity of each ventricle is computed (fig. 6). This ratio is 0.47 in IHSS and 0.90 in normal subjects, a difference which is significant (P < 0.001). No normal subject had a ratio less than 0.63, and only one of 16 IHSS subjects had a ratio greater than 0.62. This more obvious separation is caused jointly by the decreased septal and increased posterior wall velocities in IHSS.

The mean Vcf of the patients with IHSS averaged 1.62 circ/sec. This velocity was significantly higher than that of 1.24 circ/sec in the normal subjects (P < 0.005).

Discussion

Early descriptions of IHSS presented pathologic evidence of asymmetric septal hypertrophy. Histologic examination of the interventricular septum in IHSS has revealed unusual cellular morphology, supporting consideration of this entity as a primary muscle disorder. More recent echocardiographic
analysis has confirmed the concept of asymmetric hypertrophy,7 and has suggested that the increased septal thickness is an important diagnostic feature7 as well as a genetic marker.14 Because of this anatomic abnormality, however, the hyperdynamic ventricular function observed in IHSS is unexplained. The present study demonstrates that regional ventricular function is preserved only in those areas not likely to be involved by the myopathic process, and that the functional correlate of the disordered cellular architecture in the interventricular septum is indeed decreased contractility.

The interventricular septum in IHSS does not thicken normally during systolic contraction. Whereas normal septums thickened by 76%, the thickening was only 22% in IHSS. These results confirm similar conclusions by Tajik and Giuliani15 and Rossen et al.,16 and suggest the individual contributions of septal and posterior wall contraction to over-all ventricular function in IHSS are not comparable. However, the greatly increased end-diastolic thickness of the IHSS septum is mathematically weighted against normal systolic thickening. Although our experience confirms the data of Rossen and co-workers16 documenting normal septal thickening in ventricles with concentric left ventricular hypertrophy, additional evidence was sought to support the impression of depressed septal function in IHSS.

The velocity of septal contraction in IHSS was also depressed. Whereas the septum and posterior wall approached each other at almost equal rates in the normal ventricle, the septal velocity in IHSS was less than one-half that of the posterior wall. Thus, septal function is abnormal in IHSS. The presented data also im-

**Figure 4**
Ratio of septal to posterior wall systolic thickening in 16 normal subjects (right) and 16 patients with idiopathic hypertrophic subaortic stenosis (IHSS) (left). The horizontal line in each column depicts the average ratio in each group.

**Figure 5**
 Velocity of septal (left) and posterior wall (right) contraction in 16 normal subjects and 16 patients with idiopathic hypertrophic subaortic stenosis (IHSS). The horizontal line in each column represents the average wall velocity.

**Figure 6**
Ratio of septal ($V_s$) to posterior wall ($V_{pw}$) velocity in 16 normal subjects (right) and 16 patients with idiopathic hypertrophic subaortic stenosis (IHSS) (left). The horizontal line in each column represents the average ratio in each group.
ply that the posterior wall in this disorder may be truly hyperdynamic, perhaps to compensate for the decreased septal function. Although the ventricular dimension was smaller in our patients with IHSS than the normal subjects, normalization of velocities as proposed by Quinones et al. had no appreciable effect on the significance of our observations.

Extensive histologic investigations have documented the presence of bizarre cell structure and abnormal cell orientation in IHSS. Such observations justify consideration of this entity as a cardiomyopathy. In most specimens the abnormalities have been restricted to the interventricular septum, and it is these subjects who have outflow tract obstruction and echocardiographic evidence of mitral valve involvement. All IHSS patients reported here had mitral valve movement abnormalities documented by echocardiography. Therefore, histology of the posterior wall would be expected to be normal. This expectation is consistent with the observation of normal and even enhanced functional activity in this section of the left ventricle.

The mean velocity of circumferential fiber shortening as determined by echocardiography has recently been shown to be a reliable quantitative index of ventricular function. In our IHSS patients, as well as those of Quinones and co-workers, the V_{ct} is significantly elevated. It would thus appear that the enhanced function of the posterior wall in these ventricles more than compensates for the depressed contractility of the interventricular septum. The smaller ventricular size in IHSS is also probably a contributing factor. It should be noted, however, that the accuracy of mean V_{ct} as an index of ventricular function may be diminished in ventricles with regional differences of contractility.

Anatomic, histologic, and now functional evidence support the view that IHSS is an asymmetric entity. The abnormal septum moves as expected for a myocardial ventricle, while the remainder of the left ventricular myocardium compensates by contracting vigorously. The over-all result is a hyperdynamic, seemingly hypercontractile ventricle.

References

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