Echocardiographic Assessment
of the Effects of Surgery and Propranolol
on the Dynamics of Outflow Obstruction
in Hypertrophic Subaortic Stenosis

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SUMMARY
The long-term effects of surgery (ventriculomyotomy) and oral propranolol therapy were assessed by echocardiographic recordings in 51 studies conducted on 37 patients with hypertrophic subaortic stenosis. The incidence and severity of echocardiographic findings in 19 patients treated with propranolol and in 18 not so treated showed no significant differences. Likewise these findings were unaltered by administration of propranolol in 12 patients who were studied both while they were on the drug and while they were not. In contrast, of 14 patients studied after surgery, only one had persistently abnormal mitral valve motion, two had inconstant abnormality, and 11 had no abnormality at rest. The echocardiographic findings correlated well with independent postoperative hemodynamic assessment. The echocardiographic studies provide a noninvasive objective method for longitudinal evaluation of patients with hypertrophic subaortic stenosis (HSS).

Additional Indexing Words:
Mitral valve motion Ventriculomyotomy

ECHOCARDIOGRAPHY has been successfully used in the diagnosis of hypertrophic subaortic stenosis (HSS). An abnormal systolic movement of the anterior mitral valve leaflet, initially documented angiographically, has also been demonstrated consistently by echocardiography and is felt to represent the localization of the left ventricular (LV) outflow obstruction. It may also provide an explanation for the consistent association of obstruction and mitral regurgitation. The ultrasonic technic has recently been shown to be highly specific in the diagnosis of HSS as well as capable of separating patients with persistent resting obstruction from those with latent and labile obstruction. It appears to be a suitable noninvasive method for following the course of patients with this condition in a prospective longitudinal manner. The present study evaluated the effects of surgical and propranolol therapy on this specific systolic abnormality of the mitral valve movement.

Methods
All ultrasonic recordings were made by using a commercially available ultrasonic generator. The
addition of a dual-beam slave oscilloscope permitted the simultaneous recording of the ultrasonic motion pattern and four channels of physiologic data. Records were made on 35-mm film with an oscilloscope record camera which permitted the recording of more than 100 consecutive cardiac cycles for each patient. In every case, the electrocardiogram, the phonocardiogram, and the external carotid pulse were recorded with the ultrasonic data at rest and following Valsalva maneuver and amyl nitrite inhalation. In two patients, left ventricular and systemic artery pressures were recorded simultaneously with the echocardiographs at rest and during several of the interventions, such as Valsalva maneuver, amyl nitrite inhalation, isoproterenol infusion, angiotensin infusion, and the induction of ectopic beats.

Thirty-seven patients with hypertrophic subaortic stenosis were studied. The ages ranged from 12 to 59 years. Twenty-one were males. Nine were studied at the University of Rochester School of Medicine and 28 at Toronto General Hospital. Two of us (P.M.S. and R.G.) made all of the echocardiographic observations without knowledge of clinical and hemodynamic data. The clinical and hemodynamic assessment of the patients was carried out independently by two of us (A.G.A. and E.D.W.) and subsequently the clinical and hemodynamic data and the echocardiographic findings were correlated.

A total of 51 studies were made in the 37 patients; these included 18 studies while patients were receiving no therapy, 19 while on long-term oral propranolol therapy, and 14 following surgery. The daily dose of propranolol varied from 60 to 300 mg and was adjusted on the basis of clinical response. The average pressure gradient across the LV outflow in these 19 patients was 47 mm Hg (8 ± 22.7). Four patients had a resting pressure gradient of 10 mm Hg or less, the rest having a gradient of 25 mm Hg or greater. Twelve patients were studied both while on and while off propranolol therapy on two separate occasions at 6-month intervals. Five of these patients were untreated when studied initially and had been on propranolol therapy for several months prior to the second study. Seven others were on propranolol therapy at the time of the initial study and the drug was withdrawn 7 to 10 days before the last study 6 months later. Two additional patients were studied before, and 8 to 10 weeks after, surgery.

The echocardiographic findings were classified as follows:

1. An abnormal systolic anterior movement of the mitral valve leaflet which consistently obliterated the LV outflow tract on

the echocardiographic recordings. This category of patients has previously been shown to have persistent pressure gradients.

2. An inconstant systolic abnormality of the mitral valve movement observed only in occasional beats at rest, that did not completely obliterate the LV outflow space on the echocardiograms. This group has been shown to have latent or labile pressure gradients.

3. No abnormality at rest. This group has been shown to have no resting gradients across the LV outflow.

Results

The overall results of 51 studies in 37 patients are summarized in table 1.

Untreated Group

Fourteen of the 18 studies on untreated patients had echocardiographic findings of complete and constant systolic anterior movement of the mitral valve. Partial and inconstant abnormalities showed in two; and in two no abnormalities were observed at rest but were unmasked on provocation (fig. 1).

Propranolol Group

Sixteen of the 19 patients studied while receiving propranolol therapy had the echo findings of complete and constant abnormality at rest. Two showed a partial and inconstant abnormality, and in one the abnormal motion was demonstrated only on provocation.

The echocardiographic findings of the 12 patients studied both during and without propranolol therapy showed no significant

Table 1

Results of 51 Studies on 37 Patients

<table>
<thead>
<tr>
<th>Abnormal systolic motion at rest*</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Untreated</td>
</tr>
<tr>
<td>Persistent and complete •</td>
<td>14</td>
</tr>
<tr>
<td>Partial and inconstant ◊</td>
<td>2</td>
</tr>
<tr>
<td>Absent ◊</td>
<td>2</td>
</tr>
<tr>
<td>Total studies 51 in 37 patients*</td>
<td>18</td>
</tr>
</tbody>
</table>

*Symbols same as in figure 3.
Two types of echocardiographic abnormalities of anterior mitral leaflet motion are depicted. (Left panel) A complete or total abnormality consists of the anterior leaflet moving against the interventricular septum with obliteration of outflow space (arrow). (Right panel) An example of partial abnormality. This consists of a shallow movement (arrow) with only partial obliteration of outflow space in front. MV = mitral valve, anterior leaflet; CP = carotid pulse; PCG = phonocardiogram; ECG = electrocardiogram.

change between the two studies in any patient. In each patient the resting heart rate was slower by 10 to 20 beats/min while on propranolol therapy. Other objective clinical findings, including the loudness of the murmur, showed no significant change. Symptomatic improvement noted by some patients while on propranolol therapy could not be correlated with any objective change in physical findings nor with the echocardiographic observations.

Post surgery Group

Of the 14 patients with HSS studied after ventriculomyotomy, only one had the echo findings of complete and constant abnormality at rest; two had partial and inconstant abnormalities, and 11 had normal mitral valve motion. One of the two patients studied both before and after surgery demonstrated resolution of the preoperative abnormality to normal mitral valve echo postoperatively (fig. 2). In the second patient the abnormality of mitral valve motion persisted after surgery.

Nine of these patients were also evaluated by cardiac catheterization studies following surgery. In eight, such studies were independent of the echocardiographic examination. The effects of surgery on pressure gradients are compared with the echo findings at the postoperative evaluation (fig. 3). Each of the nine patients demonstrated a drop in pressure gradient across the left ventricular outflow. Postoperative hemodynamic findings correlated well with the echo findings in each patient studied.

Simultaneous recordings of the echocardiogram, the left ventricular and aortic pressures, the electrocardiogram, and the phonocardiogram in one patient (V.R.) during the
Figure 2

Echocardiogram of mitral valve (MV) recorded before and after surgery shows presence of significant abnormality before surgery (left panel—arrow), which disappeared after surgery (right panel). Resting pressure gradient ($P_o$) across LV outflow was reduced from 60 mm Hg to zero following surgery.

Discussion

Evaluation of a therapeutic intervention in hypertrophic subaortic stenosis is difficult because of the dynamic and variable nature of LV outflow obstruction. Objective measures, such as intensity of the systolic murmur, appearance of arterial pulse wave, and multiple cardiac catheterization studies, have been employed. The present study employed echocardiography as a noninvasive method for objective evaluation of patients. In the previous studies we reported a good overall correlation between echocardiographic and hemodynamic data.

Effectiveness of surgery in the amelioration of LV outflow obstruction in HSS has been demonstrated by several authors.\textsuperscript{8-12} The echocardiographic assessment of patients following ventriculomyotomy is consistent with the reported hemodynamic and clinical improvement. A persistent abnormality of the motion of the anterior leaflet of the mitral valve indicative of resting outflow obstruction was present in only one of 14 patients after surgical treatment for HSS compared to 14 of 18 untreated patients with HSS. Eleven of the 14 surgically treated patients had no echocardiographic abnormality at rest after operation as compared with two of the 18 untreated patients. In nine surgically treated patients in whom independent hemodynamic and echocardiographic evaluations were made postoperatively, correlation was good between the presence of a pressure gradient across the LV outflow and the presence of an abnormal systolic mitral valve motion on ultrasound studies.

The introduction of the beta-adrenergic blocking agents appeared to offer some hope in an effective medical form of therapy, since beta-adrenergic stimulation accentuates LV
outflow obstruction.13–14 Heightened adrenergic stimulation may play a causative role in the development and progression of the disease.15 Clinical trials of oral propranolol therapy in HSS have reported initial symptomatic improvement in over two thirds of the patients.16–21 Studies have suffered from lack of sizable patient population and lack of rigid controls of the clinical drug trials. Several studies have also pointed out that in many patients the initial improvement is not sustained with continued therapy.7, 10, 20 Objective evidences of improvement are few and largely unimpressive. Hemodynamic studies have revealed little or no change in the level of gradient in most patients with resting obstruction.21 Abolition of pressure gradient in an occasional patient must be interpreted with caution in this disease as the severity of the obstruction may be extremely variable. It has been shown, however, that propranolol ameliorates the intensification of the pressure gradients following exercise,22 thus providing a rational explanation for part of the symptomatic improvement.

Echocardiographic observations of mitral valve motion during rest showed no significant difference between patients on propranolol and untreated patients. Twelve patients studied both while on and while off therapy demonstrated no significant change in echo findings. Provocative maneuvers such as the Valsalva maneuver and inhalation of amyl nitrite were associated with similar ultrasound findings in both groups. The echocardiographic findings in the present study are in general agreement with the hemodynamic data. These observations support the suggestion that propranolol is unlikely to bring about major improvement in those with persistently high gradients across LV outflow.7–21 Its use in the symptomatic relief of angina in HSS has been demonstrated.16

Mechanisms by which LV outflow obstruction results in HSS have been elucidated in recent years. Abnormal anterior motion of the free edge of the anterior mitral leaflet appears to form the basis of outflow obstruction.1–4 The factors responsible for this abnormal motion of the mitral valve are not clear. A Venturi effect due to the rapid early ejection or excessive traction by a hypertrophied and distorted papillary muscle may provide the explanation. It is, however, of considerable interest that this abnormal motion is corrected by ventriculotomy and is unaltered by beta-adrenergic blocking agents. This observation points to the hypertrophied interventricular septum as the basic anomaly initiating the outflow obstruction. Several factors, such as Valsalva maneuver, respiration, beta-adrenergic stimulation, vasopressor and vasodepressor agents, and altered inotropic state, are known to affect the LV outflow obstruction as well as mitral valve motion in HSS. These diverse maneuvers must alter the dynamic behavior of hypertrophied interventricular septum which may secondarily influence the function of the anterior mitral leaflet.

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