Hypertrophic obstructive cardiomyopathy (HOCM) is defined as a primary, sometimes familial and genetically determined form of hypertrophy of the ventricular myocardium, frequently favoring the interventricular septum (IVS), it is often possible to observe changes in the papillary muscles and mitral valve (3). HOCM is the most frequent cause of stress-induced syncope or sudden cardiac death in patients <30 years old (4). Therapeutic approaches aim to reduce the extent of the outflow tract obstruction, thus improving clinical symptoms. Negatively inotropic substances (beta-adrenergic blocking agents [5–7] and calcium antagonists of the verapamil type [6,8]), the implantation of a DDD pacemaker (9–11), as well as surgical myectomy (12–20) have all been used successfully. Through transitory balloon occlusions of a septal branch, a reduction in the intraventricular gradient could be established in individual cases (21,22). In 1995, as a result of these positive experiences, Sigwart (22) was the first to introduce the concept of percutaneous transluminal septal myocardial ablation (PTSMA) in symptomatic patients with hypertrophic obstructive cardiomyopathy (HOCM).

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Manuscript received May 7, 1997; revised manuscript received July 18, 1997, accepted October 29, 1997.

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describe the successful nonsurgical ablation of hypertrophied septal myocardium in three patients, with a consecutive decrease in the obstruction, later to be followed by other investigators (23–26). We report the hemodynamic acute and 3-month follow-up results in 25 patients who were treated with this new procedure.

**Methods**

**Patients.** Between January and August 1996, we treated 25 patients (13 women, 12 men; mean age 54.7 ± 15.0 years) with a mean [±SD] disease duration of 7.4 ± 4.0 years. The patients were all symptomatic despite therapy with verapamil or beta-blockers; the mean New York Heart Association functional class was 2.8 ± 0.6. Three patients, who had shown clinical improvement after an operative myectomy 7 to 10 years earlier, had once more become symptomatic; in one of these patients, even the implantation of a DDD pacemaker had not led to a decrease in symptoms. The clinical baseline data of the patients are shown in Table 1.

After initial reports about the potential of nonsurgical catheter treatment for their clinical symptoms (22), the viability and novelty of this therapeutic procedure were explained to the symptomatic patients. They gave their written consent to the procedure but not before they had been informed about all other possible forms of therapy.

In all patients, the diagnosis HOCM was confirmed by clinical and noninvasive criteria. Before as well as 4 to 6 days after the intervention, the systolic pressure gradient of the left ventricular outflow tract (LVOT) was determined by Doppler echocardiography, both with medication and after a 24-h washout phase. Using echocardiography, the end-diastolic thicknesses of the left ventricular posterior wall (LVPW) and IVS were measured, as well as the dimensions of the left atrium (LA), left ventricular end-diastolic diameter (LVEDD) and left ventricular end-systolic diameter (LVESD). The extent of the occurrence of the systolic anterior movement of the mitral valve (SAM) phenomenon was classified as follows: 0 = no SAM phenomenon; I = SAM phenomenon without contact with the IVS; II = SAM phenomenon with short-term systolic contact with the IVS; III = SAM phenomenon with holosystolic septal contact. These measurements were carried out before and 4 to 6 days as well as 3 months after percutaneous transluminal septal myocardial ablation (PTSMA).

After both noninvasive and invasive preinterventional diagnoses that excluded an aortic valve gradient and coronary artery disease, as well as a 24-h medication break, the intervention was carried out. Only two highly symptomatic patients underwent the examination with continued verapamil therapy. First, a 4F pacemaker lead was placed through the left femoral vein in the right ventricle. After puncture of the right femoral vein, a Brockenbrough catheter was introduced into the left ventricular inflow tract through the mitral valve, after transseptal puncture. After puncture of the right femoral artery, a 7F or 8F guiding catheter was placed into the ascending aorta. The LVOT gradient was then determined at rest, after the Valsalva maneuver, after extrasystole and, in some cases, after wing provocation with orciprenaline. This was followed by the intravenous application of 10,000 U of heparin to prevent thromboembolic complications. The standard premedication usual for coronary dilation, namely, 500 mg of acetylsalicylic acid, was only administered to the first seven patients. The left main coronary artery was then intubated and visualized (Fig. 1A), after which the first septal branch was probed with a 0.014-in thick guide wire. Then, an over the wire angioplasty catheter with a balloon diameter and length of 2.5 mm and 0.4 cm (Atlantis) or 2.0 mm and 1.0 cm (Cobra, Boston Scientific Corp.), respectively, was placed in the proximal part of the septal branch. After the balloon was inflated to a pressure of 6 bar, the correct balloon position was determined using an injection of contrast medium into the left coronary artery.
main artery (Fig. 1B), and the supply area of the septal branch was determined using an injection of contrast medium through the balloon catheter (Fig. 1C). If a reduction in the outflow tract obstruction could be established after 5 min of septal occlusion, myocardial ablation of the septal branch supply area was then carried out by an injection of 96% alcohol. Ten minutes later, the balloon catheter was deflated, and the morphologic result was examined by visualizing the left main coronary artery (Fig. 1D). If a sufficient reduction in the outflow tract gradient could be achieved, another septal branch was occluded. After renewed determination of the LVOT gradient (Fig. 2), the investigation was brought to an end.

Postinterventional monitoring of the patients was carried out in the intensive care unit. The vascular sheaths were removed after normalization of the coagulation variables. Intensive care included both electrocardiographic monitoring and determination of creatine kinase (CK) and CK-MB fraction values every 4 h, followed by daily electrocardiographic checkups and, before discharge from hospital, ergometry. The corrected QT interval (QTc) was estimated according to the Bazett formula: $QTc = QT/RR\text{ interval}^{-2}$.

After 3 months, all patients underwent clinical and noninvasive follow-up examinations. Eighteen patients were additionally examined invasively.

**Statistics.** Continuous variables are expressed as mean value ± SD. Frequencies are given for discrete variables. Comparison of continuous variables at various times was carried out using the paired Student $t$ test. A $p$ value <0.05 was considered statistically significant. Statistical analyses were performed using the program Winstat 3.1.

**Results**

**Acute results.** **Technical course of the treatment.** During the intervention, a mean of $1.4 ± 0.6$ (range 1 to 3) septal branches were occluded by injection of $4.1 ± 2.6$ ml (range 1.5 to 11.0) of alcohol. Having occluded a septal branch with an insufficient gradient reduction in one female patient with a previous operative myectomy, it was not possible successfully to probe a second branch with the balloon catheter. After stopping the procedure because of its long duration and high consumption of contrast medium, this branch could be probed and occluded without any problems in a second session, with a complete reduction of the LVOT gradient. The mean catheterization time was $101.8 ± 33.3$ min (range 46 to 173), with a mean radiation time of $18.4 ± 12.7$ min (range 5.6 to 44.5);
253.1 ± 121.2 (range 130 to 550) ml of contrast medium was required.

**Hemodynamic results.** A reduction in LVOT gradient could be attained in 22 patients (88%): complete reduction in 4 (16%), >50% in 16 (64%) and 20% to 49% in 2 (8%). During the first intervention in three patients (12%), a gradient reduction could not be attained; however, a second intervention was successful in all three. The mean systolic pressure difference in the LVOT at rest sank from a mean of 61.7 ± 29.8 mm Hg (range 4 to 152) to 27.2 ± 19.0 mm Hg (range 1 to 67, p < 0.0001) after exploratory balloon occlusion and after occlusion by alcohol to 19.4 ± 20.8 mm Hg (range 0 to 74, p = 0.015 vs. balloon occlusion). The predictive value of the balloon-induced LVOT gradient reduction for the final result was not always low (Postprocedural LVOT gradient = -1.09 + 0.71 × LVOT gradient after balloon occlusion; r = 0.70). The postextrasystolic gradient could be reduced from 141.4 ± 45.3 mm Hg (range 76 to 240) before therapy to 61.1 ± 40.1 mm Hg (range 8 to 135, p < 0.0001). During the Valsalva maneuver, the LVOT gradient sank from 108.3 ± 35.7 mm Hg (range 38 to 188) to 39.4 ± 32.6 mm Hg (range 0 to 119, p < 0.0001).

**Echocardiographic course.** Both at rest and during the Valsalva maneuver, LVOT gradients were significantly reduced (Fig. 3). The mean SAM phenomenon was acutely reduced from 2.4 ± 0.8 (range 1 to 3) to 1.6 ± 1.0 (range 0 to 3, p < 0.001). At final echocardiography, new wall motion dyskinesia could be seen in the basal septum in all patients.

**Electrocardiographic changes.** During ablation, persistent broadening of the QRS complex and temporarily lengthened QTC intervals could be observed in all patients. In addition, a trifascicular block occurred during intervention in 13 patients (52%); which made temporary pacemaker stimulation necessary in 8 (32%) and permanent (DDD) pacemaker stimulation necessary in 5 (20%). In 13 patients (52%), new bundle branch block patterns could be observed (Table 2).

**Clinical course.** During the alcohol injection, all patients complained of a marked feeling of pressure in the left thorax, making administration of 0.3 mg of buprenorphine necessary in 24 patients. Postinterventionally, patients reported a feeling of pressure in the thorax lasting up to 24 h. After a mean duration of 11.1 ± 5.9 h, a maximal increase in CK to 780.0 ± 427.3 U/liter (range 305 to 1,810) was registered, with an MB fraction of 102.8 ± 63.4 U/liter (range 45 to 281). The patients were monitored in the intensive care for 5.0 ± 3.3 days (range 2 to 14). Twenty-four patients could leave the hospital after 11.3 ± 5.4 days (range 5 to 24), after a cardially uncomplicated...
catheter with side holes was used without any further problem. In the second patient, the cause was mechanical irritation through the extremely distally positioned guide wire. One 86-year old female patient, in whom the therapy had been carried out with a good hemodynamic acute result after several previous cardiac decompensations, died 8 days after the intervention, at the end of a clinical course that up to then had been uneventful, of the consequences of uncontrollable ventricular fibrillation. We traced this event to an overdose of beta-sympathomimetics in conjunction with known chronic obstructive pulmonary disease. In another female patient, gastrointestinal bleeding after an erosive gastritis was an extracardial complication during the clinical course. A blood transfusion was not necessary. We observed no neurologic complications.

Three-month follow-up. Clinical course. After 3 months, a clinical follow-up examination was carried out in all 24 surviving patients. At this time, there was a significant improvement in the clinical symptoms, with the mean functional class rising to 1.2 ± 0.8 (p < 0.001 vs. baseline). Twenty-one patients (88%) had improved subjectively; 3 patients (12%) reported no change in their cardiac symptoms; and 6 patients (25%) were able to tolerate a maximal stress load. Exercise capacity during ergometry increased from 67.0 ± 28.0 mm Hg to 110.7 ± 49.7 W (p = 0.008). There were no cardiac complications during follow-up. Three patients with unsatisfactory primary results underwent successful intervention at that time.

Echocardiographic course. Echocardiographic results could be compared in all 24 patients. In eight patients (34%), there was complete reduction of the LVOT gradient. Compared with baseline values, 13 patients (54%) had a reduction of LVOT gradient >50%, whereas 3 (12%) showed no significant change. Compared with the acute results, a further reduction in LVOT gradient had occurred in 14 patients (58%) and a renewed increase in 1 (4%). In 8 patients (34%), no further change had occurred. The need of DDD pacemaker implantation after PTSMA had no influence on the results. Mean LVOT gradient, both at rest (p = 0.008) and during the Valsalva maneuver (p = 0.011), had significantly decreased compared with that directly after the intervention (Fig. 3). The changes in left heart dimensions are shown in Table 3.

Hemodynamic course. In 18 patients (75%), recatheterization was carried out in addition to the noninvasive checkup. The six remaining patients did not consent to invasive diagnostic procedures because of the significant decrease in their symptoms. There was complete reduction of the LVOT gradient in eight patients with recatheterization (45%), six of whom (33%) demonstrated a reduction of >50% of their original values. Compared with the acute hemodynamic result after septal occlusion, a further reduction of the gradient could be observed in seven patients (39%). In eight patients (44%), no further change had occurred, but in three (17%), the gradient had increased. In these three patients, repeat PTSMA was successful. Compared with those directly after intervention, the mean values had not significantly changed, either at rest (18.4 ± 28.0 mm Hg) or after extrasystole (47.8 ± 45.1 mm Hg). The reduction in left ventricular end-diastolic pressure from 21.6 ± 7.9 mm Hg (before intervention) to 19.1 ± 7.2 mm Hg (3 months after intervention) was not significant because of the low number of patients examined. No change in global left ventricular ejection fraction could be observed in any patient, whereas all patients demonstrated limited akinesia of the basal septum and occluded septal branches.

Discussion

HOCM was first described as a disease entity in its own right in the late 1950s (27). A morphologic difference is made between subaortic obstruction and the far more rare midventricular obstruction (3). Patients become symptomatic in the form of angina pectoris, dyspnea, stress-induced syncope or heart failure caused by diastolic and systolic dysfunction. Atrial fibrillation, ventricular tachycardia (28,29) and myocardial scintigraphic proof of ischemia (30) are all prognostically unfavorable factors. Evaluation of the prognostic significance of LVOT obstruction varies (6,31–33).

Table 2. Bundle Branch Blocks After Percutaneous Transluminal Septal Myocardial Ablation

<table>
<thead>
<tr>
<th>Bundle Branch Block</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trifascicular</td>
<td>13</td>
</tr>
<tr>
<td>Temporary</td>
<td>8</td>
</tr>
<tr>
<td>Permanent</td>
<td>5</td>
</tr>
<tr>
<td>Left bundle</td>
<td>2</td>
</tr>
<tr>
<td>Right bundle</td>
<td>6</td>
</tr>
<tr>
<td>Right bundle and left anterior bundle</td>
<td>3</td>
</tr>
<tr>
<td>Right bundle and left posterior bundle</td>
<td>1</td>
</tr>
<tr>
<td>Left anterior bundle</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 3. Comparison of Echocardiographic Variables Before (baseline) and Three Months (follow-up) After Percutaneous Transluminal Septal Myocardial Ablation

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Follow-Up</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LA (mm)</td>
<td>48.0 ± 8.1</td>
<td>45.7 ± 8.1</td>
<td>0.04</td>
</tr>
<tr>
<td>LVEDD (mm)</td>
<td>46.6 ± 5.3</td>
<td>48.8 ± 6.1</td>
<td>0.08</td>
</tr>
<tr>
<td>LVESD (mm)</td>
<td>27.2 ± 5.0</td>
<td>30.8 ± 6.6</td>
<td>0.01</td>
</tr>
<tr>
<td>IVS (mm)</td>
<td>21.9 ± 3.5</td>
<td>17.0 ± 6.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LV PW (mm)</td>
<td>14.3 ± 2.6</td>
<td>12.3 ± 5.5</td>
<td>0.09</td>
</tr>
<tr>
<td>SAM</td>
<td>2.4 ± 0.8</td>
<td>0.7 ± 0.9</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Data presented are mean value ± SD. IVS = interventricular septum; LA = left atrium; LVEDD = left ventricular end-diastolic diameter; LVESD = left ventricular end-systolic diameter; LV PW = left ventricular posterior wall; SAM = septal anterior movement of mitral valve.
Previous forms of therapy for HOCM. Treatment of symptomatic patients with HOCM aims at reducing the outflow tract gradient. This reduction in LVOT obstruction could be achieved with drug therapy through the administration of negatively inotropic substances, especially beta-blockers (5–7) and calcium antagonists of the verapamil type (6,8). The implantation of a DDD pacemaker system was able to reduce the outflow tract gradient by >30% (9–11), also leading to a decrease in symptoms in patients without altering septal thickness. However, when determining the optimal atrioventricular interval, it is important not to hinder sufficient left ventricular filling by shortening the atrioventricular activation time too drastically (34). Because of these restrictions, DDD pacemaker therapy still cannot be generally recommended (35).

Surgical therapy gained increasing significance after its introduction by Cleland in 1958 (12–20). The operative procedure is complicated by a high mortality rate of 1.6% to 10.0% and the possibility of perioperative complications, such as the emergence of a ventricular septal defect, total atrioventricular block and cerebral embolism, particularly in connection with an intraoperative myectomy. When perioperative mortality was not considered, a prognostic improvement was achieved in postoperative patients compared with patients treated conservatively with drug therapy, so that extension of the indication for operative myectomy to low level symptomatic patients was discussed as early as 1983 (14).

Results of PTSMA. After first investigations in patients with HOCM were able to establish a reduction in intracavitary pressure gradient through transitory occlusion of a septal branch (21,22), Sigwart (22) was then the first to report a successful nonsurgical myocardial reduction in cases of HOCM through occlusion of the septal branch using pure alcohol. After we successfully completed our initial experience with this technique in six patients (25), we considered it feasible for use in a larger patient population.

The chemical ablation procedure had been previously described for treatment of ventricular arrhythmia (36). Similar to the surgical technique, this method aims to achieve a reduction in septal muscular mass through a limited therapeutic infarction, thus reducing the extent of the outflow tract obstruction. Compared with the surgical procedure, a significant advantage is that through occlusion of the septal branch, the therapeutic effect may be predicted and with a nondetectable reduction in the outflow tract gradient, chemical occlusion of the septal branch need not be carried out. However, our results lead us to conclude that the significance of transitory balloon occlusion for prediction of acute hemodynamic results is not very high. Particularly in patients with several small septal branches, the difficulty of this procedure lies in identifying the septal branch supplying the myocardial area responsible for the existence of the outflow tract obstruction. As initial experiences have shown, myocardial contrast echocardiography could be helpful here (37). This procedure may also lead to septal branches that atypically originate from side branches of the left anterior descending coronary artery being identified as responsible for supplying the septal area responsible for gradient formation.

In the series presented here, a complete reduction in LVOT gradient could be achieved in 4 patients (16%) and a reduction of >50% in 16 (64%). In two patients (8%), the acute reduction was 20% to 49%. Short-term follow-up observations show that a further reduction in LVOT gradient may be expected in the subsequent course in >50% of patients. This is presumably due to a remodeling process comparable to that after acute myocardial infarction. The ongoing reduction of the SAM phenomenon may be another reason for the progressive LVOT gradient reduction.

We were also able to show that PTSMA can be easily repeated in case of an initial failure. In three patients (12%), LVOT gradient reduction could not be achieved on the first attempt. In one female patient with a previous operation, in whom a second septal branch could not be reached with the balloon catheter during the first intervention because of technical problems, a hemodynamically and clinically good acute result could be achieved with a second intervention. In the other two patients who could not be treated successfully during the first intervention, the LVOT gradient was reduced by means of intraoperative myocardial contrast echocardiography at the 3 month follow-up catheterization.

The observation of further gradient reduction over the short-term course due to remodeling after induced therapeutic infarction, as well as the nonproblematic repeatability of PTSMA, render a staged procedure preferable, if several slender septal branches are present, to reduce the theoretic risk of systolic dysfunction through the loss of a large proportion of septal myocardium.

As with any new therapeutic procedure, the PTSMA of HOCM presented here is essentially limited by the occurrence of significant complications. After induction of a therapeutic limited myocardial infarction, all patients had symptoms of angina pectoris for a period of 24 h. The most frequent complication observed to date has been trifascicular blocks, which occurred in 60% of patients and made a permanent pacemaker necessary in 20%. For such patients, implantation of a DDD pacemaker system is recommended, such that atrioventricular activation time is optimized, as described earlier. A larger series of patients help to identify those patients requiring definitive pacemaker implantation as early as possible to reduce the hospital stay.

To avoid potential tachycardial arrhythmias in conjunction with an acute infarction, as seen in our 86-year old female patient, monitoring of rhythm is necessary for several days. It should be noted, that acute ventricular rhythm disturbances were not seen during alcohol injection. As with surgical therapy, the possibility of ventricular septal defect formation must also be considered. To reduce the risk of acute complications, it may be helpful to minimize the ablated septal area by using myocardial contrast echocardiography.

The long-term effects of the present therapeutic procedure on ventricular function and prognosis of the primary disease are not predictable. Because the primary disease is accompanied by restricted diastolic ventricular function, we currently consider permanent medical therapy with low dose beta-blockers or calcium antagonists to be necessary. In addition, clinical follow-up observations must confirm whether the fa-
vorable midterm results reported here and elsewhere (38) can be confirmed over the long term.

Conclusions. These initial results confirm the experience of Sigwart (22) and show that the new interventional technique represents a promising alternative to the previous treatment of HOCM and is able, insofar as clinical symptoms are concerned, to achieve results equally as good as surgical myocardial resection and probably equally as good or even better results than pacemaker therapy. Possible complications are trifascicular blocks requiring permanent pacemaker implantation and tachycardiac rhythm disturbances. Long-term effects of the procedure on the prognosis of the patients and left ventricular function remain to be investigated in prospective studies. Finally, PTSMA has to be compared with myectomy and DDD pacemaker therapy in a prospective, randomized trial to estimate its definitive significance in the treatment of symptomatic patients with HOCM.

We thank Sarah L. Kirkby for linguistic assistance in the preparation of the manuscript.

References