Pericutaneous Versus Surgical Treatment for Patients With Hypertrophic Obstructive Cardiomyopathy and Enlarged Anterior Mitral Valve Leaflets

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Background—The purpose of this study was to compare percutaneous transluminal septal myocardial ablation (PTSMA) and septal myectomy combined with mitral leaflet extension (MLE) in symptomatic hypertrophic obstructive cardiomyopathy patients with an enlarged anterior mitral valve leaflet (AMVL). Both PTSMA and myectomy reduce septal thickness and left ventricular outflow tract (LVOT) gradient; however, an uncorrected enlarged AMVL may predispose to residual systolic anterior motion (SAM) after successful standard myectomy or PTSMA. Myectomy with MLE previously demonstrated superior hemodynamic results compared with standard myectomy, but its value relative to PTSMA is unknown.

Methods and Results—Twenty-nine patients (aged 44±12 years) underwent myectomy with MLE, and 43 patients (aged 52±17 years) underwent PTSMA. Mitral leaflet area was similar in both groups (16.7±3.4 versus 15.9±2.7 cm², respectively). After PTSMA, 2 patients died, 4 needed a reintervention, and 4 required a permanent pacemaker for complete heart block. After surgery, only 1 patient needed a reintervention. At 1-year follow-up, LVOT gradients did not differ between surgical and PTSMA patients (17±14 versus 23±19 mm Hg, respectively). Preinterventional mitral regurgitation grade was more severe in the surgical group, but with myectomy combined with MLE, the residual grade was similar to that of PTSMA. Mean SAM grade decreased significantly more after surgery (from 2.9±0.3 to 0.5±0.7 mm Hg versus from 2.8±0.5 to 1.3±0.9 mm Hg, P<0.05).

Conclusions—PTSMA in these selected patients with hypertrophic obstructive cardiomyopathy had more periprocedural complications and resulted in more reinterventions. Hemodynamic results (SAM grade and reduction in mitral regurgitation) were better in surgical patients. (Circulation. 2005;112:482-488.)

Key Words: hypertrophy • cardiomyopathy • ablation • ablation, septal • alcohol

Hypertrophic obstructive cardiomyopathy (HOCM) is characterized by asymmetrical septal hypertrophy that causes a left ventricular outflow tract (LVOT) gradient. The severity of the LVOT gradient is usually correlated with the degree of complaints. In patients who remain symptomatic despite optimal medical treatment, several invasive therapeutic modalities have been introduced. Septal myectomy, a surgical technique developed by Morrow, is regarded as the standard approach to reduce septal thickness and LVOT gradient. This technique proved to be safe, with excellent hemodynamic results. Percutaneous transluminal septal myocardial ablation (PTSMA) is a nonsurgical technique to reduce septal thickness. During this procedure, ethanol is injected into 1 or more septal branches of the left anterior descending coronary artery (LAD), which results in a local myocardial infarction with contractile septal dysfunction followed by septal thinning, LVOT widening, and eventual LVOT gradient reduction.

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The mitral valve apparatus frequently demonstrates anomalies in HOCM (for instance, increased mitral leaflet area, length, and laxity, as well as anterior displacement of the papillary muscles). All of these abnormalities may predispose to residual systolic anterior motion (SAM) after successful myectomy. To avoid persistence of LVOT gradient and mitral regurgitation (MR), we developed the technique of mitral leaflet extension (MLE) in addition to myectomy. Previously, we reported beneficial effects of this novel technique compared with standard myectomy.
rently, it is not known whether PTSMA is equally effective in these selected patients. Here, we present hemodynamic and clinical 1-year outcomes in HOCM patients with an enlarged anterior mitral valve leaflet (AMVL) who underwent PTSMA or myectomy in combination with MLE.

Methods

Patient Selection
The study population comprised 72 patients with symptomatic HOCM despite optimal medical treatment. All subjects demonstrated a dynamic LVOT gradient of at least 50 mm Hg at rest or on provocation and a mitral leaflet area >12 cm². Between 1986 and 1999, 29 patients underwent surgical septal myectomy in combination with MLE. After August 1999, 43 consecutive patients underwent PTSMA. Our institutional review committee approved the study, and all patients gave informed consent.

Echocardiographic Analysis

Transthoracic echocardiography was routinely performed to evaluate the site of hypertrophy, mitral valve anatomy, and LVOT gradient. Mitral valve opening area was measured in the parasternal short-axis view by tracing the innermost margins of the mitral valve at the point of maximal opening. Mitral leaflet area was calculated with a previously validated formula (4.64+2.17×mitral valve opening area).17 Follow-up measurements included septal thickness at the site of treatment, LVOT gradient, MR grade, severity of SAM, and left atrial and ventricular dimensions. Septal thickness was measured in the parasternal long-axis view in an end-diastolic still frame. Peak LVOT gradient was calculated from the color-guided, continuous-wave Doppler velocity by the modified Bernoulli equation. MR severity was assessed by color flow Doppler echocardiography and graded on a scale from 0 (no regurgitation) to 4 (severe regurgitation). SAM of the AMVL was graded as 0 (absent), 1 (mild; minimal mitral-septal distance >10 mm during systole), 2 (moderate; minimal mitral-septal distance ≤10 mm during systole), or 3 (marked; brief or prolonged contact between the AMVL and septum).18 Dimensions of the left atrium and left ventricle (LV) were measured with standard M-mode echocardiography from the parasternal long-axis view. In the apical 2- and 4-chamber views, the end-systolic and end-diastolic still frames were manually traced to assess LV ejection fractions.19

Surgical Myectomy in Combination With MLE

Cardiac surgery was performed with standard techniques of cardiopulmonary bypass with moderate hypothermia and myocardial preservation. After aortotomy, the septum was partially resected to the left of an imaginary line through the nadir of the right coronary cusp by a locally designed modified electrocutting technique. If myectomy had been completed, the surgeon performed MLE (Figure 1).6,20 In this procedure, an autologous pericardial patch is placed by a locally designed modified electrocutting technique. If myectomy was weaned by blood flow against the leaflet is proportional to its area, which extends the width but not the length of the AMVL, which shifts the centrally attached chordae laterally. As a result, the chordae are stretched and erected, which will enhance leaflet coaptation. Finally, because force produced by blood flow against the leaflet is proportional to its area, the increased leaflet will be pressed posterior, with a decrease in SAM and MR. Postoperative results were assessed by transeosophageal and epicardial echocardiography immediately after the patient was weaned from bypass (Figure 3). There were no suboptimal results that required reinstitution of bypass.

Percutaneous Transluminal Septal Myocardial Ablation

The right and left femoral arteries were cannulated by standard techniques. A temporary pacemaker lead (5F temporary pacing electrode catheter [Bard], which was later replaced by a 5F bipolar electrode catheter [Arrow]) was positioned in the right ventricle.
procedure, the pacemaker lead was left in situ for at least 48 hours, and the patient was transferred to the clinical department for telemetric observation.

Follow-Up

One-year follow-up data included mortality, New York Heart Association (NYHA) class, medication use, and the above-described echocardiographic variables (septal thickness, LVOT gradient, MR, SAM grade, and left atrial and ventricular dimensions). The clinical status was assessed by one cardiologist (F.J.C.) and therefore not subject to interobserver variability. We performed a MEDLINE search (1995 to the present) on studies in English language. Using the search terms “hypertrophic cardiomyopathy” in combination with “septal ablation” or “myectomy,” we found 158 and 276 articles, respectively. On the basis of the abstracts, we selected 3 articles that compared septal ablation and septal myectomy.21–23

Statistical Analysis

Continuous variables were presented as mean±SD values and were compared by the Student unpaired t test. Categorical variables were presented as counts and percentages and compared with the χ² test or, when appropriate, with Fisher’s exact test.

Results

Baseline Clinical Characteristics

Baseline clinical characteristics of patients treated by surgery or PTSMA only differed with respect to age (Table 1). PTSMA patients were older at time of intervention (P<0.05).

Baseline Echocardiographic Measurements

Mean septal thickness, LVOT gradient, and mitral leaflet area in the surgical group matched that in the PTSMA group. Only MR grade was higher in the surgical group. All patients demonstrated typical SAM of the AMVL.

Clinical Outcome

Preinterventional and postinterventional data at 1-year follow-up are presented in Table 1.

Outcome After Surgery

There were no deaths associated with surgery. Three months after surgery, 1 patient was hospitalized with shortness of breath. Echocardiography demonstrated severe MR at the site of the patch due to dehiscence. After surgical correction, the patient’s clinical course was further uncomplicated. Mean NYHA class in the surgical group improved from 2.8±0.4 to 1.3±0.4 (P<0.05) at follow-up.

Outcome After PTSMA

Two patients died in the PTSMA group. One patient died during the procedure owing to refractory ventricular fibrillation after induction of the infarction. The other patient died after the procedure owing to cardiac tamponade caused by right ventricular perforation by a pacemaker lead. Since then, we have changed the type of pacemaker lead to avoid this complication. Five other patients were successfully resuscitated for ventricular fibrillation within 24 hours after the intervention. One patient with late recurrence of ventricular fibrillation and another patient with late occurrence of non-
sustained ventricular tachycardia were treated with an implantable cardioverter defibrillator. Four patients underwent permanent pacemaker implantation because of complete atrioventricular heart block after the procedure. In 1 patient, a large anterior myocardial infarction (maximal creatine kinase 4700 U/L) was induced because of spill of ethanol in the LAD. Four patients underwent repeat PTSMA after a mean follow-up period of 10 months for recurrence of complaints and significant LVOT gradient. Mean NYHA class in PTSMA patients improved from 2.4 ± 0.5 to 1.5 ± 0.7 (P < 0.05) at follow-up.

Echocardiographic Follow-Up Data
As seen in Table 1, the decreases in septal thickness and LVOT gradient at 1-year follow-up were comparable in both groups. Mean residual MR after surgery did not differ from that in the PTSMA group; however, postsurgical MR decreased at least 2 grades in 75% of surgical patients, whereas this improvement was reached in only 10% of the PTSMA patients (P < 0.0001). Mean SAM grade decreased significantly more after surgery (P < 0.001). In both groups, mean LV end-diastolic dimensions did not change. LV end-systolic dimension remained unchanged after surgery, whereas it increased significantly after PTSMA (P < 0.05). In both groups, LV ejection fractions remained preserved at follow-up.

Discussion
Both surgical septal myectomy and PTSMA were developed to reduce septal hypertrophy and to relieve LVOT gradient in patients with HOCM. Some of these patients also demonstrate structural anomalies of the mitral valve apparatus that are not corrected with either intervention, however. This may predispose to residual SAM, suboptimal alleviation of LVOT gradient, and residual MR. Surgical implantation of a mitral valve prosthesis is not attractive because of the risks of thromboembolism and bleeding related to the need for anticoagulation therapy.24 One alternative that preserves native valve tissue is mitral valve plication.25 In our center, myectomy in combination with MLE is used in patients with an enlarged AMVL. Previously, we reported superior hemodynamic results compared with myectomy alone16 and sustained hemodynamic improvement during long-term follow-up.7 In the present study, we compared this modified surgical procedure with PTSMA in patients with an enlarged AMVL. We observed more periprocedural complications and necessity for reinterventions in PTSMA patients. In addition, hemodynamic results (reduction in SAM and MR grade) were better in surgical patients.

Comparison of Echocardiographic Parameters After PTSMA and Surgery in Other Studies
As summarized in Table 2, 3 earlier published studies compared the hemodynamic effects and clinical outcome of PTSMA versus septal myectomy.21-23

LVOT Gradient
Acute LVOT gradient reduction after PTSMA happens mainly owing to a lesser peak acceleration rate of blood flow proximal to the obstruction.26 This may be caused by inhomogeneity in LV contraction due to ischemic septal dysfunction27 and/or conduction abnormalities due to ischemia-induced bundle-branch block.28 Obviously, myectomy results in immediate septal thinning, LVOT widening, and gradient reduction. In the long-term follow-up, maximal gradient

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**TABLE 1. Clinical and Echocardiographic Data at Baseline and at 1-Year Follow-Up**

<table>
<thead>
<tr>
<th>Clinical data</th>
<th>Preprocedure</th>
<th>One-Year Follow-Up</th>
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<tr>
<td></td>
<td>Myectomy (n=29)</td>
<td>PTSMA (n=43)</td>
</tr>
<tr>
<td>Mean age, y</td>
<td>44 ± 12*</td>
<td>52 ± 17</td>
</tr>
<tr>
<td>NYHA class</td>
<td>2.8 ± 0.4</td>
<td>2.4 ± 0.5</td>
</tr>
<tr>
<td>No. of drugs</td>
<td>1.5 ± 0.7</td>
<td>1.5 ± 0.9</td>
</tr>
<tr>
<td>Echocardiographic data</td>
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<td></td>
</tr>
<tr>
<td>Septal thickness, mm</td>
<td>23 ± 4</td>
<td>21 ± 4</td>
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<td>LVOT gradient, mm Hg</td>
<td>100 ± 20</td>
<td>101 ± 34</td>
</tr>
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<td>MR grade</td>
<td>2.1 ± 1.1*</td>
<td>1.5 ± 0.8</td>
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<tr>
<td>SAM grade</td>
<td>2.9 ± 0.3</td>
<td>2.8 ± 0.5</td>
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<tr>
<td>Left atrium, mm</td>
<td>47 ± 9</td>
<td>47 ± 7</td>
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<td>LV EDD, mm</td>
<td>43 ± 5</td>
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</tr>
<tr>
<td>LV ESD, mm</td>
<td>27 ± 5</td>
<td>25 ± 5</td>
</tr>
<tr>
<td>LV ejection fraction, %</td>
<td>72 ± 6</td>
<td>71 ± 5</td>
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<td>MLA, cm²</td>
<td>16.7 ± 3.4</td>
<td>15.9 ± 2.7</td>
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</table>

n indicates number of patients; EDD, end-diastolic diameter; ESD, end-systolic diameter; and MLA, mitral valve leaflet area.

*P < 0.05 vs PTSMA; †P < 0.05 vs baseline value.

 β-Blocker and/or calcium antagonist.
TABLE 2. Comparison of Published Studies Comparing Surgical Myectomy and PTSMA

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of Patients</th>
<th>Follow-Up, mo</th>
<th>Pre</th>
<th>Post</th>
<th>Pre</th>
<th>Post</th>
<th>Pre</th>
<th>Post</th>
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<td></td>
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</tr>
<tr>
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<td>12</td>
<td>2.8±0.4</td>
<td>1.3±0.4</td>
<td>100±20</td>
<td>17±14</td>
<td>2.1±1.1</td>
<td>0.6±0.6</td>
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<td>PTSMA</td>
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<td></td>
<td>2.4±0.5</td>
<td>1.5±0.7</td>
<td>101±34</td>
<td>23±19</td>
<td>1.5±0.8</td>
<td>0.8±0.8</td>
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<tr>
<td>Nagueh et al21</td>
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<td>12</td>
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<td></td>
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<tr>
<td>Myectomy</td>
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<td></td>
<td>78%</td>
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<td>78±30</td>
<td>4±7†</td>
<td>83%</td>
<td>51%†</td>
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<tr>
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<td></td>
<td>90%</td>
<td>0%†</td>
<td>76±23</td>
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<td>Myectomy</td>
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<td>3.3±0.5</td>
<td>1.5±0.7</td>
<td>62±43</td>
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<td>28±12</td>
<td>8±5†</td>
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<td>3.5±0.5</td>
<td>1.9±0.7</td>
<td>64±39</td>
<td>24±19†</td>
<td>23±12</td>
<td>9±3†</td>
</tr>
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<td>Firoozi et al23</td>
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<tr>
<td>Myectomy</td>
<td>24</td>
<td></td>
<td>2.4±0.6</td>
<td>1.5±0.7</td>
<td>83±23</td>
<td>17±12†</td>
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</tr>
<tr>
<td>PTSMA</td>
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<td>2.3±0.5</td>
<td>1.7±0.8†</td>
<td>91±18</td>
<td>21±12†</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

Pre indicates preintervention; Post, postintervention; IVS, interventricular septal thickness; EDD, end-diastolic dimension; ESD, end-systolic dimension; LA, left atrium; and NA, not available.

*P<0.05 vs PTSMA; †P<0.05 vs baseline value.

diminish, which results in decreased SAM. In the long-term, however, LVOT widening may be of more importance than changes in LV ejection dynamics. In the present study, we noticed a greater reduction in SAM after surgery than with PTSMA. This result favors the hypothesis that MLE has additional advantages over PTSMA for patients with an enlarged AMVL.7,16,32 These advantages include (1) stiffening of the central part of the buckling AMVL to prevent SAM by insertion of a pericardial patch,14,33–35 (2) erection of the lax chordae attached to central portions of the AMVL through lateral shift caused by enlargement of the horizontal width of the anterior leaflet,32 (3) maintenance of valve tethering due to an enlarged leaflet area once the streamlines of flow are straightened after septal myectomy,32 and (4) enhanced reduction in MR provided by greater leaflet area. The observation that the preinterventional higher grade of MR in the surgical group was abolished to the same extent as after PTSMA confirms the observation that a larger leaflet contact area reduces MR for any given degree of SAM.17

Comparison of Clinical Parameters After PTSMA and Surgery

Both the present and prior studies reported no difference in mean postinterventional NYHA classification between PTSMA and surgery.

Complications and Reinterventions After PTSMA and Surgery

As summarized in Table 3, more complications were noticed after PTSMA. The need for permanent pacemaker implantation, as noticed in other studies, occurred more often after PTSMA, despite careful contrast identification of the target septal branch. This difference in incidence may be caused by induced transmural myocardial infarction as opposed to well-controlled, more precise myectomy. As seen in the present study, PTSMA also has some relatively unique complications, such as spill of ethanol into the LAD and

reduction after PTSMA is achieved owing to LVOT remodeling that results in widening of the LVOT. That short-term LVOT gradient reduction may indeed be better with surgery was shown in the 3-month follow-up study by Qin et al.22 Retrospective analysis of our data at 3 months also showed a significantly better reduction in LVOT gradient with myectomy (16±11 versus 27±22 mm Hg after PTSMA, P<0.05). At 1-year follow-up, however, there were no significant differences between surgery and PTSMA in the present study and the studies by Nagueh et al21 and Firoozi et al.23 Notably, all studies demonstrated a tendency towards a better reduction with surgery. At present, it is not known whether the timing of maximal LVOT reduction after an intervention is important in reducing morbidity and mortality. The small mean differences in alleviation of the LVOT gradient between surgery and PTSMA may be of importance, because the severity of LVOT gradient is an independent risk factor for functional deterioration.29 After PTSMA, a residual LVOT gradient in the catheterization laboratory was an independent predictor of adverse outcome at later follow-up in a study by Chang et al.30 After myectomy, it was an independent predictor of mortality at prolonged follow-up in a study by Mohr et al.31

SAM of the AMVL

In the study by Qin et al.22 MR as well as SAM of the AMVL were reduced equally after surgery and PTSMA. In the study by Nagueh et al.21 who only reported on MR, an equal reduction was achieved with both treatment modalities. Interestingly, Qin et al22 described 2 patients with an elongated AMVL who did not benefit from PTSMA. In contrast to this observation, Flores-Ramirez et al26 reported that PTSMA could indeed be effective in HOCM patients with redundant mitral leaflet valves. They stated that after successful PTSMA, the streamlines of flow are straightened, and ejection velocity proximal to the LVOT decreases. Consequently, the drag forces that pull the AMVL into the LVOT will
ventricular fibrillation due to induced myocardial ischemia.
In addition, more reinterventions were needed after PTSMA.
In contrast to other studies, we could not find a relation
between reinterventions, the amount of ethanol used, and
peak creatine kinase values.

Study Limitations
This study was not a randomized trial but an analysis of 2
cohorts treated with a surgical and percutaneous therapy. The
present results may not be generalized, because all patients
were selected by mitral leaflet area. Furthermore, the groups
were dissimilar with respect to age and severity of MR. The
choice of treatment, however, was not influenced by these
parameters, because after 1999, all patients were treated with
PTSMA. It is unlikely that the advanced age in this group
would have influenced the differences in hemodynamic
outcome compared with surgery. As described by Chang et
al., age was not a predictor of outcome after PTSMA. It is
not clear whether the lesser degree of MR in the PTSMA

group influenced the outcome in the present study, but in
actual clinical practice, it is likely that patients with more
severe MR would be referred to surgery.

Implications and Conclusions
Both myectomy and PTSMA are effective therapies to
diminish the LVOT gradient by reduction in septal thickness.
After myectomy, maximal gradient reduction is achieved
immediately. As mentioned above, the gradient reduction
after PTSMA appears to follow a biphasic course, and the
maximal reduction is achieved somewhat later in time. In
HOCM patients with an enlarged AMVL, myectomy in
combination with MLE offers the aforementioned additional
effects to further reduce SAM. In the present study, we found
more periprocedural complications and need for reinterven-
tions in PTSMA patients. Whether the immediate LVOT
gradient reduction with the combined surgical approach will

TABLE 2. Continued

<table>
<thead>
<tr>
<th>SAM Grade</th>
<th>IVS, mm</th>
<th>LV EDD, mm</th>
<th>LV ESD, mm</th>
<th>LA EDD, mm</th>
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<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
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<tr>
<td>2.9 ± 0.3</td>
<td>0.5 ± 0.7†</td>
<td>23 ± 4</td>
<td>17 ± 2†</td>
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<td>2.8 ± 0.5</td>
<td>1.3 ± 0.9†</td>
<td>21 ± 4</td>
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<td>20 ± 6</td>
<td>17 ± 5†</td>
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TABLE 3. Reported Complications After Myectomy or PTSMA

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<thead>
<tr>
<th>Study</th>
<th>No. of Patients</th>
<th>Death, n (%)</th>
<th>Acute MI, n (%)</th>
<th>Ventricular Fibrillation, n (%)</th>
<th>Permanent Pacing, n (%)</th>
<th>Automated ICD, n (%)</th>
<th>Reintervention, n (%)</th>
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<td>Myectomy</td>
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<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (3)*</td>
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<td>PTSMA</td>
<td>43</td>
<td>2 (5)</td>
<td>1 (2)</td>
<td>6 (14)</td>
<td>4 (9)</td>
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<td>4 (9)</td>
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<td>Nagueh et al21</td>
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<tr>
<td>Myectomy</td>
<td>41</td>
<td>0 (0)</td>
<td>1 (2)</td>
<td>6 (14)</td>
<td>4 (9)</td>
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<td>PTSMA</td>
<td>41</td>
<td>1 (2)</td>
<td>9 (22)</td>
<td>1 (2)</td>
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<td>2 (8)</td>
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<td>Myectomy</td>
<td>24</td>
<td>1 (4)</td>
<td>1 (4)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PTSMA</td>
<td>20</td>
<td>1 (4)</td>
<td>3 (15)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

MI indicates myocardial infarction; ICD, internal cardiac defibrillator.
*Reintervention because of patch dehiscence.
result in a better clinical outcome than with PTSMA during a longer follow-up period is unknown and merits further research.

References


Percutaneous Versus Surgical Treatment for Patients With Hypertrophic Obstructive Cardiomyopathy and Enlarged Anterior Mitral Valve Leaflets
Chris van der Lee, Folkert J. ten Cate, Marcel L. Geleijnse, Marcel J. Kofflard, Chiara Pedone, Lex A. van Herwerden, Elena Biagini, Wim B. Vletter and Patrick W. Serruys

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