Sustained Improvement After Combined Anterior Mitral Leaflet Extension and Myectomy in Hypertrophic Obstructive Cardiomyopathy

Chris van der Lee, MD; Marcel J.M. Kofflard, MD; Lex A. van Herwerden, MD; Willem B. Vletter, MSc; Folkert J. ten Cate, MD

Background—Mitral leaflet extension (MLE) combined with septal myectomy is a new surgical approach to treat hypertrophic obstructive cardiomyopathy (HOCM) and an enlarged mitral leaflet area. The study presents the long-term clinical results and outcome of this technique.

Methods and Results—MLE entails grafting a glutaraldehyde-preserved autologous pericardial patch onto the center portion of the anterior mitral valve leaflet. Twenty-nine patients with HOCM were studied. Mean follow-up (±SD) was 3.4±2.1 years (range 3 months to 7.7 years). The preoperative calculated mitral leaflet area was 16.7±3.4 cm². New York Heart Association functional class improved significantly from 2.8±0.4 to 1.3±0.4 (P<0.05), width of the interventricular septum decreased from 23±4 to 17±2 mm (P<0.05), left ventricular outflow tract gradient decreased from 100±20 to 17±14 mm Hg (P<0.01), severity of mitral regurgitation graded on a scale from 0 to 4+ decreased from 2.5±0.9 to 0.5±0.6 (P<0.01), and severity of the systolic anterior motion of the mitral valve graded on a scale from 0 to 3+ decreased from 2.9±0.3 to 0.5±0.7 (P<0.01) postoperatively. There were no deaths associated with surgery.

Conclusions—Long-term follow-up shows sustained improvement in functional status, reduction of outflow tract obstruction, and attenuation of mitral regurgitation and systolic anterior motion of the mitral valve. In this respect, the new technique widens the surgical applications in HOCM. (Circulation. 2003;108:2088-2092.)

Key Words: cardiomyopathy ■ surgery ■ mitral valve

Hypertrophic obstructive cardiomyopathy (HOCM) is a heterogeneous disease characterized by asymmetrically distributed left ventricular hypertrophy and left ventricular outflow tract (LVOT) obstruction. Dynamic LVOT obstruction is induced by thickening of the interventricular septum and systolic anterior motion (SAM) of the mitral valve. Several invasive therapeutic modalities have been developed to diminish outflow tract obstruction by reduction of the interventricular septum width. The most commonly performed intervention is surgical myectomy according to the technique developed by Morrow et al. Hypertrophic cardiomyopathy, however, frequently presents with several anatomic alterations of the mitral valve apparatus, including increased mitral leaflet area (MLA), length, and laxity, as well as anterior displacement of the papillary muscles. These structural abnormalities, which are not corrected after a successful myectomy, may predispose to residual SAM and result in a suboptimal outcome with persistence of outflow obstruction and mitral regurgitation. We therefore performed anterior mitral leaflet extension (MLE), one of several repair techniques originally developed by Carpentier, in combination with myectomy in patients with HOCM and an enlargement of the anterior mitral leaflet. We have shown that the combined technique resulted in good short-term functional and hemodynamic outcome compared with myectomy alone in these patients. In this report, we present the long-term follow-up results of this combined surgical approach.

Methods

Patient Selection

Patients are selected for surgery at our hypertrophic cardiomyopathy clinic on the basis of the following indications: (1) a significant LVOT gradient ≥50 mm Hg at rest or on provocation and (2) New York Heart Association (NYHA) functional class II to IV despite optimal medical treatment consisting of β-blocking agents, calcium channel blockers, or both. Both cardiac catheterizations for invasive hemodynamic measurements and visualization of the coronary anatomy and transthoracic echocardiography were performed routinely before surgery. The echocardiographic images were collected by a single echocardiographer and stored on videotape for offline analysis.
The mitral valve leaflet area was used as a selection criterion to perform MLE in conjunction with myectomy. First, the mitral valve opening area was measured offline from transthoracic echocardiographic images in the parasternal short-axis view by tracing the innermost margins of the mitral valve at the point of maximal opening. The demarcated area was calculated with a dedicated software program. Next, the leaflet area was calculated with the formula previously validated by Klues et al: mitral valve leaflet area = 4.64 + 2.17 x mitral valve opening area.

Between 1991 and 1999, 32 patients were accepted for surgical correction, and 29 patients met the selection criteria for MLE. The final decision to perform MLE was made perioperatively by the surgeon after visual inspection and epicardial echocardiographic observation of papillary muscle length and mitral valve laxity, as well as leaflet area. If, in the surgeon’s view, these morphometric abnormalities made mitryctomy alone unlikely to yield optimal results, the leaflet-extending patch was additionally grafted. The surgical procedures, which were approved by the local institutional review committee, were performed by one surgeon (L.A.v.H.). All subjects gave oral informed consent.

Surgical Technique
Cardiac surgery was performed by standard techniques of cardiopulmonary bypass with moderate hypothermia and crystalloid cardioplegic arrest (St Thomas’s solution). An autologous pericardial patch was harvested, trimmed of fat and extraneous tissue, immersed for 10 minutes in 0.62% glutaraldehyde, and then placed in a normal saline bath. The patch was treated with glutaraldehyde for ease of manipulation and collagen cross-linking. After the ascending aorta was opened by an oblique incision, myectomy was performed to the left of an imaginary line through the nadir of the right coronary cusp with a locally designed electrocautery device, described in detail elsewhere. The entire surgical procedure was monitored with epicardial echocardiography by the surgeon.

When, in the surgeon’s opinion, adequate septal myectomy had been achieved, anterior MLE was performed. The procedure has been explained previously. In brief, a gap was created in the anterior mitral leaflet through a longitudinal incision, starting at the subaortic hinge point to the rough zone. Then, an oval autologous pericardial patch, ~2.5 cm wide and 3 cm long, was grafted onto the center portion of the anterior mitral leaflet with 2 running polypropylene sutures. The surgical results were assessed with transesophageal and epicardial echocardiography immediately after the patient was weaned from bypass and at a systolic blood pressure of ≥100 mm Hg, with special attention to the width of the interventricular septum, residual LVOT gradient, mitral valve regurgitation, and SAM. None of the patients had an indication for reinstitution of cardiopulmonary bypass because of a suboptimal surgical result.

Follow-Up
The clinical characteristics collected before the intervention included assessment of symptoms, NYHA functional class, and drugs prescribed. Physical examination and baseline laboratory studies were performed, including electrocardiography, transthoracic echocardiography, and cardiac catheterization.

The echocardiographic data were reviewed by 2 physicians who were unaware of the patient’s medical history. Echocardiography was performed 1 week before surgery and was subsequently repeated 1 week, 3 months, and at yearly intervals after surgery.

At the site of myectomy, the mean interventricular septal thickness was calculated from the septal width in diastole from both the parasternal short-axis and long-axis views. The severity of the mitral regurgitation was graded (on a scale from 0 to 4+) by color flow Doppler echocardiography. The severity of the SAM of the anterior mitral valve was determined from the 2D images and was graded on a scale from 0 to 4+ depending on the mitral-septal distance (grade 0 indicates no SAM and grade 3+ indicates brief or prolonged contact between mitral valve and septum). Peak LVOT gradient was estimated with Doppler echocardiography by the modified Bernoulli equation (P = 4V²), where P is the pressure gradient and V is Doppler-determined blood velocity. MLA was calculated as described above from the preoperative echocardiograms.

Follow-up information was obtained at the hypertrophic cardiomyopathy clinic by 1 cardiologist (F.H.C.). Because echocardiography has become a noninvasive and standard routine to assess postoperative results, repeated catheterization was not performed in this group.

Statistical Analysis
Data are expressed as mean±SD values. The paired Student’s t test was determined to compare continuous variables. Preoperative and postoperative patient characteristics compared were NYHA functional class, number of drugs prescribed, width of the interventricular septum, LVOT gradient, severity of mitral regurgitation, and grade of the SAM of the anterior mitral valve leaflet.

Results
Baseline Characteristics
The baseline characteristics of the 29 patients are listed in Table 1. Fifteen patients were male. Mean age was 44±13 years (range 21 to 64 years). The majority of patients (76%) had class III symptoms according to NYHA classification, and 24% of patients had class II symptoms. Two patients had been resuscitated successfully from an out-of-hospital cardiac arrest. All patients were treated with drugs. β-Blocking agents, calcium antagonists or the combination of these drugs were prescribed in 41%, 38%, and 21% of patients, respectively.

Interventricular septal thickness averaged 23±4 mm (range 17 to 35 mm), and mean left ventricular posterior wall thickness was 13±3 mm (range 9 to 19 mm). The mean LVOT gradient was 100±20 mm Hg. Most patients had moderate to severe mitral valve regurgitation (mean grade 2.5±0.9). All patients had typical marked SAM of the anterior mitral valve leaflet (mean grade 2.9±0.3). The calculated MLA was 16.7±3.4 cm² (normal <12 cm²). Significant coronary artery disease was demonstrated in a single patient in whom bypass grafting was performed simultaneously during the MLE and myectomy procedure.

### Table 1. Baseline Characteristics of the 29 Patients With HOCM Treated With Myectomy and MLE

<table>
<thead>
<tr>
<th>Gender, male/female, n (%)</th>
<th>15 (52/14 (48)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age ±SD, y</td>
<td>44±13</td>
</tr>
<tr>
<td>Years of follow-up, mean±SD</td>
<td>3.4±2.1</td>
</tr>
<tr>
<td>Symptoms, n (%)</td>
<td></td>
</tr>
<tr>
<td>Dyspnea</td>
<td>19 (66)</td>
</tr>
<tr>
<td>Angina</td>
<td>14 (48)</td>
</tr>
<tr>
<td>(Pre)syncope</td>
<td>7 (24)</td>
</tr>
<tr>
<td>Out-of-hospital resuscitation</td>
<td>2 (7)</td>
</tr>
<tr>
<td>NYHA class, n (%)</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>7 (24)</td>
</tr>
<tr>
<td>III</td>
<td>22 (76)</td>
</tr>
<tr>
<td>Medical therapy, n (%)</td>
<td></td>
</tr>
<tr>
<td>β-Blocker</td>
<td>12 (41)</td>
</tr>
<tr>
<td>Calcium antagonist</td>
<td>11 (38)</td>
</tr>
<tr>
<td>Combination</td>
<td>6 (21)</td>
</tr>
</tbody>
</table>
Clinical Outcome
Preoperative and postoperative data at 3 months and at the latest follow-up are presented in Table 2. The mean follow-up was 3.4 ± 2.1 years (range 3 months to 7.7 years). None of the patients died during surgery or during short-term follow-up. One surgical complication occurred at 3 months’ follow-up and involved a patient with rapid-onset dyspnea. Echocardiography revealed a severe mitral valve regurgitation jet at the side of the inserted patch. At acute surgical intervention, the patch appeared dehiscent because of a loosened suture. After correction, the patient’s clinical course was uncomplicated. During the follow-up period, patients were either asymptomatic or had mild symptoms (70% of them were in NYHA functional class I, and 30% were in class II). The number of cardiac drugs prescribed decreased significantly; before intervention, the number of cardiac drugs used was 1.5 ± 0.7, whereas after surgery, the number of drugs decreased to 0.5 ± 0.7. In 1 of the 2 patients with atrial fibrillation before surgery, sinus rhythm was restored and was maintained under medical treatment postoperatively. No patient needed permanent cardiac pacing.

In relation to the preoperative data, we found a mean reduction in septal thickness of 5.9 ± 2.3 mm after the surgical procedure. Moreover, short-term follow-up demonstrated that the LVOT gradient, mitral regurgitation, and SAM of the mitral valve were significantly reduced. At the latest patient visit, the beneficial results were maintained compared with the data at 3 months’ follow-up.

Preoperative and postoperative echocardiograms from the same patient after MLE and myectomy are shown in the Figure.

Discussion
LVOT is present in 20% to 25% of HOCM patients and results primarily from septal hypertrophy. Besides the myocardium, the anatomy of the mitral valve apparatus also frequently appears anomalous and may add to the obstruction component. Normally, the mitral valve leaflets coapt below the outflow tract as they are pulled posteriorly by the papillary muscles, where they do not impede the outward-directed blood flow. Well-recognized elements that may disrupt this coaptation mechanism are valve elongation and anterior displacement of the papillary muscles, which predispose to systolic anterior motion. Consequently, outflow tract obstruction and mitral regurgitation may persist after successful surgical myectomy. Therefore, mitral valve replacement has been alternatively performed to counteract residual SAM in patients regarded as less-suitable candidates for septal myectomy. The thromboembolic complications due to long-term use of anticoagulants restrict the beneficial use of an artificial valve prosthesis. Mitral leaflet plication has been introduced as a successful alternative to mitral valve replacement.

At our institute, we developed an alternative surgical procedure after septal myectomy that aims to reduce the risk of a residual outflow obstruction due to SAM of the mitral valve. The technique entails septal myectomy in combination...
with a patch of autologous pericardium inserted into the anterior mitral valve leaflet. Initially, patients treated with the combination of myectomy and MLE were selected primarily on the basis of the echocardiographic findings of an elongated MLA. After a short-term follow-up period, we concluded that application of the combined technique resulted in superior hemodynamic results compared with myectomy alone. In the present study, we report the long-term follow-up results of this alternative approach in a larger patient population. Within the next period, 29 of 32 patients selected for surgical myectomy demonstrated an enlarged mitral valve leaflet area (16.7±3.4 cm²), which was significantly above values of a control group of patients (<12 cm²). Clinical and hemodynamic parameters including functional class, reduction of the LVOT gradient, and attenuation of mitral valve regurgitation and SAM showed sustained improvement during this period. In 90% of the patients treated with the combined technique, SAM was reduced to grade 0 (absent) or grade I (mild). It is important to realize that the severity of mitral regurgitation is related to the presence of SAM.²⁸ Indeed, mitral valve incompetence was absent or trivial in 97% of patients in the present study.

We regard MLE as a safe addition to myectomy because there was no mortality in the present study. In addition, no ventricular septal defects or complete AV block was seen. One patient needed reoperation because of a dehiscent pericardial patch. Mitral valve function was maintained without echocardiographic observation of a restricted mitral valve opening. In this respect, the combined technique might serve as a good alternative to septal myectomy alone in selected patients.

**MLE: Why Does It Work?**

In most patients with hypertrophic cardiomyopathy, the abnormal motion of the mitral valve in systole plays a key role in creating the outflow tract obstruction.⁶,⁷ Several factors may be responsible for this phenomenon. The Venturi mechanism and flow drag of the leaflets due to increased mitral leaflet length, laxity, and anterior displacement of the papillary muscles allow the valve to protrude in the outflow tract.⁴ Also, inward displacement of the papillary muscles toward each other results in chordal slack in the central leaflet portion and consequently SAM in the central portion of the valve.⁵ To counteract these forces, the pericardial patch is grafted in the center portion of the anterior leaflet, where SAM typically reaches a maximum.⁵,⁸,¹¹,²３ By extending the patch across the bending point of the mitral valve, we hypothesize that we stiffen the central parts of the buckling anterior leaflet, preventing abnormal mobility. In addition, the patch increases the width of the leaflet, which results in a horizontal extension. The widening of the leaflet may cause a lateral shift of the chordae attaching central portions of the valve. This displacement stretches the chordae, everts them, and enhances leaflet coaptation.²⁸

Enlargement of the leaflet area could also add positively to maintenance of valve tethering once the streamlines of flow are normalized by septal myectomy.²⁸ During systole, the blood flow in the septal hypertrophied heart is forced to go around the septum and flows partially toward the posterior part of the anterior leaflet. The force of this streamline of flow pushes the valve into the LVOT. After septal myectomy, the flow stream straightens, hitting the mitral valve onto the anterior surface and pressing the leaflets toward the left atrium. The force that directs the enlarged valve posteriorly is linear to the leaflet area exposed to that flow. In fact, the patch appears tightened in systole, the anterior leaflet is directed toward the left atrium, and SAM and mitral regurgitation are abolished (Figure).

Septal myectomy is the most widely used surgical therapy in drug-refractory hypertrophic cardiomyopathy, with beneficial results in reducing outflow obstruction and mitral regurgitation. Because the outflow tract obstruction is multifactorial in origin, several different methods besides the classic myectomy have been developed to treat this heterogeneous disease. The present study cohort consisted of selected patients who demonstrated enlarged MLAs and typical SAM, as previously described by Klues et al.¹⁹ This subset of patients with obstructive cardiomyopathy is particularly predisposed to residual SAM after a successful myectomy and would therefore benefit from the MLE procedure.

Mitral valve plication is another approach to avoid residual obstruction in selected patients.³ It was designed to avoid mitral valve repair with a prosthesis, and hemodynamic results were encouraging, as in the present study. The selection criteria for plication included not only a relatively thin ventricular septum or an abnormal mitral valve apparatus but also a persistent obstruction after myectomy. In the present study, we did not treat previously operated patients. Also, we could not compare MLE to the results with valve prosthesis because this has not been a routine procedure at our institute.

Recently, percutaneous transluminal septal myocardial ablation (PTSMA) has been introduced as a new, nonsurgical approach to reduce septal width.²⁹ The procedure leads to localized thinning and contractile dysfunction of the septum, expansion of the LVOT, and thus reduction of the LVOT gradient. The anatomy of the mitral valve apparatus, however, remains unaltered, and at this moment, it is unknown whether comparable results can be obtained in this patient group with PTSMA. The present technique appears especially useful for patients with failed PTSMA and persisting mitral valve regurgitation.

**Conclusions**

MLE in combination with myectomy is an effective and safe treatment for patients with HOCM. Long-term follow-up demonstrates sustained improvement in functional class, reduction of obstruction, and reduction in the severity of SAM and mitral insufficiency. Because the present technique offers a broadening of the surgical possibilities, we believe that MLE could become the preferred choice in persistent LVOT and SAM after PTSMA. The technique appears to be especially effective in patients with an enlarged anterior MLA. Future randomized studies will need to examine the status of the different techniques in patients with hypertrophic cardiomyopathy and obstruction.
References
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