A contemporary European experience with surgical septal myectomy in hypertrophic cardiomyopathy

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Aims

The recent American College of Cardiology and American Heart Association Guidelines on hypertrophic cardiomyopathy (HCM) have confirmed surgical myectomy as the gold standard for non-pharmacological treatment of obstructive HCM. However, during the last 15 years, an extensive use of alcohol septal ablation has led to the virtual extinction of myectomy programmes in several European countries. Therefore, many HCM candidates for myectomy in Europe cannot be offered the option of this procedure. The purpose of our study is to report the difficulties and results in developing a myectomy programme for HCM in a centre without previous experience with this procedure.

Methods and results

The clinical course is reported of 124 consecutive patients with obstructive HCM and heart failure symptoms who underwent myectomy at a single European centre between 1996 and 2010. The median follow-up was 20.3 months (inter-quartile range: 3.9–40.6 months). No patients were lost to follow-up. A cumulative incidence of HCM-related death after myectomy was 0.8, 3.3, and 11.2% at 1, 5, and 10 years, respectively, including one operative death (procedural mortality 0.8%). The left ventricular (LV) outflow gradient decreased from 95 ± 36 mmHg before surgery to 12 ± 6 mmHg at most recent evaluation (P < 0.001), with none of the patients having a significant residual LV outflow gradient. Of the 97 patients in New York Heart Association functional class III–IV before surgery, 93 (96%) were in class I–II at most recent evaluation (P < 0.001).

Conclusion

Our results show that the development of a myectomy programme at a centre without previous experience with this procedure is feasible and can lead to highly favourable clinical results.

Keywords

Myectomy • Surgery • Hypertrophic cardiomyopathy

Introduction

The recommendations of the American College of Cardiology and European Society of Cardiology Expert Consensus Conference on the management of hypertrophic cardiomyopathy (HCM), and the recent American College of Cardiology and American Heart Association Guidelines on HCM, have confirmed surgical septal myectomy as the gold standard for non-pharmacological treatment of obstructive HCM.1,2 However, in recent years, percutaneous alcohol septal ablation has been strongly promoted in Europe as a less invasive and safer alternative to the myectomy operation for patients with obstructive HCM.3–10 This policy has led to the virtual extinction of surgical myectomy programmes in several European countries with a long tradition for surgical treatment of patients with HCM.11 Therefore, many European patients with HCM and severe symptoms of heart failure cannot be offered...
the gold-standard treatment suggested by the HCM international guidelines, but only the alternative of alcohol septal ablation.

However, recent data have generated concern regarding the possibility that the transmural infarction and scar caused by septal ablation may increase the risk for life-threatening ventricular tachyarrhythmias and sudden death in HCM.12–20 Moreover, evidence has accumulated on the important role of abnormal papillary muscles and mitral valve chordae in contributing to left ventricular (LV) outflow obstruction in HCM.21–29 Such abnormalities of the mitral valve apparatus cannot be treated by alcohol septal ablation, but only with surgical intervention. In this context, we considered of interest to report our experience with developing a surgical programme for the myectomy operation.

Methods

Study population

The present investigation includes 124 consecutive symptomatic patients with obstructive HCM who underwent extended surgical myectomy at our institution between January 1996 and July 2010. Before surgery, each of the study patients had an LV outflow gradient of ≥50 mmHg at rest and disabling heart failure symptoms despite medical therapy. Operative mortality included any death within 30 days after operation. Follow-up data were obtained between January and September 2010 in each of the surviving study patients.

Diagnosis and echocardiographic evaluation

The diagnosis of HCM was based on the echocardiographic demonstration of a hypertrophied and non-dilated LV (wall thickness ≥15 mm in adults, or the equivalent relative to the body surface area in children) in the absence of another cardiac or systemic disease that could produce a comparable magnitude of LV hypertrophy.30,31 Echocardiographic measurements were obtained as described previously.30,31 Left ventricular outflow tract obstruction was defined as a peak instantaneous outflow gradient of ≥30 mmHg by continuous-wave Doppler under basal conditions.31–33

Surgical procedures

After induction of general anaesthesia, intraoperative transoesophageal echocardiography (TEE) was performed to determine the extension of the myectomy, as well as to assess the morphology of the mitral valve and the presence of associated primary mitral valve abnormalities.34 Transoesophageal echocardiography was repeated immediately after surgery, in the operating room and off cardiopulmonary bypass, in order to detect a residual LV outflow tract gradient and aortic or mitral valve regurgitation, as well as to identify potential surgical complications, such as ventricular septum perforation or coronary fistula. The septal myectomy (in the present era commonly referred to as ‘extended myectomy’) was performed during cardiopulmonary bypass through an aortotomy. Two longitudinal incisions are started in the basal septum, 2–3 mm below the aortic valve, and extended distally to the base of the papillary muscles (equatorial zone), creating a trapezoidal trough which is wider towards the apex than at the subaortic level.23,24,27,35 Great care was taken to excise the cardiac muscle specimen in one piece in order to leave a smooth surface on the remaining septum. In patients with LV outflow obstruction in whom a mid-ventricular obstruction due to markedly hypertrophied papillary muscles or muscle bundles was also present, an additional small resection was made around the base of the papillary muscle.23,27,35 After the excision of the cardiac muscle (myectomy), the operative procedure was completed by interventions on the subvalvular mitral apparatus. Fibrous or muscular structures connecting the papillary muscles to the ventricular septum or LV free wall are present in almost all patients with obstructive HCM and limit the mobility of the papillary muscles.23,27,35 Such structures, identifiable only at the time of surgery, were present and systematically excised and/or dissected free (up to the base of the papillary muscle) in each of our study patients in order to increase the papillary muscle mobility. Anomalous chordal structures or fibrous attachments of the mitral leaflets to the ventricular septum or free wall are found in a minority of patients with HCM and, whenever present in our study patients, were excised or divided.23,26,35 Anomalous attachments of the papillary muscle directly into the anterior mitral leaflet are uncommon in HCM and, in our patients, were resected when attached to the body (not the margin) of the leaflet.23,24 The extended myectomy operation was performed by the senior surgeon (P.F.) in 115 (93%) of the 124 study patients and by a surgeon in training for the myectomy operation in the remaining 9 patients (S.P.). Concomitant surgical procedures were also performed in selected patients.

During the last 3 years, myectomy was associated with surgical therapy of atrial fibrillation in patients presenting with paroxysmal or persistent atrial fibrillation. Lines of ablation were performed by using a bipolar radiofrequency energy device (Atricure, Inc., Cincinnati, OH, USA). The lesion set included an epicardial encircling of the pulmonary veins and a crux line on the external side of the left atrial appendage.

Statistical methods

The median and the inter-quartile range (IQR) of follow-up were calculated according to the reverse Kaplan–Meier method. Comparisons of continuous variables were performed with the Wilcoxon test. Analyses of change for parameters evaluated before surgery and at the most recent evaluation were performed by means of the McNemar change test and sign test, for binary and continuous variables, respectively. The crude cumulative incidence function estimates of HCM-related death were computed according to Kalbfleisch and Prentice. All reported P-values are two-sided. SPSS statistical software (SPSS, Chicago, IL, USA) and SAS System 9.2 (SAS Institute, Cary, NC, USA) were used for the calculations.

Results

Baseline characteristics

The clinical characteristics of the 124 study patients are summarized in Table 1. In the study cohort, age ranged from 2 to 81 years (mean 51 ± 17; median 54 years), with five of the patients being <18 years old and two patients <12 years old at the time of surgery. Of the 124 patients included in the study, 97 (78%) were in New York Heart Association (NYHA) functional class III–IV at the time of the operation. In 26 of the remaining 27 study patients, myectomy was performed because of the persistence of drug-refractory symptoms, including heart failure symptoms, chest pain, and/or recurrent syncopal episodes, that interfered with everyday activity and quality of life. The remaining study patient who underwent myectomy in the absence of functional class III–IV symptoms was a woman with marked LV outflow obstruction who had developed severe heart failure symptoms during her first pregnancy, but wished to have a second pregnancy. In this patient, myectomy was performed to reduce the risk...
of complications during pregnancy. Her second pregnancy was un-
complicated by HCM-related symptoms.

Septal myectomy was a repeat procedure in five (4%) patients
who had previously undergone a myectomy operation at other
institutions, but had a significant residual LV outflow gradient
under basal conditions and severe symptoms of heart failure.
Septal myectomy was associated with mitral valve repair in 7
(5.6%) and mitral valve replacement in 2 (1.6%) of the 124 study
patients. Of the two patients with mitral valve replacement, one
was in cardiogenic shock due to rupture of the mitral valve
chordae and the other had severe chronic obstructive pulmonary
disease and rupture of the posterior leaflet chordae. Other opera-
tive procedures concomitant to ventricular septal myectomy, in-
cluding the operative interventions on the subvalvular mitral
apparatus, are summarized in Table 2. In particular, fibrous or mus-
cular structures connecting the papillary muscles to the ventricular
septum or LV free wall were present and excised in each of our
study patients, in order to increase the papillary muscle mobility
(Figure 1).

The number of septal myectomy operations was unequally dis-
tributed during the 15 years covered by the present investigation

| Variable | Demographic data |
|----------|------------------|
| Age (years), mean and SD (median) | 51 ± 17 (54) |
| Male sex, n (%) | 56 (45) |

| Clinical status |  |
|-----------------|---|
| Shortness of breath, n (%) | 120 (97) |
| Syncope, n (%) | 24 (19) |
| NYHA functional class III or IV, n (%) | 97 (78) |
| History of prior myectomy, n (%) | 5 (4) |
| History of prior atrial fibrillation, n (%) | 27 (22) |

| Pre-operative echocardiographic data |  |
|-------------------------------------|---|
| Septal LV wall thickness (mm), mean and SD | 23 ± 6 |
| LV end-diastolic cavity dimension (mm), mean and SD | 42 ± 7 |
| Resting LV outflow gradient (mmHg), mean and SD | 95 ± 36 |
| Moderate or severe mitral valve regurgitation, n (%) | 56 (45) |

| Treatment, n (%) |  |
|------------------|---|
| β-Blockers | 102 (82) |
| Calcium antagonists | 12 (10) |
| Diuretics | 48 (39) |
| Amiodarone | 15 (12) |

| NYHA, New York Heart Association; LV, left ventricular; SD, standard deviation. |

| Variable | Operative procedures concomitant to septal myectomy in the 124 study patients |
|----------|-----------------------------------------------------------------------------|
| Coronary artery bypass graft, n (%) | 9 (7.3) |
| Mitral valve replacement, n (%) | 2 (1.6) |
| Mitral valve repair, n (%) | 7 (5.6) |
| Aortic valve replacement, n (%) | 2 (1.6) |
| Epicardial cardioverter defibrillator, n (%) | 1 (0.8) |
| Subvalvular mitral apparatus |  |
| Resection of fibrous–muscular attachments between papillary muscle and ventricular septum or LV free wall, n (%) | 124 (100) |
| Excision of anomalous chordal attachments between mitral valve leaflets and ventricular septum or LV free wall, n (%) | 11/91 (12.1) |
| Resection of anomalous attachment of the papillary muscle into the anterior mitral valve leaflet, n (%) | 2/91 (2.2) |

| Data were available in 91 of the 124 study patients. |

Figure 1 Intraoperative transthoracic echocardiographic images before (A), and after (B), the excision of fibrous–muscular structures connecting the papillary muscles to the ventricular septum and left ventricular free wall. The area of excision of the fibrous–muscular structures is indicated by arrows.
and increased exponentially in recent years, with 109 (88%) of the 124 procedures being performed during the last 5 years (Figure 2A). The mean weight of the excised myocardium at the time of surgery in the 124 study patients was 4.2 ± 1.9 g. A specimen of the excised myocardium is shown in Figure 3.

Of the 124 study patients, 9 (7.3%) had received an implantable cardioverter defibrillator (ICD) before cardiac surgery. In one of these nine patients, the percutaneous ICD was upgraded to an epicardial cardioverter defibrillator at the time of surgery, because of massive LV hypertrophy (a maximal wall thickness of 51 mm). In one patient, an ICD was implanted during follow-up. Of the 10 (8.1%) study patients in whom a cardioverter defibrillator had been implanted either before myectomy operation or during follow-up, 1 received an appropriate intervention of the device (overdrive pacing) for ventricular tachycardia. No patients received inappropriate shocks.

**Clinical course after myectomy operation**

The median duration of follow-up in the 124 study patients was 20.3 months (IQR: 3.9–40.6 months). Of the 124 study patients, 1 patient (0.8%), a 78-year-old woman, died 14 h after surgery as a consequence of a massive bleeding due to perforation of the free wall contiguous to the anterior septum.

A total of two HCM-related deaths occurred after hospital discharge. A 21-year-old patient with extreme LV wall thickness (a pre-operative maximal wall thickness of 36 mm) refused implantation of an ICD and died suddenly 31 months after myectomy. A 50-year-old patient died of an ischaemic cerebrovascular event 6 years after surgery. A total of two non-HCM-related deaths occurred during follow-up, one due to pneumonia in an 89-year-old patient, 7 years after surgery, and the second due to lung cancer in a 67-year-old patient, 2 years after surgery (Table 3). Including one operative death (procedural mortality...
A clinical and echocardiographic follow-up evaluation was performed in a dedicated HCM clinic between January and September 2010. The LV outflow tract gradient before surgery and at most recent evaluation was available in 113 (91%) of the 124 study patients. The LV outflow gradient decreased from $95 \pm 36$ mmHg (range: 52–180 mm Hg) before surgery to $12 \pm 6$ mmHg at most recent evaluation ($P < 0.001$). None of these patients had a significant ($\geq 30$ mmHg) residual LV outflow gradient under basal conditions or at Valsalva manoeuvre at most recent evaluation. Of these 113 patients in whom resting LV outflow gradient measurements were available before surgery and at most recent evaluation, 9 had a residual gradient of $\geq 25$ mmHg. Using colour and pulsed Doppler ultrasound, the site of the gradient was located at the mid-ventricular cavity, below the mitral valve leaflets, in each of these nine patients. At most recent evaluation, only one of these nine patients had significant heart failure symptoms (NYHA functional class III). The left atrial dimension before surgery and at most recent evaluation was available in 109 (88%) of the study patients and decreased significantly after surgery ($P < 0.001$). Data on NYHA functional class before surgery and at most recent evaluation were available in 116 (94%) of the study patients. Of the 97 patients in NYHA functional class III–IV before surgery, 93 (96%) were in functional class I–II at most recent evaluation ($P < 0.001$). Of the four patients with severe heart failure symptoms at most recent evaluation, one had shown clinical deterioration to NYHA class III–IV 18 months after surgery. In this patient, an echocardiogram identified severe mitral valve regurgitation and TEE documented perforation of the anterior mitral leaflet. At surgery, a 2 mm perforation of the anterior mitral leaflet was identified and repaired, and an anomalous attachment of the papillary muscle to a posteriorly retracted
fibrous leaflet was excised. At most recent evaluation, the patient was in NYHA class II and the echocardiogram showed mild mitral valve regurgitation.

Of the 124 study patients, 27 (22%) had a pre-operative history of paroxysmal or persistent atrial fibrillation. None of the study patients were in permanent atrial fibrillation.

The patients with atrial fibrillation were older (60 years, IQR: 50–64) than patients without atrial fibrillation (51 years, IQR: 36–62) (P = 0.020) and had a significantly higher median left atrial dimension (59 mm, IQR: 56–61 vs. 46 mm, IQR: 43–50) (P < 0.001). At most recent evaluation, 25 (92%) of the 27 patients with preoperative history of paroxysmal or persistent atrial fibrillation were in sinus rhythm and 2 were in permanent atrial fibrillation. During the last 3 years, 9 of the 27 patients with a pre-operative history of atrial fibrillation had undergone surgical therapy for atrial fibrillation at the time of the myectomy operation. Each of these nine patients was in sinus rhythm at most recent evaluation.

Discussion

The ACC and ESC Expert Consensus Conference and the recent ACC and AHA guidelines on HCM have stated that surgical septal myectomy is the gold-standard and primary treatment option for patients with obstructive HCM and severe symptoms of heart failure and that alcohol septal ablation should be selected when the surgical risk is considered unacceptable because of serious co-morbidities or advanced age. However, after the introduction of percutaneous alcohol septal ablation, the surgical myectomy operation has almost disappeared in European countries, including some with a long and extensive experience with this operation. Therefore, many severely symptomatic European patients with obstructive HCM are denied the option of surgical septal myectomy, which is the primary treatment strategy recommended by the HCM international guidelines.

Conversely, in recent years, the surgical septal myectomy operation has become the most frequently selected treatment at North American referral centres that offer both expert surgical myectomy and alcohol septal ablation as possible treatment options for patients with obstructive HCM. This preference for surgical treatment has probably been driven by the growing evidence of the favourable long-term results of myectomy, when performed by surgeons experienced with this procedure. Furthermore, morphological abnormalities of the mitral valve apparatus that limit the mobility of the papillary muscles and mitral valve leaflets are present in the majority of patients with obstructive HCM and can be treated only by surgery. These anomalies include fibrous or muscular structures connecting the papillary muscles to the ventricular septum or LV free wall, anomalous chordal structures or fibrous attachments of the mitral leaflets to the septum or free wall, or, less commonly, a direct insertion of the papillary muscle into the anterior mitral leaflet.

We believe that European patients with HCM should be offered the option of surgical septal myectomy, as indicated by the HCM international guidelines. Therefore, we report here our results with developing a surgical referral programme for the myectomy operation. Our experience shows that it is possible to obtain favourable results for an elective procedure such as the myectomy operation, by relying initially on the expertise of a single surgeon and gradually establishing a dedicated surgical and cardiological HCM team through a close collaboration with cardiology centres with large experience in the clinical management of patients with HCM.

Survival was excellent in our consecutive 124 patients with HCM who underwent surgical myectomy since 1996, with a single hospital death and two HCM-related deaths during follow-up. At most recent evaluation, none of the surviving study patients had a significant residual LV outflow gradient, and the large majority had mild or no symptoms of heart failure (NYHA class I or II). In most patients, this important symptomatic improvement was already evident in the first days after myectomy. This rapid amelioration of the clinical condition after surgical myectomy is consistent with the experience of other centres with large myectomy programmes and can be explained by the underlying pathophysiology of the disease. Surgical myectomy in HCM relieves the high LV systolic pressure overload due to the LV outflow gradient, as well as the volume overload secondary to mitral valve regurgitation, in a ventricle with a high end-diastolic pressure and a small cavity but preserved ejection fraction. Therefore, in most HCM patients, LV haemodynamics and symptoms improve, often dramatically, within days after surgery.

The number of surgical septal myectomies performed at our centre has grown rapidly during the last 5 years. A similar increase in myectomy operations has also been reported in recent years by centres with a long tradition for HCM surgery in North America. This increasing request for surgical myectomy underlines the need for referral centres with myectomy programmes in European countries where such programmes are not available. About two to three referral centres for surgical myectomy would probably be sufficient for a country with ~60 million people, because of the low absolute number of HCM candidates to surgery. At present, there are about five surgical referral centres for myectomy operation in the USA, a country of 300 million people.

The learning curve for surgical myectomy may be long because HCM patients with severe clinical expression of the disease are uncommon, and only a portion of such patients are surgical candidates. The specific experience required for this operation is also increased by the unusual surgical technique, which is based on an extensive cardiac muscle resection through an aortotomy, with limited visualization of the septum and the risk of causing a ventricular septal defect or damaging the aortic or mitral valve. During the last two decades, TEE guidance at the time of surgical myectomy, as well as modern cardiac preservation techniques, has contributed to make this operation easier than it was in the pioneer years of the early 1960s and have permitted to extend the septal muscle resection to the mid-ventricular level, allowing more complete reconstruction of the LV outflow tract and improving clinical results. Previous surgical experience with the treatment of congenital heart diseases associated with LV outflow tract obstruction, such as discrete subaortic membrane, subaortic fibromuscular tunnel, subaortic obstruction in complex cardiac anomalies, and post-correction of the atrio-ventricular canal, may also contribute importantly to reduce the learning curve for myectomy.
However, establishing a myectomy programme in a centre without previous experience with HCM surgery remains a complex undertaking and requires that a number of important pre-conditions are met. We believe that several components played a determinant role in our favourable results. The senior surgeon at our centre had acquired an initial experience with septal myectomy at another institution about two decades previously, and this experience was combined with an extensive expertise in reconstructive surgery for congenital heart disease and mitral valve repair. Moreover, our prolonged collaboration with cardiology centres with particular experience in the clinical management of patients with HCM allowed us to develop an integrated surgical and cardiological team for the evaluation and treatment of patients with obstructive HCM.

In conclusion, in Europe, a growing cardiological referral for septal myectomy in patients with obstructive HCM is confronted with an inadequate number of centres with experience with surgical myectomy. We believe that European patients with HCM should be granted the option of surgical septal myectomy, as indicated by the HCM international guidelines. Our results show that the initial establishment and subsequent gradual expansion of a myectomy programme at a centre without prior experience with this procedure is feasible and can lead to highly favourable clinical results, given that a number of critical preliminary conditions are met.

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