

Original Research

Surgical Septal Myectomy for Hypertrophic Cardiomyopathy in Greece: A Single-Center Initial Experience

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Introduction: Surgical septal myectomy is thought to be the gold standard of treatment for obstructive hypertrophic cardiomyopathy (HCM) with obstruction symptoms refractory to optimal medical therapy. In Europe, during the last 2 decades, myectomy has been set aside, while alcohol septal ablation has been widely promoted. In this paper, we analyze our first experience of surgical septal myectomy in a small cohort of patients with HCM coming from a single tertiary center.

Methods: Thirty-two patients (16 male, 50%) with a mean age of 58.1 ± 14.4 (range 12-79 years) underwent myectomy for HCM symptoms refractory to negative inotropic agents. The technique used for the myectomy was the one introduced by Andrew Morrow. Mean follow-up time after procedure was 16.8 ± 13.3 months with a median of 13 months (range 4-58 months).

Results: Post-myectomy, there was a significant improvement in patients' NYHA class (from 3.3 ± 0.46 to 1.38 ± 0.49 , $p < 0.0005$), while interventricular septum thickness was reduced from 2.3 ± 0.4 cm to 1.6 ± 0.4 cm ($p < 0.0005$), and peak gradient at the site of obstruction from 94.9 ± 29 to 16.7 ± 7.9 mmHg ($p < 0.0005$). During the follow-up period, only 1 out of 32 patients died, from non-cardiovascular causes, with the overall survival post-myectomy being 97.2% (95%CI: 94.5-99.9%) at 1-year follow up.

Conclusions: Surgical septal myectomy in patients with HCM and drug-refractory symptoms is a safe procedure that greatly improves symptoms and quality of life. Further follow-up of our patients is mandatory in order to determine whether the good survival rate achieved at 1 year will persist.

Hypertrophic cardiomyopathy (HCM) is predominantly a disease of the left ventricular outflow tract (LVOT), since 70% of patients exhibit obstruction, either at rest or during exercise.¹ Obstruction of the LVOT is one of the major determinants of symptom development and prognosis.² Patients with obstructive HCM and heart failure symptoms (class III or IV according to the New

York Heart Association [NYHA] classification) that are refractory to optimal medical therapy with negative inotropic agents should be treated with an interventional method that alleviates the obstruction and relieves symptoms. The gold standard of treatment is thought to be surgical septal myectomy,³⁻⁸ although alcohol septal ablation (ASA) has been applied as an alternative method during the last 2 de-

cases.^{9,10} In Europe, during the same period of time, myectomy has been set aside, while ASA has been strongly promoted.¹¹ In this paper we analyze our first experience of surgical septal myectomy in a small cohort of patients with HCM coming from a single tertiary center.

Methods

Study design

We conducted a retrospective study to evaluate the course and outcomes of patients with severe symptomatic HCM who underwent surgical septal myectomy, focusing on the effect of the procedure on LVOT obstruction amelioration and relief of heart failure symptoms.

Selection of patients

The study population was selected from a cohort of more than 400 patients with HCM, who were treated at the Cardiomyopathies Center of AHEPA University Hospital and St. Luke's Cardiac Surgery Institution, Thessaloniki, Greece. The diagnosis of HCM was based on the echocardiographic appearance of a hypertrophied non-dilated left ventricle, in the absence of any other cause able to produce the magnitude of the observed hypertrophy. Obstruction of the LVOT was defined as a peak gradient (estimated by placing the continuous wave Doppler vector in the outflow tract point where peak turbulent flow was observed) of at least 30 mmHg at rest, or a provokable gradient of at least 50 mmHg obtained easily with a Valsalva maneuver or during a standing position. In 36 patients diagnosed with HCM, presenting with rest or provokable gradient ≥ 50 mmHg and NYHA class III-IV, the severity of their symptoms, despite optimal medical treatment with negative inotropic drugs (beta-blockers and disopyramide), led to a recommendation for surgical septal myectomy. Among these, 1 patient preferred to undergo ASA, 3 refused any procedure, and 32 provided written informed consent to undergo surgery. These patients were referred for surgical myectomy to St. Luke's Cardiac Surgery Institution in Thessaloniki, Greece, between February 2007 and June 2011. Prior to this, coronary angiography was performed in patients aged >40 years (30 patients) to exclude underlying coronary artery disease. In all patients, an echocardiogram was obtained a few days prior to myectomy and post-myectomy before discharge from hospital. In subjects

who were taking antihypertensive agents that had a potential impact on the severity of the gradient estimated (such as angiotensin-converting enzyme inhibitors or angiotensin receptor blockers), antihypertensive medication was stopped for at least 2 half-lives before the gradient was measured, and in particular for the measurement obtained a few days prior to myectomy.

Surgery

The technique used for the myectomy was the one introduced by Andrew Morrow. This comprises an aortotomy, through which two parallel longitudinal incisions are made in the basal septum, connected by a third vertical incision just below the right coronary cusp of the aortic valve, creating a trough approximately 4-5 cm in length that extends to just beyond the mitral-septal contact.⁵⁻⁸ In some cases the incision was extended more distally, as far as the base of the papillary muscles (extended myectomy). The target was to resect 5-10 g of myocardium.

The extent of myectomy was monitored by intraoperative transesophageal echocardiography, which also provided additional information regarding the morphology of the mitral valve and the presence of other cardiac abnormalities. LVOT evaluation during the final stages of the operation was crucial in order to exclude the presence of residual gradient and to detect any possible complications, such as perforation of the septum.

Whenever necessary, a concomitant procedure (such as coronary artery bypass grafting [n=1], Maze procedure [n=3], mitral valve repair using the edge-to-edge Alfieri technique [n=3], aortic valve replacement [n=3] or repair [n=1], or pulmonary vein ablation [n=1]) was performed. All the operations were performed by the same surgical team in the same theatre. Twelve patients underwent operation in 2011, 11 patients during 2010, 7 patients in 2009 and 2 patients in 2007.

Although it is beyond the scope of this paper, we should report that, apart from the group of 32 patients with LVOT obstruction who were treated surgically, 2 other patients suffering from mid-ventricular HCM underwent a successful extended mid-left ventricular myectomy, and 2 patients suffering from pure apical HCM underwent a successful apical myectomy, using a double approach technique in both cases, i.e. transaortic and transapical. The latter cases are a subject of a forthcoming paper.

Statistical analysis

Statistical analyses were performed using SPSS software (version 19.0, IBM SPSS Statistics, Chicago, Illinois). All analyses were two-tailed and p-values were considered significant if <0.05 . The change in NYHA score was assessed using the Wilcoxon test. The changes in the pressure gradient in the LVOT, in interventricular septum thickness, and in mitral regurgitation (MR) severity were assessed using a paired sample t-test. The survival of patients after myectomy was evaluated with Kaplan–Meier curves.

Ethical considerations

All the patients gave their signed informed consent on their first visit to our center, permitting the use of their anonymized data for investigational or scientific purposes. The study protocol was approved by the Institutional Ethics Committee.

Results

Patients' demographic, clinical and echocardiographic characteristics are outlined in Table 1. There were 16 males (50%) and the mean age pre-myectomy was 58.1 ± 14.4 years (range 12-79 years). The mean follow-up time after the procedure was 16.8 ± 13.3 months, with a median of 13 months (range 4-58 months). Before surgery, all 32 patients received b-blockers while 12 (37.5%) also received disopyramide up to a maximum dose of 400 mg. Amiodarone was

administered to 8 patients (25%) and anticoagulants to 7 (21.9%), as per indications. Four patients suffered from hypertension and were taking angiotensin-converting enzyme inhibitors or angiotensin receptor blockers. In addition, 2 (6.25%) patients in our cohort were being treated for diabetes mellitus, while during the preoperative assessment 2 (6.25%) patients were discovered to have coronary artery disease.

There was a significant improvement in patients' NYHA class, from a mean of 3.3 ± 0.46 pre-myectomy to 1.38 ± 0.49 post-myectomy ($p < 0.0005$). Interventricular septum thickness was reduced, from 2.3 ± 0.4 cm to 1.6 ± 0.4 cm, after the procedure ($p < 0.0005$), as was the peak gradient at the site of obstruction, from 94.9 ± 29 mmHg to 16.7 ± 7.9 mmHg postoperatively ($p < 0.0005$) (Figures 1 & 2). Mean absolute and percentile gradient difference pre- and post-myectomy were 78.2 ± 30 mmHg (range 34-160 mmHg) and $81 \pm 11\%$ (range 53-97%), respectively. There was no significant correlation between septal thickness reduction and LVOT gradient reduction (absolute or percentile) due to myectomy ($p = 0.156$). The mean myocardial tissue weight removed from the interventricular septum was 8.4 ± 3 g (range 3.3-12.5 g).

Alleviation of LVOT obstruction accompanied by reduction of the systolic anterior motion of the mitral leaflets led to significant regression of MR, since 14/32 (43.7%) patients had moderate to severe MR pre-myectomy, while no patient had signs of moderate or severe MR after the procedure. Pre-myectomy, 8 patients (25%) displayed permanent atrial fi-

Table 1. Basic demographic, clinical and echocardiographic characteristics of patients with hypertrophic cardiomyopathy before and after myectomy. Data are presented as absolute numbers (percentage) and mean \pm standard deviation.

Variable	Pre-myectomy	Post-myectomy	p
Sex (male)	16 (50%)	–	–
Age (years)	58.1 ± 14.4	–	–
NYHA class:			
I	0	20 (62.9%)	<0.0005
II	0	12 (37.5%)	
III	23 (71.9%)	0	
IV	9 (28.1%)	0	
Peak gradient (mmHg)	94.9 ± 29	16.7 ± 7.9	<0.0005
IVS diastole (cm)	2.3 ± 0.4	1.6 ± 0.4	<0.0005
MR:			
No	1 (3.1%),	13 (40.6%)	<0.0005
Mild	6 (18.8%)	18 (56.3%)	
Moderate	23 (71.9%)	1 (3.1%)	
Severe	2 (6.3%)	0	
Tissue weight removed (g)	–	8.4 ± 3	–

NYHA – New York Heart Association; IVS – interventricular septum; MR – mitral regurgitation.

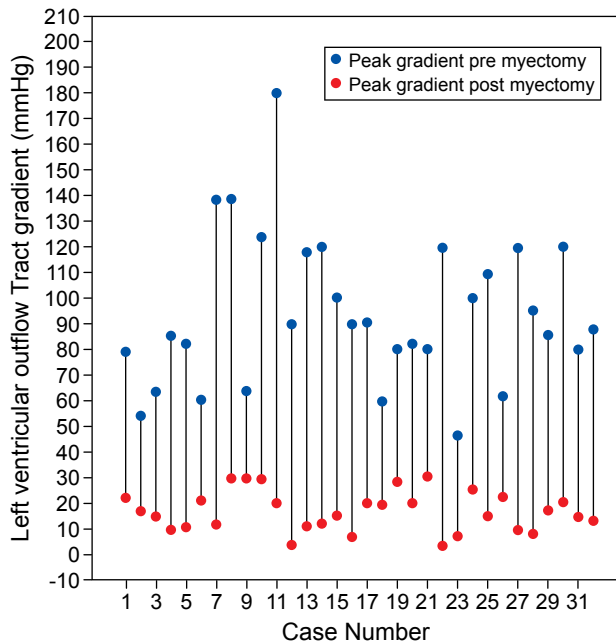


Figure 1. Graphical representation of left ventricular outflow tract gradients (in mmHg) recorded pre- and post-myectomy in each patient of our cohort with obstructive hypertrophic cardiomyopathy.

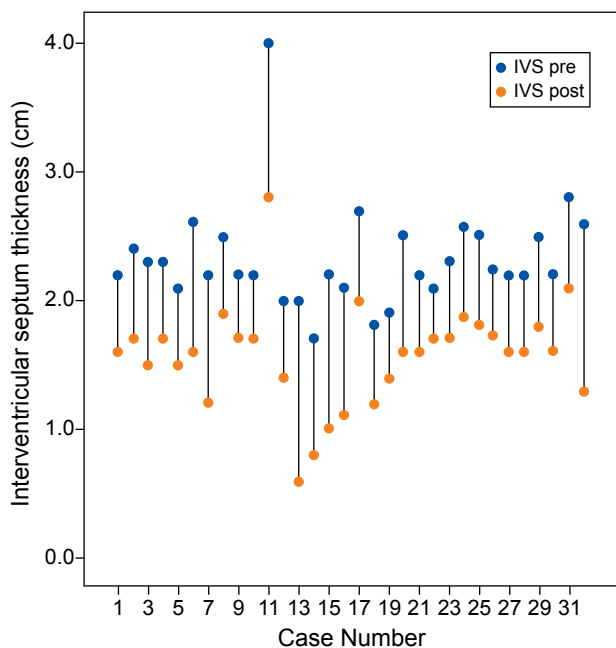


Figure 2. Graphical representation of interventricular septal thickness (IVS) during diastole (in cm) measured pre- and post-myectomy in each patient of our cohort with obstructive hypertrophic cardiomyopathy.

brillation, while no new cases of atrial fibrillation developed after surgery. Twenty-two patients (68.8%) developed new left bundle branch block post-procedure; one of them had a permanent pacemaker implanted 3 months postoperatively for complete atrioventricular block. One patient received an implantable-cardioverter defibrillator (ICD) preoperatively, while no patient needed an ICD during follow up. One patient developed a ventricular septal defect during myectomy, which was closed surgically.

Survival after myectomy

No deaths were recorded during the perioperative period or before hospital discharge. During a mean follow-up period of 16.8 ± 13.3 months after myectomy (median 13 months, range 4-58 months), only 1 patient died, from non-cardiovascular causes, about 1 year after myectomy. More specifically, the patient underwent a spinal cord neurosurgical intervention followed by weaning failure, sepsis, and finally death due to septic shock 2 months after the operation. The overall survival post-myectomy was 97.2% (95%CI: 94.5-99.9%) at 1 year follow up.

Discussion

Our study clearly demonstrates that surgical myectomy offers a great clinical benefit to HCM patients with refractory symptoms of heart failure, by reducing the LVOT gradient without causing serious complications and with excellent survival post-procedure (**Figure 3**). All of our patients who were initially in NYHA class III or IV improved to NYHA class I or II after myectomy. The improvement reached 100%, or in other words there was significant symptom relief of from 1 to 3 NYHA classes, a finding that is in concordance with older studies with patient populations similar to ours.¹²⁻¹⁶ Our results were also comparable with those of other studies in terms of gradient reduction (78.2 ± 30 mmHg) and post-myectomy measured gradient (10-15 mmHg).^{12,17} It is of great interest that no patient underwent mitral valve replacement. In 14 of the 32 patients with moderate to severe MR, we had almost complete relief of the MR by myectomy *per se*, while in only 3 patients was mitral repair (using the Alfieri technique) performed. The Alfieri technique (edge-to-edge repair) was chosen because the MR was due to organic disease of the valve (ruptured *chordae* of the A2 in 2 cases and the P2 in 1 case) and not due to systolic anterior mo-

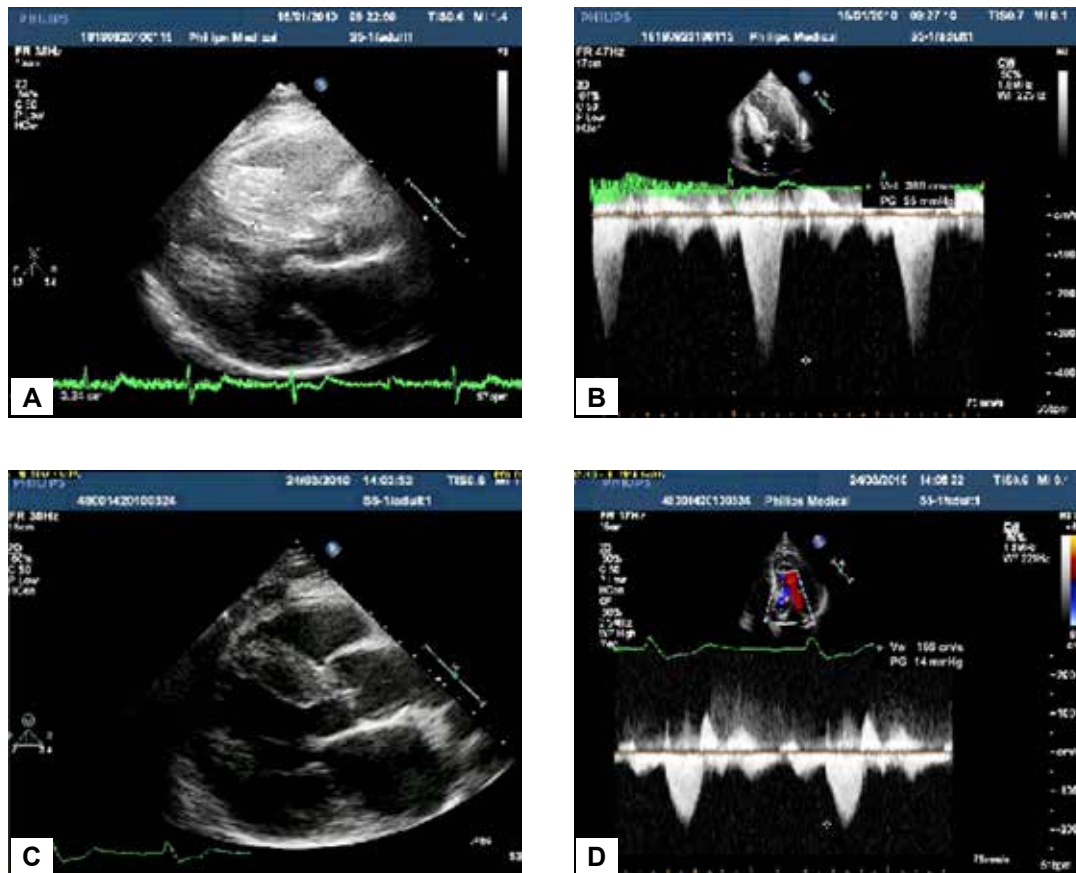


Figure 3. Echo images from the same patient before and after myectomy. Panel A represents a parasternal long-axis view showing an excessive septal thickness (>30 mm) causing left ventricular outflow tract obstruction. In Panel B, continuous wave Doppler recording at the left ventricular outflow tract demonstrates a peak gradient equal to 55 mmHg. After myectomy, the septal thickness has diminished significantly (C), while the peak gradient at the outflow tract is 14 mmHg (D).

tion (SAM) of the mitral leaflets alone. MR due to SAM alone is best treated by septal resection and does not require any additional measures. The trans-aortic Alfieri technique was preferred over a formal repair, with synthetic *chordae* and/or resections plus the use of rings through another incision (atriotomy), in order to minimize the cross-clamp time and also to avoid the use of a ring, which is a risk factor for iatrogenic SAM, even more so in the case of basal septal hypertrophy. Nevertheless if we had to perform a formal mitral valve repair through an atriotomy, we would have chosen a partial flexible ring (some type of band) only for the posterior mitral annulus, in order to avoid pushing the mitral apparatus towards the LVOT and thus creating SAM.

All patients were alive at hospital discharge and the 1-year total survival rate was 97.3%. Other studies reported a 5-year survival rate of 92-97%,^{12,16,18} a 10-year rate of 80-88%,^{12,13,15,18} and an approximate

20-year survival rate of 72% after myectomy,^{12,13,15} indicating that the good operative result is maintained for many years. Data from the Mayo Clinic have shown that operated patients with HCM displayed a survival rate comparable to that of the general age-matched US population,⁶ while according to a very recent paper from the same center, the continuously growing experience with ASA has offered treated patients remarkable survival rates, reaching those of septal myectomy.¹⁹ In another study from the same center, surgical myectomy performed in patients with HCM was associated with a marked reduction in the frequency of appropriate ICD discharge and a reduction in the risk of sudden cardiac death.^{17,20}

Although surgical myectomy is an established intervention to cure patients with severe symptomatic HCM, only a limited number of cardiothoracic centers worldwide are performing the technique nowadays, probably because of the lack of experienced

surgeons in this field. Most of the centers reporting a substantial number of patients (>100 patients) treated by surgical myectomy are in the US,^{6,18,21-23} and to a lesser degree Toronto.²⁴ Recently, a paper from Italy, concerning myectomy in 124 patients with obstructive HCM over 15 years, has also been published,²⁵ while myectomy programs in Switzerland⁸ and Germany,¹² although once robust, are now (and have been for years) essentially non-existent.

Limitations

Our study includes the data of patients who were treated in our specialized Cardiomyopathies Center and, although this is a retrospective study, we have a complete database concerning demographic, clinical, echo and operation details. We included a small number of patients with a satisfactory sex (50% male) and age (range 12-79 years) stratification, even though the follow-up period is still short. Additionally we should emphasize the substantial increase in the number of treated patients per year (23 patients during 2010 and 2011).

Conclusions

Our data presented here provide considerable evidence that surgical septal myectomy in patients with HCM and drug-refractory symptoms is a safe procedure that greatly improves symptoms and quality of life. Further follow up of our patients is required in order to determine whether the good survival rate that we achieved over 1 year will persist over a longer period.

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