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Review

# Does a standard myectomy exist for obstructive hypertrophic cardiomyopathy? From the *Morrow variations* to precision surgery

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ABSTRACT

*Objectives:* The purpose of this work is to revisit the history of surgical treatment for obstructive hypertrophic cardiomyopathy (oHCM) over the last 60 years, in the light of advancing knowledge of the pathophysiology of obstruction.
*Methods:* In this narrative review the contribution of the different surgical approaches to the field will be assessed in our personal experience in Florence.
*Results:* Septal myectomy is the treatment of choice in patients with obstructive hypertrophic cardiomyopathy who remain symptomatic despite optimal medical treatment. Over the decades, numerous "theme variations" of the Morrow operation have been proposed, each of them targeting a specific pathophysiological determinant of left ventricular outflow tract obstruction.
*Conclusions:* Precision surgery in oHCM patients today depends on the ability of the surgeon to combine and master these variations, with the bird's eye view allowed by climbing on the shoulders of giants.

## 1. Introduction

In 1958 a patient with a suspected congenital subaortic stenosis was referred to Dr. W.P. Cleland at Hammersmith Hospital (London). During the intervention, he noticed a markedly enlarged septum partially protruding into the left ventricular outflow tract (LVOT), but no evidence of fixed stenosis. Therefore, he decided to remove part of the hypertrophied septum and so performed the first myectomy. [1,2] Dr. Andrew G. Morrow, two years later, used septal myotomy to abolish the continuity of the muscular bundles believed to create a sphincter-like contraction in a young patient with hypertrophic cardiomyopathy and pre-operative evidence of severe LVOT obstruction (LVOTO). [2] Over the years he refined the technique associating myotomy to proper myectomy finally composing the "main theme" of LVOTO surgical treatment. [3] The approach worked, although no one at the time really knew why. Indeed, the rationale became evident only after 20 years, following the introduction of echocardiography and the description of systolic anterior motion of the mitral valve (SAM).

Over the decades, numerous "theme variations" of the Morrow operation have been developed, each of them targeting a specific pathophysiological determinant of LVOTO. While some variations have been later abandoned, other have contributed with peculiar aspects still in use, allowing tailored approaches in individual patients. Precision surgery in obstructive hypertrophic cardiomyopathy (oHCM) patients today depends on the ability of the surgeon to combine and master these variations, with the bird's eye view allowed by climbing on the shoulders of giants. The purpose of this work is to revisit the history of surgical treatment for oHCM over the last 60 years, in the light of advancing knowledge of the pathophysiology of obstruction. The surgical techniques described below are summarized in Fig. 2 and in Table 1.

## 2. Pathophysiology of left ventricular outflow tract obstruction

LVOTO is a multifactorial, dynamic phenomenon that functional and

*Abbreviations:* ASA, alcohol septal ablation; AML, anterior mitral leaflet; AV, atrioventricular; FU, follow-up; LV, left ventricle/ventricular; LVOTO, left ventricular outflow tract obstruction; oHCM, obstructive hypertrophic cardiomyopathy; PM, pacemaker; PML, posterior mitral leaflet; SAM, systolic anterior motion; RPR, resection-plication-release.

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**Table 1**
FU: follow-up. FS: full sternotomy. LV: left ventricular. LVOT: left ventricular outflow tract. MS: ministernotomy. PM: pacemaker. Pt: patient/patients, * Major complications include reoperation for bleeding, need for intra-aortic balloon pump, stroke, pneumonia, mediastinitis, and renal failure requiring dialysis.

| Surgeon, year | Place and Year | Technique | Results |
|---|---|---|---|
| Cleland 1958 | Hammersmith Hospital, London | Excision of a Small amount of LV septum in 1 patient. [1] | |
| Morrow 1960 | Clinic of Surgery, National Heart Institute, Bethesda | Subaortic Ventriculomyotomy in 2 patients. [2] | |
| Bigelow 1961 | Toronto General Hospital Toronto, Canada | Subaortic Ventriculomyotomy in 4 patients. [51] | |
| Morrow 1960–1975 | Clinic of Surgery, National Heart Institute, Bethesda | Left ventriculomyotomy and myectomy From two myotomic parallel incisions and a transverse incision connecting the proximal portions of the two, a rectangular bar of muscle is detached. | 83 patients 7.2% (6 pt) hospital mortality, 3.6% (3 pt) PM implantations for complete AV block, 6% (5 pt) had residual interventricular septal defects, 1 closing reintervention needed, 71% (59 pt) survived after a mean FU of 5.7 years. [3] |
| Messmer 1979–1992 | University Hospital, Aachen, Germany | Extended myectomy (additional resection at the junction of the septum with the lateral and posterior ventricular wall) together with mobilisation and partial excision of papillary muscles. | 58 pt. 1.7% (1 pt) hospital mortality, 5.1% (3 pt) PM implantations, 1.7% (1 pt) transient cerebral attack, 86% survived after a FU of 7 years. [8] |
| Dearani and Danielson 1975–2002 | Rochester, Minnesota, Mayo Clinic | Further extended myectomy with all bulging septal muscle apical and rightward to the initial classical resection resected, making the trough much wider at the apex than at the base of the heart. | 199 pt. 1.5% (3 pt) hospital mortality, 1% (2 pt) PM implantation, 83 ± 4% survived at 10 years of FU. [10] |
| Dearani, Schaff, Nguyen 2005–2014 | Rochester, Minnesota, Mayo Clinic | Transaortic septal myectomy and additional mitral procedures | 1486 pt. 0.2% (4 pt) inhospital mortality, 2% (36 pt) PM implantation. Survival estimates at 5 years 95%. [11] |
| Cooley 1970–1976 | Texas Heart Institute, Houston | Mitral valve replacement without myectomy. Mitral valve annuloplasty associated with myectomy presented. | 33 pt. 3% hospital mortality (1 pt), 72% (24 pt) survived at FU. 84.9% (28 pt) significant LVOT relief. [13] 98 pt. 0% hospital |

**Table 1** (*continued*)

| Surgeon, year | Place and Year | Technique | Results |
|---|---|---|---|
| Van Herverden 1991–2012 | Erasmus Medical Center, Rotterdam | Combined Myectomy and Anterior Mitral Leaflet Extension | mortality, 4% (4 pt) PM implantation, 90% (86 pt) survived at 8 years FU. [20] |
| Ferrazzi 2000–2010 | Policlinico di Monza, Italy | Shallow septal myectomy and chordal cutting | 39 pt. 0% hospital mortality, 87% were in NYHA class I and had LVOT gradient<15 mmHg after 2 years of FU. [21] |
| Swistel 2000–2014 | NYU/Langone Medical Center, New York | RPR procedure—resection, plication, relaease | 400 pt. 0.7% (3 pt) hospital mortality. All post-operatively, gradients<25 mmHg on provocation, NYHA class is 1.2 ± 0.5. [24] |
| Bhudia 1997–2001 | Cleveland, Ohio, Cleveland Clinic Foundation | Extended myectomy + edge-to-edge (Alfieri) mitral repair | 14 pt. 14% (2 pt) reoperated for persistent obstruction. [29] |
| Shah 2014–2015 | Duke University Medical Center, Durham | Extended myectomy + edge-to-edge (Alfieri) mitral repair | 24 pt. 4% (1 pt) hospital mortality, 12% (3 pt) PM implantation, Mean LVOT gradient improved from 78 ± 48 preoperatively to 19 ± 20 after myectomy ($p <$ 0.001), mean postoperative mitral gradient 4.5 mmHg. [27] |
| Yacoub 2005–2008 | Azienda Ospedaliera Universitaria Careggi, Florence | Extended myectomy + removal of the fibrous tissue covering the fibrous trigones to restore subaortic curtain mobility | 44 pt. 0% in hospital mortality. 0% PM implantation. Mean LVOT gradient improved from 68 ± 27 preoperatively to 9 ± 6 after myectomy ($p <$ 0.0001). [31] |
| Bouchard 1999–2016 | Montreal Heart Institute, Canada | Minimally invasive septal myectomy through a right anterior minithoracotomy | 24 pt. 0% in-hospital mortality, 4% (1 pt) conversion to sternotomy, 20% (5 pt) PM implantation, 2 (8%) residual SAM. Mean LVOT gradient improved from 78 mmHg to 15 mmHg. [35] |
| Ralph J. Damiano 1999–2016 | Washington University School of | Minimally invasive septal myectomy | 86 pt. MS vs 34 FS No in-hospital deaths in both |

(*continued on next page*)

**Table 1** (*continued*)

| Surgeon, year | Place and Year | Technique | Results |
|---|---|---|---|
| | Medicine Barnes-Jewish Hospital, St. Louis, MO USA | through ministernotomy | groups. Overall major complications: MS 8% (7 pt) vs 12% (4 pt) in FS* ($p = 0.5$). After 2.0 ± 3.4 years of FU NYHA class distribution ($P = 0.684$) and rest LVOT gradient (11 mmHg ±15 vs 9 mmHg ±13, $P = 0.381$) were similar between groups. [36] |
| Wierup | Cleveland Clinic, Ohio 2020 | Robotic Trans-Mitral Septal Myectomy and Papillary muscle reorientation combined with or without Mitral valve repair [33] | |
| Meghana R. Kunkala, Schaff, Dearani 1997–2012 | Mayo Clinic, Rochester, Minnesota | Transapical approach to myectomy for midventricular obstruction | 46 pt. 5 transaortic myectomy, 32 transapical approach and 19 combined transaortic and transapical incisions. 13 apical aneurysm repairs. No in-hospital deaths, LVOT gradient reduced from 64 ± 32 mmHg before myectomy to 6 ± 12 mmHg postoperatively ($p \leq 0.0001$). 1-year survival 100%, 5-year survival 95%. [37] |
| Sun, Schaff Dearani 1997–2018 | Mayo Clinic, Rochester, Minnesota | Transapical or combined transapical/ subaortic approach for midventricular obstruction | 196 pt. 1% (2 pt) perioperative mortality, 1.53% (3 pt) PM implantation. Survival estimates at 5 years 98%. [38] |

anatomical abnormalities conjure to generate, largely due to the existence of abnormally enlarged mitral leaflets in a small, hypercontractile left ventricle (LV) and interventricular septum hypertrophy. The elongated mitral leaflets, typical of HCM, coapt anteriorly and are incompletely held by slack and redundant chordae, often attached to abnormally positioned papillary muscles. The latter may be thickened, fixed to each other and to LV walls, even directly inserted into the mitral valve leaflets forcing the mitral valve into an anomalous position. The asymmetric hypertrophy localized at the septum mis-directs the outflow backward and laterally, generating drag forces which drive the leaflets towards the LV septum in early systole (the so-called SAM) leading to LVOTO (Fig. 1). These forces are magnified by the enhanced LV contractility typical of HCM. SAM progressively increases the mitral surface exposed to drag forces, generating a "crescendo" outflow gradient as well as loss of mitral coaptation and functional mitral

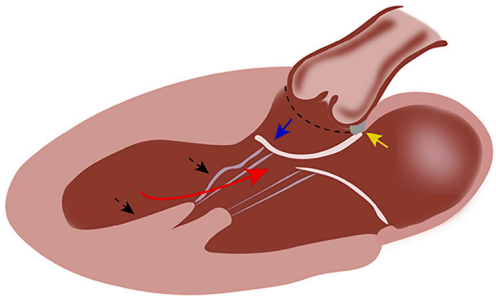

**Fig. 1.** Pathophysiology of left ventricular outflow tract obstruction (LVOTO). The hypertrophic and hypercontractile left ventricle (LV) generates a misdirected drag force (red arrow) which drive the elongated mitral leaflets towards the LV septum in early systole (i.e., systolic anterior motion of the mitral valve) leading to LVOTO (blue arrow). The mitral leaflets coapt anteriorly and are incompletely held by slack and redundant chordae often attached to abnormally positioned papillary muscles (dotted arrows). Fibrosed mitral trigones may contribute by reducing LVOT size physiological excursion of the subaortic curtain (yellow arrow). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

regurgitation. A challenging subset of patients present with systolic narrowing of the mid ventricle caused by juxtaposition of anomalous papillary muscles to the septum, causing late-systolic midventricular obstruction, which may or may not be associated with LVOTO. This variant may by complicated by apical aneurysm and thrombus formation. Fibrosed mitral trigones contribute by reducing LVOT size and physiological excursion of the subaortic curtain. Finally, posterior calcification of the mitral annulus and sigmoid septal morphology are often present in older individuals, promoting the peculiar SAM seen in this age group.

When all these components are taken into due account, LVOTO in HCM emerges as a true pathophysiological conspiracy, requiring a skilled and personalized approach.

## 3. Main theme: the Morrow myectomy

The classical Morrow myectomy requires a vertical aortotomy and aortic valve cusp retraction to visualize the septum bulging into the outflow tract. Two myotomies are made, one 2 to 3 mm to the right (clockwise) of the center of the right coronary leaflet, the second parallel to the first and about 1 cm to the left (counterclockwise). The incisions are deepened, if necessary, by digital splitting of the muscle fibers and connected with a transverse incision at the base of the right coronary leaflet. Finally, the muscular bar between the vertical incisions is detached and the apical portion resected. The result is a rectangular channel about 1 × 1.5 cm created from the valve ring towards the apex for a distance of about 4 cm. The depth of the channel is function of the septal thickness evaluated preoperatively by echocardiography and intraoperatively by palpation (left index finger in the left ventricle, left thumb over the septum externally). A limitation of this technique is that the remaining distal septal bulge still redirects the outflow, so that systolic anterior motion (SAM) and obstruction may persist (Fig. 2, Panel 1). [8]

## 4. Variation 1: extended myectomy

The Morrow technique was refined and extended by Messmer, targeting the subvalvular mitral apparatus anomalies typical of oHCM. According to Messmer, the bulging septum is pulled forward into the view of the surgeon using a sharp triple-hook retractor. The myectomy is performed through 3 septal incisions (two parallel and one transverse) resecting a deep wedge of septal tissue. Importantly, the incision is carried apically beyond the point of mitral-septal contact (usually marked by a fibrous friction lesion) and additional resection is

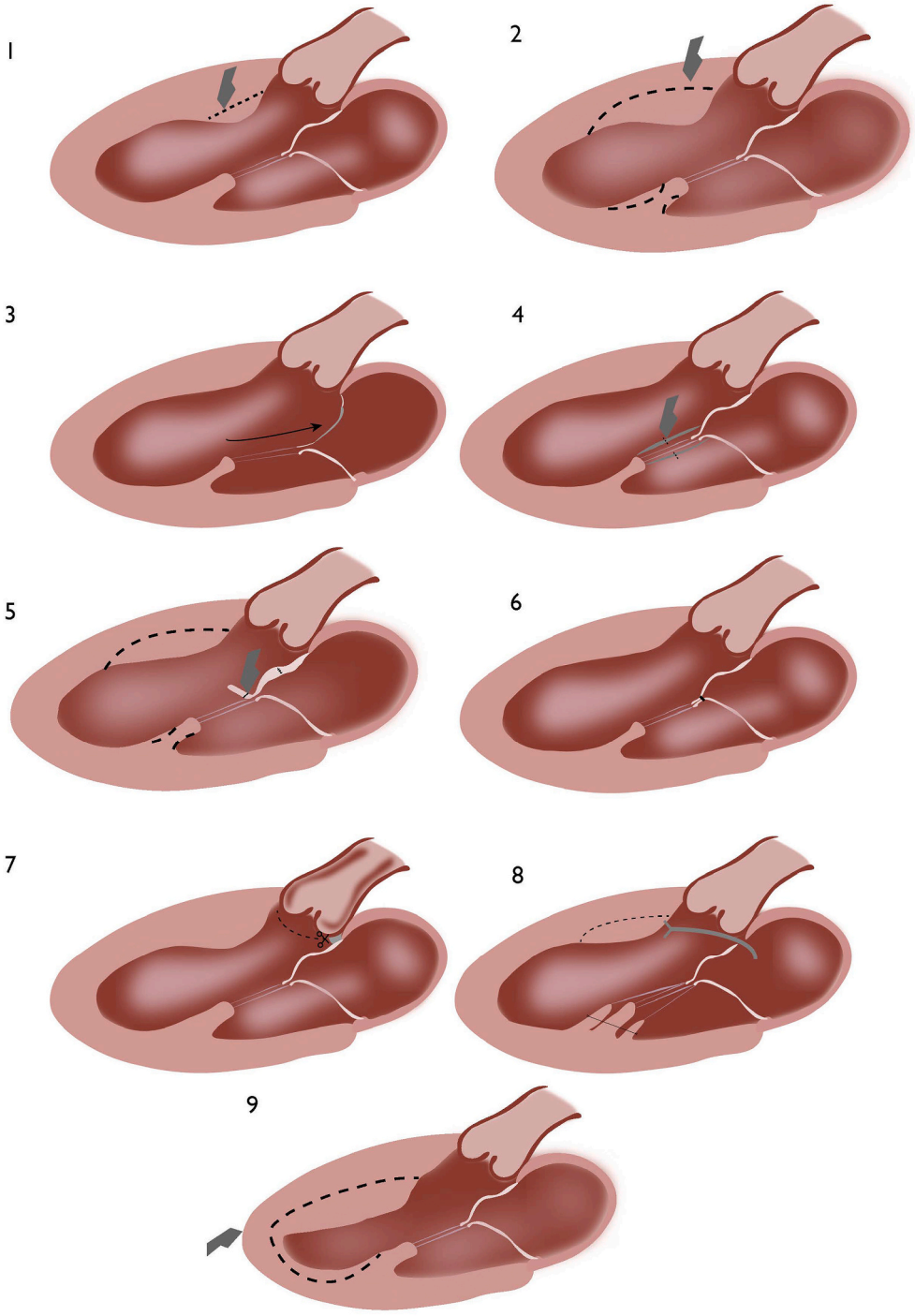


**Fig. 2.** Different surgical approaches to treat left ventricular outflow tract obstruction. Panel 1: Morrow's myectomy. Panel 2: Extended myectomy. Panel 3: Anterior mitral leaflet extension. Panel 4: Chordal cutting. Panel 5: Resection-plication-release repair. Panel 6: Alfieri stitch. Panel 7: left ventricular outflow tract remodeling. Panel 8: Robotic assisted septal myectomy. Panel 9: transapical septal myectomy.

performed at the junction of the septum with the lateral and posterior ventricular wall. Notably, a muscle rim of 4 to 5 mm is left underneath the aortic annulus to prevent secondary aortic insufficiency. After the creation of a muscular channel of at least 2 cm in diameter the intra-ventricular structures are exposed. The chordae are grasped with a nerve hook and their traction gives a view of the antero-lateral papillary muscle, which is freed from all secondary attachments to the lateral ventricular wall and the opposite papillary muscle. After this procedure, the papillary muscles should be completely mobile and remain "like slim columns inside the ventricle" (Fig. 2, Panel 2). [6,7] This approach was performed by Messmer in 58 patients from 1979 and 1992 with low hospital mortality rate (1.7%), perioperative complication rate and mortality (1.4% per patient/year). Most patients experienced a post-operative symptoms amelioration that persisted after 7 years of follow up (FU). [6,8]

The extended myectomy has been further improved by Danielson, Schaff and Dearani at the Mayo clinic. [9] Their technique includes the engagement of the distal portion of the septum with a hook to expose its rightward portion. All bulging septal muscle apical to this area and rightward to the initial classical myectomy is resected, making the

trough much wider at the apex than at the base of the heart. [10] In a recent cohort of 1486 adult patients who underwent transaortic septal myectomy between January 2005 and December 2014 at Mayo Clinic resting LVOT gradients (mmHg) was reduced by a median of 50 mmHg and provoked gradient by >100 mmHg. Four postoperative deaths have been reported and PM implantation due to AV block has been necessary in 2% of patients ($n = 36$). [11]

The Mayo approach is now considered the nearest thing to a gold standard in oHCM surgery for "classic" LVOT obstruction.

Of note, considering high- and low-volume institutions, after myectomy in-hospital mortality increases to 5.2% across US institutions, and also the rate of pacemaker implantation becomes similar to alcohol septal ablation (ASA) (10%) [12]. Therefore, referral to centers of excellence for this procedure should be strongly encouraged.

## 5. Variation 2: mitral valve replacement – vertical plication

Dr. Cooley has been the first to treat LVOTO through mitral valve replacement with a disc prosthesis, notably without excision of the hypertrophied muscle mass. From 1970 to 1976 he operated 33 patients obtaining a relief on LVOTO obstruction in all patients and symptomatic relief in most, at the expense of a 3% in-hospital mortality. [13] More specifically, mitral valve replacement is not a variation of surgical myectomy but a different approach to treat outflow tract obstruction. Currently, mitral valve replacement is considered an untoward complication in classic LVOT surgery, and should be reserved for structural abnormalities not amenable to repair, in the presence of valvular damage (i.e. post endocarditis) or calcification. [14,15] In the same paper, however, Cooley described a case of asymmetric septal hypertrophy and prolapse of the anterior mitral leaflet into the aortic outflow tract creating symptomatic LVOTO, successfully relieved with "left ventricular septectomy" and mitral valve annuloplasty. He described the advantages to such approach in abolishing SAM without incurring in long-term anticoagulation and prosthetic valve complications. [13] Mitral plasty is today an option in oHCM, particularly in the presence of leaflet abnormalities or minimal LV hypertrophy. However, the placement of an annuloplasty ring has been largely abandoned since it tends to displace the mitral annular plane anteriorly and may itself promote SAM. [14] At the beginning of the 90s, Cooley and McIntosh pioneered mitral valve repair to avoid SAM, by introducing a plication parallel to the long axis of the mitral valve with interrupted sutures termed "vertical plication", decreasing the size of the leaflet and hence drag forces, chordal and leaflet slack. [16,17] This approach has not been developed further, as vertical plication has been found to perturb the coaptation line of the anterior leaflet favouring central mitral regurgitation.

## 6. Variation 3: anterior mitral leaflet extension

A counterintuitive approach, almost opposite to vertical plication, was later introduced by Van Herwerden at the Erasmus medical center in Rotterdam, called anterior mitral leaflet extension. After performing the classical septal myectomy through a specific electrocautery device, an oval pericardial patch is inserted into the ventricular surface of the AML, at the site of a previous incision. The patch extends the width but not the length of the AML, shifting the centrally attached chordae laterally. As a result, the leaflet is stiffened and the chordae are stretched and erected, enhancing coaptation and preventing SAM. As the blood flow presses posteriorly the AML, the patch creates a ballooning structure moving the mitral valve away from the septum ("spinnaker sail" effect) (Fig. 2, Panel 3). [18,19] From 1991 to 2012, 98 patients underwent myectomy combined with AML extension. None of the patients died during the hospital stay and 4% of patients needed a pacemaker (PM) implantation. Patients showed immediate and sustained improvement of both NYHA functional class and LVOT gradient with mid-term survival rates comparable to the general population. [20]

This approach has not been adopted by other institutions. Potential limitations include the development of mitral regurgitation due to patch dehiscence, as well as the technical challenge of correct sizing of the patch to prevent persistence of SAM.

## 7. Variation 4: chordal cutting

In patients with minimal LV hypertrophy, in whom the myectomy is necessarily shallow, a "chordal cutting" technique has been recently introduced by Ferrazzi et al. [21] This approach consists of appropriate cutting of retracted and fibrotic secondary chordae tenting up the anterior mitral leaflet into the outflow tract, leading to satisfactory relief of obstruction without the need for extensive removal of septal myocardium (Fig. 2, Panel 4). After surgery the leaflet coaptation point is positioned closer to the posterior LV wall and farther from the outflow tract, with a consequent increase in the LV outflow tract size, a reduction in tenting area and LVOT gradient. [21] The procedure is not limited to patients with minimal hypertrophy, but may represent a useful adjunct in any oHCM patients. However, it requires experienced and careful evaluation of the anatomy and physiology of the subvalvular apparatus at preoperatory assessment, to prevent iatrogenic damage to the valve.

## 8. Variation 5: mitral plasty

### 8.1. Resection-plication-release technique

In order to correct all aspects of the complex dynamics of obstruction, Drs Swistel and Sherrid have devised the resection-plication-release (RPR) technique. The first step, consists of an extended myectomy as described by Messmer. The second step, includes a horizontal plication of the body of the leaflet (perpendicular to the long axis), to reduce redundancy and chordal slack. The third step is required when the excessively elongated AML is the primary cause of SAM, due to mismatch with the posterior leaflet. A portion of the AML protruding beyond the coaptation point of the mitral valve is removed and chordal slack reduced by a leaflet excision termed "ReLex", importantly leaving about 1 cm of coaptation length to maintain valvular competence (Fig. 2, Panel 5). [22] During the release phase the connections between the anterior papillary muscle and anterior free wall are dissected, allowing the valve to fall back into the LV cavity explicitly out of the flow stream. Papillary muscle heads inserting directly onto the AML and accessory secondary chordae tenting the leaflet anteriorly can be resected if other supporting structures are present. [14,23,24] After surgery all 400 patients treated at Langone Medical Center between 2000 and 2014 achieved relief of obstruction (provoked gradient<25 mmHg) and NYHA class improvement with a 0.7% mortality rate. [24]

### 8.2. Alfieri stitch

Creating a double-orifice valve by suturing the free edges of A2 and P2 is the main characteristic of the edge-to-edge technique designed by Alfieri et al. to treat mitral regurgitation (Fig. 2, Panel 6). [25,26] The technique is effective in various settings, and long-term risk of mitral stenosis is low. [27,28] The Alfieri stitch was employed as an addition to myectomy in 14 oHCM patients, two of them requiring reintervention for persistent obstruction at the Cleveland Clinic. [29] The same approach was adopted by Shah et al. [27] in 24 oHCM patients, obtaining marked post-operative LVOT gradient reduction. In this cohort, 1 patient died due to the development of ventricular septal defect. This technique allows addressing both the hypertrophied septum and the abnormal mitral valve through the aortotomy, avoiding bicaval cannulation, left atrial exposure and thus, a shorter operative time, and decreased surgical trauma. It may be used in case of long or fibrotic AML and when LV hypertrophy is minimal and the myectomy unavoidably shallow. However, due to concerns regarding long term performance of mitral valve function and potential development of stenosis, cordal

cutting or mitral plasty should be preferred, when feasible

## 9. Variation 6: LVOT remodeling

The subaortic curtain is composed of fibrous tissue which links the aortic annulus to the AML below (ventricular-aortic junction) stretched between the trigones. The subaortic curtain during the cardiac cycle moves anteriorly during diastole and posteriorly during systole, causing enlargement of the mitral orifice relative to the LVOT area and vice-versa. In oHCM, the LVOT turbulence triggers a fibrotic reaction of the trigones reducing the mobility and excursion of subaortic curtain, ultimately worsening obstruction. [30] Yacoub et al. proposed an extended myectomy including removal of the excess fibrous tissue at the trigons, thus restoring normal dynamics of the subaortic curtain (Fig. 2, Panel 7). This technique has been applied to 44 patients obtaining 86% reduction in LVOT gradient associated with zero 30-day mortality and PM implantation. [31]

Attention should be paid in the manipulation of both the left and right trigons. In fact, the incisions in the right fibrous trigon should be limited due to the proximity with the conduction system. An aggressive resection of the left trigon could lead to the development of aortic root aneurysms and even ruptures.

## 10. Variation 7: robotic-assisted septal myectomy

First introduced by Dr. Chitwood, robotic-assisted septal myectomy is becoming an alternative to the standard approach. [32] Dr. Wierup's team at the Cleveland clinic proposed a robotic trans-mitral septal myectomy and papillary muscle reorientation with or without mitral valve repair. [33] The procedure requires one incision for the endoscope at the 4th intercostal space 2–3 cm lateral to the nipple, and four incisions for port placement. Through left atriotomy the mitral valve is exposed. The AML is incised superiorly exposing the interventricular septum and the undersurface of the aortic valve. An extended septal myectomy is performed using the robotic scissors, and the AML is then reattached simultaneously reducing its height. Any abnormally oriented hypermobile anterior papillary muscle heads are then re-oriented by suturing each to the more centrally located posterior papillary muscle (Fig. 2, Panel 8). [33,34]

The robotic-assisted procedure is less invasive compared to the traditional approach. However, patients must be accurately screened as contraindications to the procedure include obesity, previous right thoracotomy, severe annular calcifications, poor right ventricular function and the coexistence of significant coronary artery disease or a severe valvulopathy. Furthermore, a restricted anterior mitral leaflet can not be approached with this procedure.

## 11. Variation 8: minimally invasive approach

The predominant approach for septal myectomy remains a full median sternotomy. Nevertheless, a minimally invasive technique using both a right parasternal minithoracotomy or a mini-sternotomy is emerging as a promising alternative with comparable efficacy and safety in patients not requiring wider exposure for additional procedures such as mitral valve repair/replacement or coronary artery bypass grafting. [35,36]

## 12. Variation 9: transapical approach for midventricular obstruction

Patients with midventricular obstruction are a particularly challenging subset, considered not amenable to surgery until recently. Today, experienced surgeons approach very distal transaortic myectomies in these patients, successfully relieving gradients in uncomplicated cases. In order to achieve a radical result, however, a transapical approach may be required. According to the approach proposed by Mayo Clinic group., [37] the ventriculotomy is begun over the apical dimple 1 to 2 cm lateral and parallel to the left anterior descending coronary artery; to avoid coronary compromise during the ventriculotomy closure. The myectomy is then focused on the ventricular septum and guided by the endocardial scar. Shaving of hypertrophied papillary muscles, excision of midventricular trabeculations and false chords and apical aneurysm repair may be performed. Muscular resection adjacent to the ventriculotomy is shallow to avoid closure complications (Fig. 2, Panel 9).

In a recent work from Mayo Clinic 196 patients underwent septal myectomy and showed midventricular obstruction (midventricular gradient >30 mmHg). In 64 patients (33%) with midventricular obstruction a sole transapical approach has been sufficient to relieve the obstruction. In 132 (67%) patients there was a concomitant subaortic obstruction and 124 (63% of the whole cohort) underwent a combined transaortic and transapical approach. In the remaining patients a sole transaortic approach has been adopted. Furthermore, in 30 patients an apical aneurysm was identified and repaired. During a median follow-up 6 patients died and the estimated 1-, 5- and 10- year survival probabilities were 99%, 98%, and 90% respectively. Survival was similar between patients with isolated midventricular obstruction and those with both LVOT and midventricular obstruction. A median decrease of 41 mmHg and 31 mmHg has been registered in resting and provoked intraventricular gradient, respectively. Perioperative mortality was 1%, and 3 patients received a pacemaker implantation for complete heart block ($n = 3$, 1.5%). [38]

## 13. Individualizing interventions in oHCM: the Florence experience

How often are these theme variations required in the real world? We reviewed the most recent series of patients operated at our institution comprising 133 consecutive oHCM patients underwent surgical myectomy at our centre aged from 21 to 82 years (mean 61 ± 14 years). Forty-five patients (34%) were women and preoperative NYHA class was III/IV in 89 (67%) patients. Seven patients underwent previous failed alcohol septal ablation. Mean resting LVOT gradient was 60 mmHg ±35 mmHg and 56 patients (42%) showed moderate to severe mitral regurgitation. Over the years, the operative approach changed due to the introduction of new technologies and techniques. The most frequent approach was a standard median sternotomy, although in the last 2 years 13 isolated mini-sternotomies have been performed. All patients received septal myectomy with LVOT remodeling, of whom 3 had papillary muscle debridement. Forty-four (33%) required additional cardiac procedures including mitral valve plasty ($n = 11$) and mitral valve replacement ($n = 14$). In 8 patients the following procedures on the mitral valve have been made: 3 edge to edge, 2 cleft closure, 1 annuloplasty, 1 PM quadrangular resection and 1 neochordae positioning (Fig. 3). Mitral valve replacement has been performed due to endocarditis or severe mitral annular calcification. Only one early death due to cardiac arrest in a patient who underwent septal myectomy, coronary artery bypass grafting and mitral valve repair has been reported. The former was a 78-year-old man that, one year before cardiac surgery, was admitted for heart failure and oppressive chest pain. On that occasion, he was treated percutaneously with angioplasty and the placement of one stent in the left anterior descending coronary artery and, in order to reduce LVOT obstruction first and second septal branches were embolized in a second procedure. After 6 months from the procedure, the patient had a second hospital admission for heart failure and was candidate for surgery although the elevated surgical risk. Overall early mortality was of 0.7%. Pace-maker implantation has been performed in 9 patients (7%) during hospitalization.

Follow up in 87 patients (65%) ranged up to 12 years (median 2.6 [1–6.6] years), only 2 patients died with an overall survival of 98%. Median resting LVOT gradient postoperatively was 10 mmHg (8–20 mmHg, $p > 0.001$ vs preoperatively) and mitral regurgitation was

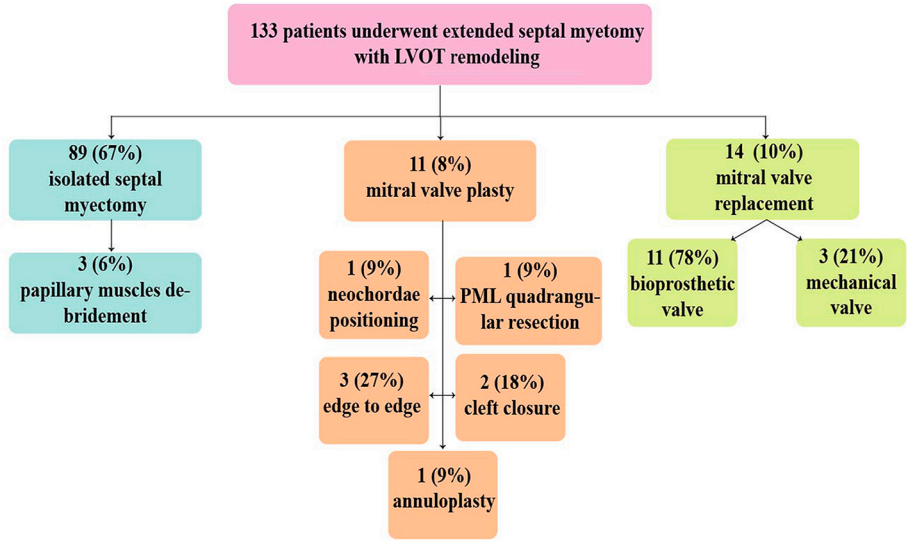


**Fig. 3.** Patients treated surgically for left ventricular outflow tract obstruction in Florence. PML: posterior mitral leaflet. LVOT: left ventricular outflow tract.

moderate in 9 patients (7%, $p < 0.001$ vs preoperatively). Postoperative NYHA class was III/IV in 26 patients (20%, $p < 0.001$ vs preoperatively).

## 14. Other therapeutic options for left ventricular outflow tract obstruction

An effective alternative to myectomy is ASA. ASA consist in the injection of absolute ethanol into an adequate septal perforator branch of the left anterior descending artery, that causes a confined septal necrosis and consequently a reduction in septal thickness and LVOT gradient. ASA is a less invasive procedure compared to myectomy and thus is characterized by a shorter in-hospital stay and faster recovery [12]. In the large, international Euro-ASA registry, ASA proved to be safe in short and long term with a 30-day all-cause mortality of 1% and with survival rates at 1, 5, and 10 years of 98%, 89%, 77%, respectively [39]. These results are comparable to those of high-volume surgical cohorts and also to mildly symptomatic/asymptomatic patients with oHCM [40–42]. Therefore, ASA and myectomy performed in high volume centres show similar low long-term mortality that is also comparable to age- and sex-matched general population [20,43]. Yet, ASA is associated with a higher rate of pacemaker implantation, a greater residual LVOT gradient and a correspondingly higher rate of repeat procedures [20,44]. Furthermore, ASA cannot address all the pathophysiological contributors to LVOTO such as papillary muscles and mitral valve abnormalities and may be less effective in presence of marked hypertrophy. [39] Thus, In symptomatic patients with oHCM who have further abnormalities requiring surgical treatment (e.g., anomalous papillary muscles, markedly elongated mitral leaflets, intrinsic mitral valve disease, CAD, valvular heart disease), surgical myectomy is recommended. [45,46] ASA is the option of choice in patients at high surgical risk (advanced age, multiple comorbidities). [45]

Mildly obstructive patients may be treated with time-honoured pharmacological options, which however rarely managed to eradicate more severe gradients in the long term.

Beta blockers are most effective for exercise induced obstruction and non-vasodilating agents are the treatment of choice (e.g. nadolol, bisoprolol and metoprolol). Nadolol is emerging as the most effective betablocker in ion channel disease, and is the first choice at our center by virtue of its single daily administration, tolerability and antiarrhythmic profile. [47,48] Beta blockers should be titrated according to symptoms to the maximally tolerated dose, although chronotropic incompetence should be avoided with care. [45] Non-dihydropyridine calcium channel blockers may be used in case of inefficacy or intolerance to beta blockers. Given the possible significant vasodilatory effect, caution is needed in case of severe resting obstruction (>80 mmHg) and marked symptoms. [45] Disopyramide is a class Ia antiarrhythmic drug and should be used as an add-on therapy to beta blockers or calcium channel blockers whenever the previous drugs are insufficient [47,49]. Disopyramide has a sarcomere-independent negative inotropic effect mediated by multichannel inhibition and a sarcomere dependent negative inotropic effect related to blunting of the the calcium-mediated activation of the myofilaments. Disopyramide has important antiarrhythmic effects in vitro, mediated by suppression of early and delayed afterdepolarizations and the transmural homogenisation of repolarization [15]. The drug can be administered in the outpatient setting [19] and its efficacy and safety have been determined in large multicenter registries. [16–18] Recent introduction of myosin inhibitors is an exciting new development with potential impact in oHCM patients, including the possibility to reduce or postpone surgery. [50] To date however, long-term data with myosin inhibitors is still missing, and surgical myectomy remains the gold standard for symptomatic obstructive HCM. [45]

## 15. Conclusions

There is no such thing as a standard myectomy for oHCM. The main theme and its variations combine to form a kaleidoscope which can be adapted to serve the need of individual patients. Surgery for oHCM is one of the safest and most rewarding in terms of clinical and pathophysiological benefits. Specific knowledge, long-standing experience and dedicated resources are key in optimizing these benefits. The diversity of patients must be met with an equivalent diversity of approaches: this is the real contemporary gold standard.

## CRediT author statement

P.S. and I·O. contributed to the conception of the work. A.A., B.B., M. Z., L.I, A.B. and A.C contributed to data acquisition and drafted the work. P.S. and I·O revised the work critically. All authors approved the final version of the work. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

## Data availability statement

The data that support the findings of this study are available from the corresponding author, [AA], upon reasonable request.

This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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