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ORIGINAL ARTICLE

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Hypertrophic cardiomyopathy with moderate septal thickness and mitral regurgitation: long-term surgical results

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Key question

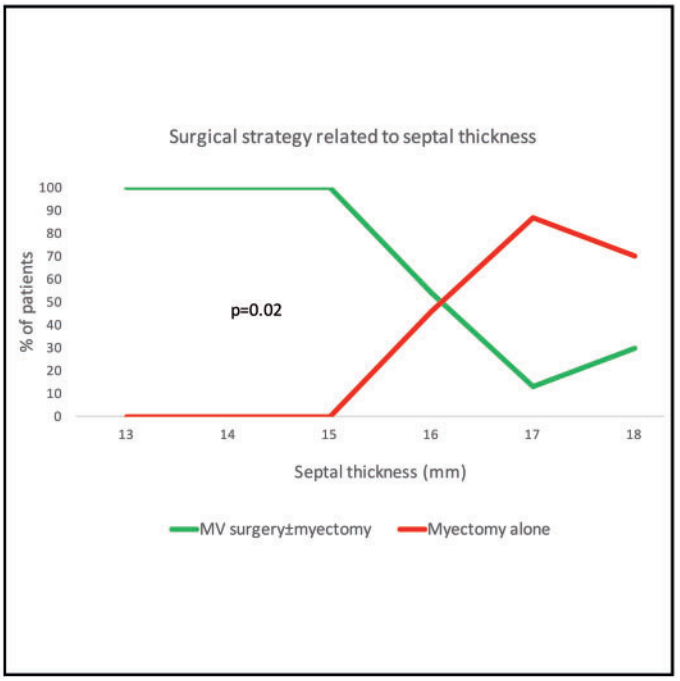
What are the long-term outcomes of different surgical strategies in HOCM with moderate septal thickness and significant MR?

Key finding(s)

9 years CIF of cardiac death was 0% in the myectomy group vs 12% in the MV surgery ± myectomy group; CIF of recurrent MR ≥ 2+ was 25% vs 3%.

Take-home message

Myectomy alone is associated with a better postoperative course and a trend towards lower cardiac mortality, despite more residual moderate MR.



Abstract

OBJECTIVES: The aim of this study was to assess the long-term outcomes of different surgical strategies in patients with hypertrophic obstructive cardiomyopathy (HOCM) with septal thickness ≤18 mm and systolic anterior motion (SAM)-related moderate-to-severe mitral regurgitation (MR).

METHODS: Seventy-six HOCM patients with septal thickness 17 [16; 18] mm, resting left ventricle outflow tract gradient 60 [41; 85] mmHg and SAM-related MR ≥2+/4+, underwent septal myectomy alone (54%) or mitral valve (MV) surgery ± myectomy (46%).

RESULTS: No hospital death and no ventricular septal defect occurred. Patients undergoing MV surgery ± myectomy had longer cardiopulmonary bypass and X-clamp times (77 [60–106] vs 51 [44–62] min, $P < 0.001$ and 56 [45–77] vs 32 [28–41] min, $P < 0.001$) and

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higher incidence of low output syndrome (11% vs 0%, $P = 0.04$). Follow-up was 98.6% complete, median 8 years [3–11]. There were no statistically significant differences in overall survival ($P = 0.069$) with survival rates at 9 years of 96 ± 4% in the myectomy alone group and 81 ± 8% in the MV surgery ± myectomy one. At 9 years, cumulative incidence function of cardiac death was 12 ± 6% in the MV surgery ± myectomy group vs 0% in the myectomy one, $P = 0.06$. Multivariable analysis identified age and previous septal alcoholization as predictors of cardiac death (hazard ratio (HR) = 1.1, 95% confidence interval (CI) 1.0–1.1, $P = 0.004$ and HR = 2.9, 95% CI 1.0–8.3, $P = 0.042$). The 9-year cumulative incidence function of recurrence of MR ≥2+, with death as competing risk, was 3 ± 2.8% in the MV surgery ± myectomy group vs 25 ± 6.9% in the myectomy one, $P = 0.005$.

CONCLUSIONS: In HOCM patients with moderate septal thickness and SAM-related MR, as the degree of septal hypertrophy decreases, addressing the abnormalities of the MV apparatus may become necessary to provide a durable resolution of left ventricle outflow tract obstruction and SAM-related MR. However, performing myectomy alone, whenever possible, seems to be associated to a better postoperative course and a trend towards lower cardiac mortality at follow-up, despite a higher rate of residual moderate MR.

Keywords: Hypertrophic obstructive cardiomyopathy • Mitral regurgitation • Systolic anterior motion • Mild septal thickness

ABBREVIATIONS

CPB	Cardiopulmonary bypass
CIF	Cumulative incidence function
EE	Edge-to-edge
HOCM	Hypertrophic obstructive cardiomyopathy
MR	Mitral regurgitation
MV	Mitral valve
SAM	Systolic anterior motion
TEE	Transoesophageal echocardiography
TTE	Transthoracic echocardiography
VSD	Ventricular septal defect

INTRODUCTION

In hypertrophic obstructive cardiomyopathy (HOCM) with septal thickness ≤18 mm and moderate-to severe mitral regurgitation (MR) due to systolic anterior motion (SAM), myectomy alone may not be enough to eliminate obstruction and SAM and restore mitral valve (MV) competence [1].

In such patients, the typical MV abnormalities present in HOCM patients are necessarily more important in causing obstruction than the modest septal thickening. Thus, mitral surgery assumes greater relevance although remains still a matter of debate [1, 2]. Some dedicated hypertrophic cardiomyopath (HCM) centres perform myectomy alone without operating on the MV [2], whereas others advocate MV or subvalvular interventions [1]. Several procedures on the MV apparatus have been proposed, including MV replacement, anterior leaflet plication/extension [3, 4], reorientation of papillary muscles [5], secondary chordae cutting [6] and edge-to-edge (EE) technique [7].

Few data are available on the long-term outcome of surgical treatment of this challenging subgroup of HOCM patients.

The aim of this study was to report the long-term clinical and echocardiographic outcomes of different surgical strategies (septal myectomy alone versus MV surgery ± myectomy) in this subset of patients.

METHODS

Study population

The study population includes the first 76 consecutive patients with primary symptomatic HOCM, septal thickness ≤18 mm and SAM-related MR ≥2+/4+ who underwent ventricular septal myectomy alone ($n = 41$, 54%) or MV surgery ± myectomy ($n = 35$, 46%), between 1999 and 2019 (Fig. 1). These 76 patients represent the 30% of the 250 patients with HOCM who were surgically treated in this time frame at our institution.

For the purpose of this study, we excluded patients with previous septal myectomy and prior MV operation including Mitraclip procedure, those affected by organic MR or with SAM-related MR <2+/4+, patients who underwent concomitant aortic valve replacement and those with apical hypertrophic cardiomyopathy (Fig. 1).

The diagnosis of HOCM was based on echocardiographic evidence of a hypertrophied non-dilated left ventricle, in the absence of any other primary cardiac or systemic aetiology [8]. Left ventricular hypertrophy was assessed according to the current guidelines [8]. Surgery was indicated when a resting or provoked (with Valsalva or exercise) left ventricle outflow tract (LVOT) peak instantaneous gradient of ≥50 mmHg was detected [14]. The severity and mechanism of MR were assessed by transthoracic echocardiography (TTE) and transoesophageal echocardiography (TEE) using an integrative approach. The degree of MR was measured by Doppler colour flow imaging and defined as mild (1+/4+), moderate (2+/4+), moderate-to-severe (3+/4+) and severe (4+/4+). Our preoperative echocardiographic protocol included exams under different haemodynamic condition such as fasting exam, postprandial re-test echo, stress echo, echo with and without beta-blockers.

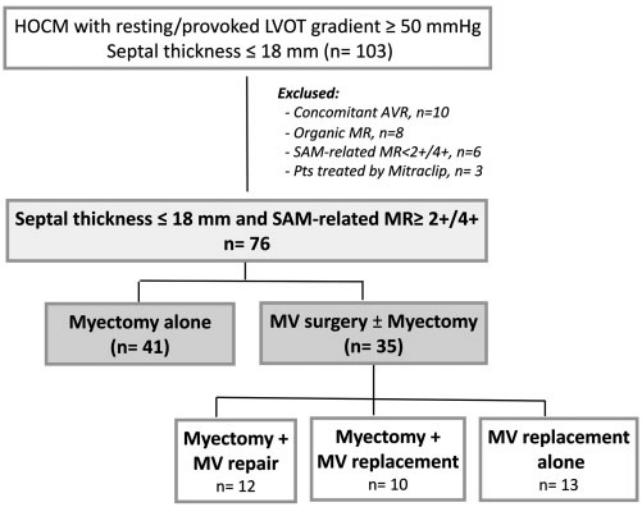

Figure 1: Flow chart depicting the study population and relative subgroups.

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The presence of abnormal chordal attachment (to the mid or base of the anterior mitral leaflet) and displacement/anomalous insertion of papillary muscles were also recorded.

The most appropriate surgical procedure for each individual patient was discussed and pre-planned within the multidisciplinary team dedicated to HOCM, after a detailed review of TEE imaging data.

Primary outcomes of the study were survival and cumulative incidence function (CIF) of cardiac death. Secondary outcomes included postoperative complications, MV reoperation, recurrence of at least moderate MR and significant LVOT gradient at long-term follow-up.

For the purpose of this study, the preoperative, intraoperative, postoperative and follow-up data were prospectively entered into a dedicated database and retrospectively reviewed. The Institutional Ethic Committee approved this study and waived individual consent for this retrospective analysis.

Follow-up

All patients underwent TTE before discharge. Clinical and echocardiographic follow-ups were performed mainly (60%) in our institutional outpatient clinic or by means of telephone interview with the patients and the referring cardiologists (40%). The cause of death was determined by death certificates or information from the physician who was caring for the patient at that time.

Follow-up was 98.6% complete, median 8 [3.5–11.3] years.

Statistical analysis

Statistical analyses were performed using Stata software version 15. Categorical data were presented as number and percentage (%) values and compared using Chi-squared test or Fisher test, as appropriate. Normal distribution of continuous variables was assessed by Kolmogorov–Smirnov test. Continuous normal distributed variables were reported as mean ± standard deviation and compared with *t*-test, while continuous non-normal data were expressed as median [25th percentile–75th percentile] and compared with Mann–Whitney test. Baseline and last follow-up measurements of continuous, normally distributed data were compared using the paired *t*-test whereas the not normally distributed data were compared using the Wilcoxon signed-rank test for related samples.

To analyse survival, Kaplan–Meier survival curve was estimated and presented as mean ± standard error and the log-rank test was used to compare survival among groups.

CIF was computed for time to cardiac death, with non-cardiac death as competing risk and for time to reoperation and time to recurrence of MR ≥2+/4+, with death as competing risk. For actuarial estimates, data were presented as failure probability ± standard error. Equality across groups was tested with the Pepe and Mori test. Fine and Gray models were adopted for the assessment of predictors of cardiac death (with non-cardiac death as competing risk) and predictors of recurrence of MR ≥2+/4+ (with death as competing risk). All variables with a *P*-value of <0.1 at univariable analysis were kept into multivariable model, as well as preop MR ≥3+ as a confounder. A *P*-value of <0.05 was employed to define statistical significance.

RESULTS

Patient characteristics

The preoperative clinical and echocardiographic characteristics of the patients are listed in Table 1.

Table 1: Baseline characteristics

	All, *n* = 76	Myectomy alone, *n* = 41	MV surgery ± myectomy, *n* = 35	*P*-value
Male sex, *n* (%)	39 (51)	22 (54)	17 (47)	0.6
Age (years), median (IQR)	60 (50; 68)	60 (54; 68)	57 (45; 71)	0.9
BMI (kg/m^2), median (IQR)	26 (24; 28)	27 (25; 29)	25 (22; 27)	0.07
Family history for HOCM, *n* (%)	8 (10)	4 (10)	4 (10)	0.9
Family history for sudden death, *n* (%)	8 (10)	5 (12)	3 (9)	0.7
Previous alcoholization, *n* (%)	2 (3)	1 (2)	1 (3)	0.9
Syncope/lipothimia, *n* (%)	39 (51)	24 (58)	15 (43)	0.1
Angina, *n* (%)	30 (39)	17 (41)	13 (37)	0.7
Acute pulmonary ooedema, *n* (%)	9 (12)	5 (12)	4 (11)	0.5
NYHA functional class, *n* (%)				0.08
I–II	37 (49)	19 (46)	18 (52)	
III	35 (46)	22 (54)	13 (37)	
IV	4 (5)	0	4 (11)	
Atrial fibrillation history, *n* (%)	24 (31)	12 (29)	12 (34)	0.8
ICD, *n* (%)	5 (7)	1 (2)	4 (11)	0.1
LVEF, %, median (IQR)	60 (60; 65)	60 (60; 65)	60 (59; 65)	0.4
SPAP, mmHg, median (IQR)	40 (30; 47)	35 (30; 45)	40 (35; 50)	0.4
LVOT gradient, mmHg, median (IQR)	60 (41; 85)	60 (46; 82)	61 (40; 89)	0.8
Septal thickness, mm, median (IQR)	17 (16; 18)	18 (17; 18)	16 (14; 18)	**0.02**
MR grade, *n* (%)				**0.02**
2+/4+	33 (43)	23 (56)	10 (29)	
3+/4+	28 (37)	14 (34)	14 (40)	
4+/4+	15 (20)	4 (10)	11 (31)	

BMI: body mass index; HOCM: Hypertrophic obstructive cardiomyopathy; ICD: implantable cardioverter defibrillator; IQR: interquartile range; LVEF: left ventricular ejection fraction; LVOT: left ventricle outflow tract; MR: mitral regurgitation; NYHA: New York Heart Association; SPAP: systolic pulmonary artery pressure.

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At hospital admission, half of the patients (39 patients, 51%) were in New York Heart Association class III or IV and 9 of them (12%) had been hospitalized due to pulmonary oedema.

The peak LVOT gradient at rest was 60 [41–85] mmHg whereas the maximum intraventricular gradient was provoked in 46 (60%) patients and reached 101 ± 33.3 mmHg with no difference between the 2 groups ($P = 0.8$).

In particular, patients who underwent MV surgery ± myectomy had thinner septum (16 [14–18] vs 18 [17–18] mm, $P = 0.02$) and more severe MR ($P = 0.02$) compared to the myectomy alone group. Indeed, as the degree of septal thickness decreased, the need for MV interventions increased (Central image).

The cause of MR was SAM (responsible for both MR and LVOT obstruction) in all patients. Anterior displacement or anomalous insertion of the anterolateral papillary muscle was present in 42 (55%) cases, abnormal chordal attachment to the MV in 22 (29%) patients and annular calcification in 23 (30%).

Procedural data

All patients were operated through a conventional median sternotomy. Standard cardiopulmonary bypass (CPB) on moderate hypothermia and cardioplegic arrest were applied. To correct outflow obstruction and MR, 41 (54%) patients underwent septal myectomy alone (transaortic resection of muscle from the basal septum) and 35 (46%) MV surgery ± myectomy. In particular, within the last group, 12 patients underwent MV repair associated to myectomy and 23 patients (23/35, 65%) MV replacement ± myectomy (Fig. 1). MV surgery was performed through a left atriotomy in all cases but 2 in whom an EE repair was done by a transaortic approach. In 2 patients undergoing MV replacement + myectomy, a transmitral approach for septal myectomy was preferred. The MV was repaired, whenever indicated, using the EE technique, as previously described [15]. In 8 cases, the presence of massive MV calcifications made impossible to repair the valve and thus a MV replacement was performed. Low-profile mechanical (16 patients) or biological (7 patients) prostheses were used. Biological prostheses were commonly used in patients ≥70 years of age. MV replacement was carried out mainly at the beginning of our experience. Indeed, 74% of patients (17/23) undergoing MV replacement were operated on before 2010.

After weaning from CPB and under optimal haemodynamic and filling conditions, a TEE was routinely performed to assess the LVOT and the final result of the repair/replacement, as appropriate.

In 7 cases (9%), MV surgery (repair in 2 patients and replacement in 5) was performed during a second pump run as a rescue procedure to eliminate residual gradient, and/or persistent SAM-related MR after the initial isolated myectomy.

As listed in Table 2, concomitant procedures were performed in 19 patients (25%): coronary artery bypass graft (CABG) (7 patients, 9%) and surgical ablation of atrial fibrillation (12 patients, 16%).

Clinical hospital outcomes

No hospital death and no ventricular septal defect (VSD) occurred. Patients undergoing MV surgery ± myectomy had longer CPB and X-clamp times (77 [60–106] vs 51 [44–62], $P < 0.001$ and 56 [45–77] vs 32 [28–41], $P < 0.001$, respectively), higher incidence of low cardiac output syndrome (11% vs 0%, $P = 0.04$) and slightly longer hospital stay (5 [4–7] vs 4 [3–6], $P = 0.05$) (Table 2). No significant differences were observed in terms of pacemaker implantation (2.9% vs 2.4%, $P = 0.9$). There were no cases of perioperative acute myocardial infarction, neurological complication and respiratory failure requiring tracheostomy in both groups.

At hospital discharge, a significant reduction in resting intraventricular gradient (median 10 [0–24] mmHg) compared to baseline ($P < 0.001$) was documented in all patients. Moreover, the TTE showed less residual moderate MR and SAM in the MV surgery ± myectomy group (0% vs 24%, $P < 0.001$ and 6% vs 29%, $P = 0.01$, respectively) (Table 2).

Follow-up

Long-term survival and cardiac death. There were no statistically significant differences in overall survival ($P = 0.069$) with survival rates at 9 years of 96 ± 4%, 95% CI [77.7–99.4] in the

Table 2: Operative and postoperative data

	All, $n = 76$	Myectomy alone, $n = 41$	MV surgery ± myectomy, $n = 35$	P-value
CPB time (min), median (IQR)	60 (48; 87)	51 (44; 62)	77 (60; 106)	**<0.001**
X-clamp time (min), median (IQR)	42 (31; 57)	32 (28; 41)	56 (45; 77)	**<0.001**
Other procedures, *n* (%)	19 (25)	9 (23)	10 (28)	0.6
Blood transfusion, *n* (%)	26 (34)	13 (29)	14 (40)	0.09
Re-exploration for bleeding, *n* (%)	3 (4)	1 (2)	2 (6)	0.5
Low cardiac output syndrome, *n* (%)	4 (5)	0	4 (11)	**0.04**
Sepsis, *n* (%)	2 (2.6%)	0	2 (5.7)	0.1
Postoperative AF, *n* (%)	32 (42)	18 (44)	14 (40)	0.7
PMK implantation, *n* (%)	2 (2.6)	1 (2.4)	1 (2.9)	0.9
ICU stay (h), median (IQR)	20 (18; 24)	19 (18; 24)	20 (18; 36)	0.8
Hospital stay (days), median (IQR)	5 (4; 6.5)	4 (3; 6)	5 (4; 7)	**0.05**
Pre-discharge SAM, *n* (%)	14 (18)	12 (29)	2 (6)	**0.01**
LVOT gradient (mmHg), median (IQR)	10 (0; 24)	10 (0; 24)	10 (0; 22)	0.9
Pre-discharge MR, *n* (%)				
0–1+/4+	66 (87)	31 (76)	35 (100)	**<0.001**
2+/4+	10 (13)	10 (24)	0	

AF: atrial fibrillation; CPB: cardiopulmonary bypass; ICU: intensive care unit; IQR: interquartile range; LVOT: left ventricle outflow tract; MR: mitral regurgitation; PMK: pacemaker; SAM: systolic anterior motion. The bold values indicate statistically significant values.

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myectomy alone group and 81 ± 8%, 95% CI [59.7–92] in the MV surgery ± myectomy one (Fig. 2). During follow-up, 14 patients died (14/75, 19%), 6 in the myectomy alone group (6/41, 15%) and 8 in the MV surgery ± myectomy one (8/34, 23%). In the myectomy alone group the cause of death was cardiac related in 3 (7%) cases (acute myocardial infarction in 1 patient and heart failure in 2 patients) and all of them died >10 years after surgery. In the MV surgery ± myectomy group, instead, cardiac deaths occurred in 5 (15%) patients (congestive heart failure with pulmonary oedema in 1 patient, sudden death in 1 patient, endocarditis in 1 patient, stroke in 1 patient and cerebral haemorrhage in 1 patient).

In particular, all the cardiac deaths in the MV surgery ± myectomy group, occurred in patients who underwent MV replacement ± myectomy (5/22, 23%) and none in patients submitted to MV repair + myectomy.

At 9 years, the CIF of cardiac death, with non-cardiac death as competing risk, was for the whole series 5 ± 3.2%, 95% CI [1.3–14.1]. In particular, there was a trend towards higher incidence of cardiac death in the MV surgery ± myectomy group (CIF at 9 years 12 ± 6.7%, 95% CI [2.8–28.3] vs 0%, $P = 0.06$) (Fig. 3).

Fine and Gray models identified age and previous septal alcoholization as predictors of cardiac death (HR = 1.1, 95% CI 1.0–1.1, $P = 0.004$ and HR = 2.9, 95% CI 1.0–8.3, $P = 0.042$, respectively), at multivariable analysis (Table 3).

Clinical outcomes. During follow-up, 3 patients (4%) developed heart failure, 1 patient underwent percutaneous transluminal coronary angioplasty (PTCA) and 2 patients catheter ablation of AF. Stroke occurred in 3 (4%) patients and major bleeding events in 1 (1.3%) case (cerebral haemorrhage). Three patients (4%) received an implantable cardioverter defibrillator, between 3 and 5 years after surgery, because of ventricular tachyarrhythmia and 3 patients required a permanent pacemaker due to bradi-AF (2 patients) or atrioventricular block (1 patient), with no difference between groups ($P = 0.2$ and $P = 0.3$, respectively). Finally, 1 patient, in permanent AF, underwent transcatheter occlusion of left atrial appendage with St. Jude Medical Amplatzer device, 18 months after surgery.

At the last follow-up, 90% of patients were in New York Heart Association class I–II and 67% in sinus rhythm, with no difference between groups ($P = 0.2$ and $P = 0.2$, respectively).

At the last echocardiography, median resting LVOT gradient decreased to 0 mmHg [0; 13] ($P < 0.001$ versus preop), systolic

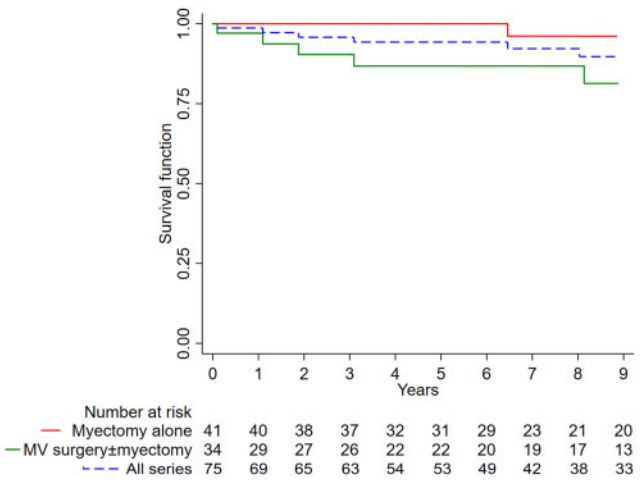

Figure 2: Kaplan–Meier estimates of overall survival.

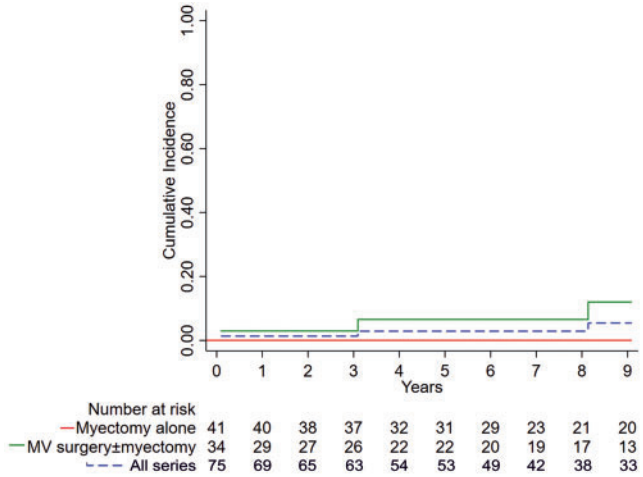

Figure 3: Cumulative incidence function of cardiac death with non-cardiac death as competing risk.

Table 3: Predictors of cardiac death

Preoperative variables	Univariable		Multivariable	
	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
Age	1.11 (1.05–1.18)	**<0.001**	1.11 (1.03–1.19)	**0.004**
Previous alcoholization	5.41 (2.20–13.36)	**<0.001**	2.93 (1.04–8.31)	**0.042**
NYHA III–IV	0.70 (0.18–2.74)	0.60		
Preoperative AF	3.15 (0.59–16.65)	0.13		
LVEF	0.90 (0.79–1.03)	0.28		
SPAP	0.90 (0.84–1.01)	0.10		
Septal thickness	1.17 (0.62–2.23)	0.63		
LVOT gradient	1.01 (0.99–1.04)	0.35		
MR ≥3+/4+	2.95 (0.64–13.67)	0.168	3.93 (0.93–16.68)	0.093
MV surgery ± myectomy	3.21 (0.87–11.81)	0.070	1.13 (0.28–4.64)	0.196

AF: atrial fibrillation; LVEF: left ventricular ejection fraction; LVOT: left ventricle outflow tract; MR: mitral regurgitation; MV: mitral valve; NYHA: New York Heart Association; SPAP: systolic pulmonary artery pressure.

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pulmonary artery pressure to 35 [30–43] mmHg ($P = 0.04$ versus baseline) and LVEF to 60% [55–60] ($P = 0.01$ versus preop).

Reoperation and recurrence of MR. During follow-up, 3 patients (4%) underwent MV reoperation. One patient in the myectomy alone group underwent MV repair, 1 month after surgery, because of severe MR related to flail of the A1 scallop of the MV. One patient, submitted to previous MV repair and myectomy, required MV replacement 9 months later, due to persistent LVOT obstruction related to anterior displacement of the anterolateral papillary muscle. Finally, 1 patient with MV replacement needed a reoperation 15 years later, due to prosthesis leak.

Considering the whole series, the 9-year CIF of reoperation, with death as competing risk, was 2.8 ± 1.2% (95% CI 0.5–8.7). No difference between the 2 groups was detected ($P = 0.8$).

At the last follow-up, 12 patients (12/75, 16%) had recurrent MR ≥ 2+, 4 patients died (3 cardiac deaths), 3 have been reoperated and 5 patients were asymptomatic in optimal medical therapy.

In particular, in the myectomy alone group, 10 (24%) patients showed moderate MR (2+/4+) at hospital discharge. However, in 5 of them, MR reduced to mild at 3-month follow-up and remained constant throughout the follow-up period. Indeed, SAM-related MR in HOCM is strongly influenced by haemodynamic and filling conditions, which are unfavourable immediately after surgery. Therefore, we decided to consider the first 3 months after surgery as a period of haemodynamic adjustment and we started to evaluate MR recurrence after that period. During follow-up, other 5 patients in the myectomy alone group and 2 in the MV surgery ± myectomy developed MR ≥2+.

At 9 years, the CIF of recurrence of MR ≥2+ with death as competing risk was 25 ± 6.9% (95% CI 13.1–39.5) in the myectomy alone group and 3 ± 2.8% (95% CI 0.22–13.0) in the MV surgery ± myectomy group ($P = 0.005$) (Fig. 4). Fine and Gray models failed to identify other predictors of MR recurrence at multivariable analysis.

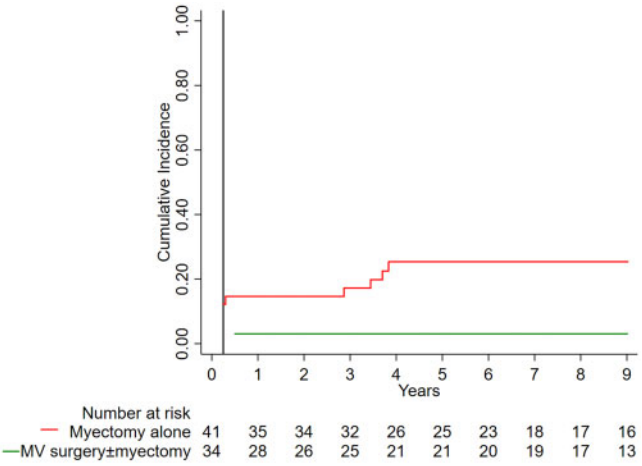

Figure 4: Cumulative incidence function of mitral regurgitation ≥2+ with death as competing risk.

DISCUSSION

The present study reports the long-term clinical and echocardiographic results of different surgical strategies (myectomy alone versus MV surgery ± septal myectomy) in HOCM patients with moderate septal thickness and significant SAM-related MR.

The major findings are that: (i) MV surgery was performed in about half of the cases, with MV replacement carried out mainly at the beginning of our experience, and (ii) patients undergoing Myectomy alone had better postoperative course and a trend towards lower cardiac mortality at follow-up, despite more residual moderate MR.

Hypertrophic cardiomyopathy has been widely described as a disease mainly characterized by marked septal hypertrophy and LVOT obstruction [9]. However, a subset of patients with only moderate/mild basal septal thickness and dynamic outflow obstruction due to SAM has been recently identified [1], raising important management implications. In such patients, the abnormalities of the MV and papillary muscles play a key role in determining dynamic LVOT obstruction and SAM-related MR [10]. Therefore, MV surgery assumes greater relevance since a mild/moderate septal thickness is unlikely to be fixed by a shallow myectomy alone. Historically, septal myectomy has been considered not advisable in patients with a basal septum thickness of <18 mm, due to a perceived increased risk of iatrogenic VSD as well as concerns regarding inadequate relief of LVOT obstruction and symptoms [11]. Thus, MV replacement, usually with a low-profile prosthesis, has been deemed as the only viable option in such patients [11]. Even though this procedure relieves both the outflow gradient and the MR, it is rarely performed nowadays, due to the increased hospital mortality [12] and the adverse sequelae of the prosthetic valve and the related long-term anticoagulation.

Nevertheless, MV surgery in this setting remains still a matter of debate. Some dedicated HCM centres perform myectomy alone without operating on the MV [2], whereas others advocate adjunctive MV procedures [1], including anterior leaflet plication/extension [3, 4], reorientation of papillary muscles [5], secondary chordae cutting [6] and EE technique [7]. All these techniques aim to decrease the mobility of the anterior leaflet and reorient the MV apparatus posteriorly, away from ventricular septum, providing a complete relief of the obstruction.

There are few studies describing the surgical treatment of HOCM in the context of moderate/mild septal thickness, and most of them have limited follow-up.

In a recent study, Nguyen *et al.* [2] reported on 1486 surgical HOCM patients stratified by basal septal thickness, 25% of whom presented a septum of <18 mm. All patients underwent septal myectomy alone, regardless of septal thickness and degree of SAM-related MR. Adjunctive procedures on the MV (8% of cases) were reserved only for patients with iatrogenic or intrinsic valve disease (such as mitral prolapse) and those who had persistent SAM, MR or LVOT obstruction after myectomy. In the group with septum <18 mm, at early postoperative follow-up, MR ≥2+ was documented in only 2% of patients and SAM in 27.5%, with no difference compared to patients with a baseline septum ≥18 mm. However, no echocardiographic data were available at longer follow-up and, therefore, it is unknown whether the myectomy alone strategy performed in that study was associated to durable results over extended periods of time, particularly in the thinner septum group.

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Patel *et al.* [1] have shown that half of the 45 surgical patients with a basal septal thickness of ≤18 mm and MV anomalies required concomitant MV procedures, while Hodges *et al.* [13] documented that the need of MV interventions was inversely related to the degree of septal hypertrophy. A study by Rowin *et al.* [14] described a series of 36 patients affected by HOCM with septum thickness ≤15 mm who were surgically treated. Thirty-two of them (89%) underwent additional procedures on the MV apparatus associated to a shallow myectomy. Finally, Sherrid *et al.* [15] have recently stated that, in the presence of a relatively thin septum ≤18 mm, they routinely perform a limited myectomy along with mitral repair. However, all these studies are limited by the lack of long-term outcomes.

In our series, MV surgery was required in 46% of patients, those who had a significantly thinner septum (median 16 vs 18 mm) and more severe MR compared to the myectomy alone group ($P = 0.02$), confirming that as the degree of septal thickness decreases, the need for MV interventions increases.

Of note, 30% of patients underwent MV replacement, much more than that reported in other series [2, 12]. However, most of those cases have been operated on at the beginning of our experience while more recently the MV has been replaced principally due to the presence of massive MV calcifications (which made impossible to repair the valve), or during a second pump run as a rescue procedure to eliminate residual gradient, and/or persistent SAM-related MR after the initial isolated myectomy. Nevertheless, patients undergoing surgery for HOCM with mild septal hypertrophy should be aware of the risk of MV replacement, particularly given the relatively youthful age at which surgery is performed in HOCM patients.

As far as the postoperative complications are concerned, it is noteworthy that in our series, no hospital death and no VSD occurred and postoperative permanent pacemaker implantation was necessary in only 2.6% of cases, with no difference in the 2 groups. These findings are consistent with the more recent outcomes reported in high volume centres [16].

However, patients undergoing MV surgery ± myectomy, in our study, had longer CPB and X-clamp times, higher incidence of low output syndrome, and slightly longer hospital stay compared to the myectomy alone group. Indeed, MV surgery in the context of hypertrophic cardiomyopathy is more challenging due to the suboptimal exposure of the MV and introduces additional surgical complexity, longer cross-clamp time, and potential complications. Moreover, the subgroup of HOCM patients herein reported appears to be particularly prone to even greater risk of complications, due to the limited basal hypertrophy. Therefore, it has to be emphasized that surgery in such patients without marked septal hypertrophy should be performed by experienced surgeons in dedicated HOCM centres since these are the key determinants of a successful outcome. Moreover, a multidisciplinary approach is of utmost importance to tailor the surgical procedure to each individual patient and achieve optimal outcomes.

Our study reports the clinical and echocardiographic results of different surgical strategies at a median follow-up of 8 [3–11] years, the longest follow-up to date in such patients.

Late survival was satisfactory and symptomatic improvement remarkable in the whole series. However, patients undergoing MV surgery had a trend towards higher incidence of cardiac death at follow-up and we speculate on the possible negative impact on cardiac mortality of MV replacement, which requires more patients to be confirmed. Conversely, the long-term recurrence of MR ≥2+ was definitely higher in the myectomy alone group compared to the MV surgery ± myectomy one.

In conclusion, in HOCM patients with moderate septal thickness, as the degree of septal hypertrophy decreases, addressing the abnormalities of the MV apparatus may become necessary to minimize the risk of iatrogenic VSD and provide a durable resolution of LVOT obstruction and SAM-related MR. However, performing myectomy alone, whenever possible, seems to be associated to a better postoperative course and a trend towards lower cardiac mortality at follow-up, despite a higher rate of residual moderate MR.

Limitations

Although data were obtained from a prospectively collected database, this was a retrospective, single-centre study and, therefore, subject to its intrinsic limitations. The inclusion period is long and the small sample size and number of events could undermine the statistical power of our analysis. However, it appears to be the largest study to date looking at long-term clinical and echocardiographic outcomes of the subset of HOCM patients with a relatively thin septum. Future studies, with larger number of patients, may lead to more robust conclusions and may help to identify the optimal strategy in this challenging population.

Furthermore, some of the echocardiographic measurements such as the length of the anterior and posterior leaflets, as well as the mitro-aortic angle and the coaptation-septum distance, due to the retrospective nature of the study, were not systematically recorded and therefore could not be analysed.

Moreover, cardiac magnetic resonance imaging is an important examination to complete the preoperative evaluation of HOCM patients providing further insights into the understanding of the complex way the MV apparatus contributes to dynamic LVOT obstruction. However, in our series, due to the long time frame taken into consideration, only the more recent patients were evaluated with magnetic resonance imaging.

Finally, although the 2 groups (myectomy alone and MV surgery ± myectomy) differed only in the septal thickness and MR grade and, therefore, have been considered as similar, such a difference might have somehow influenced the results.

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Author contributions

Elisabetta Lapenna: Conceptualization; Formal analysis; Methodology; Supervision; Validation; Writing—original draft. **Teodora Nisi:** Data curation; Methodology; Writing—review & editing. **Davide Carino:** Data curation; Methodology. **Marta Bargagna:** Data curation. **Stefania Ruggeri:** Formal analysis; Methodology; Software. **Edoardo Zancanaro:** Data curation. **Benedetto Del Forno:** Data curation; Methodology. **Davide Schiavi:** Methodology; Validation. **Eustachio Agricola:** Supervision; Validation; Writing—review & editing. **Alessandro Castiglioni:** Supervision; Validation.

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Ottavio Alfieri: Supervision; Validation; Writing—review & editing. **Michele De Bonis:** Conceptualization; Methodology; Supervision; Validation; Writing—review & editing.

Reviewer information

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