

Septal Myectomy without Correction of Moderate and Severe Mitral Regurgitation

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Abstract

Objectives: Septal myectomy (SM) is the gold standard treatment option for patients with hypertrophic obstructive cardiomyopathy (HOCM) whose symptoms do not respond to medical therapy. Extended SM adequately relieves left ventricular outflow tract (LVOT) gradients, abolishes systolic anterior motion (SAM) of the mitral valve and improves mitral regurgitation (MR). However, in patients with moderate and severe MR, controversy remains regarding the necessity of mitral intervention at the time of SM. In this study, we investigated short-term outcomes of SM without correction of moderate and severe MR, as well as risk factors for residual MR $\geq 2+$ after SM.

Materials and Methods: From January 2019 to January 2024, 207 adult patients underwent transaortic SM in our Center. Of these, 119 patients who underwent isolated SM were included in the study: group 1 (n=36) consisted of patients with no or mild MR and group 2 (n=83) consisted of patients with moderate to severe MR. The primary endpoint was the severity of MR after SM. Secondary endpoints included postoperative complications, residual LVOT gradient ≥ 30 mmHg and residual SAM.

Results: There was no residual MR in the group 1, while 9% of patients in group 2 had moderate MR. Only 3.6% of cases in group 2 required repeated aortic cross-clamping and mitral valve intervention. The mortality rate was 1.2% (1 patient) in group 2, with no deaths in group 1. Complete AV-block requiring permanent pacemaker implantation occurred in 2 patients (5.6%) in group 1 and 6 patients (7.2%) in group 2 (p=0.74). There were 2 patients (5.6%) in group 1 and 4 patients (4.8%) in group 2 with a residual LVOT gradient ≥ 30 mmHg at discharge (p=0.87). Residual SAM was identified



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in 2 patients (5.6%) in group 1 and 7 patients (8.4%) in group 2 ($p=0.58$). Multivariate regression analysis identified only residual SAM [odds ratio (OR): 13.994, 95% confidence interval (CI): 2.692-72.744, $p=0.02$] as a predictor of residual $MR \geq 2+$.

Conclusion: In our study, among patients with moderate and severe MR, only 3.6% required repeated aortic cross-clamping and mitral valve intervention. Before discharge, only 9% of patients had moderate MR. Consequently, in most patients with HOCM and moderate/severe MR not due to organic mitral valve lesion, isolated SM effectively relieves LVOT gradients, SAM of the mitral valve and the associated MR.

Keywords: Cardiovascular medicine, cardiovascular surgery, heart failure

Introduction

Hypertrophic obstructive cardiomyopathy (HOCM) is the most common hereditary cardiomyopathy characterized by left ventricular hypertrophy^(1,2). The mechanism of left ventricular outflow tract (LVOT) obstruction in patients with HOCM involves both hypertrophic interventricular septum (IVS) and mitral valve (MV) abnormalities. The leaflets of the MV and the submitral apparatus play a significant role in the formation and worsening of LVOT obstruction. Systolic anterior motion (SAM) of the MV, along with its contact with the hypertrophic IVS, results in dynamic LVOT obstruction, impaired coaptation of the MV leaflets, and mitral regurgitation (MR)^(3,4).

Currently, septal myectomy (SM) has been the treatment of choice for patients with HOCM and LVOT obstruction^(1,2). However, there remains controversy regarding whether MV procedures should be performed simultaneously. Some authors believe that isolated resection of the IVS is sufficient to eliminate MR⁽⁴⁻⁶⁾, whereas others advocate for intervention on the MV and submitral structures⁽⁷⁻¹³⁾.

The purpose of this study was to analyze the clinical and echocardiogram outcomes of SM without correction of moderate and severe MR; and to identify risk factors for residual $MR \geq 2+$ after SM.

Materials and Methods

Patient Selection

From January 2019 to January 2024, 207 patients underwent SM at our center. The exclusion criteria were: 1) age below 18 years old; 2) need for coronary artery bypass grafting and 3) organic aortic and MV disease requiring surgery. Thus, 119 patients who underwent isolated intervention were included in the study. These patients were divided into two groups: group 1 ($n=36$), consisting of patients with no or mild MR; and group 2 ($n=83$), consisting of patients with moderate or severe MR (Figure 1).

HOCM was diagnosed based on transthoracic echocardiogram and magnetic resonance imaging (MRI) results, in accordance with the clinical guidelines^(1,2). The indications for surgery included septal thickness >15 mm and LVOT pressure gradient ≥ 50 mmHg at rest or after exercise (Valsalva maneuver / exercise test). The severity of MR was measured by color Doppler ultrasonography and classified as mild (0-1+), moderate (2+), moderate/severe (3+), or severe (4+).

In accordance with the clinical guidelines, all patients received β -blockers without vasodilating effect and/or calcium channel blockers before surgery^(1,2).

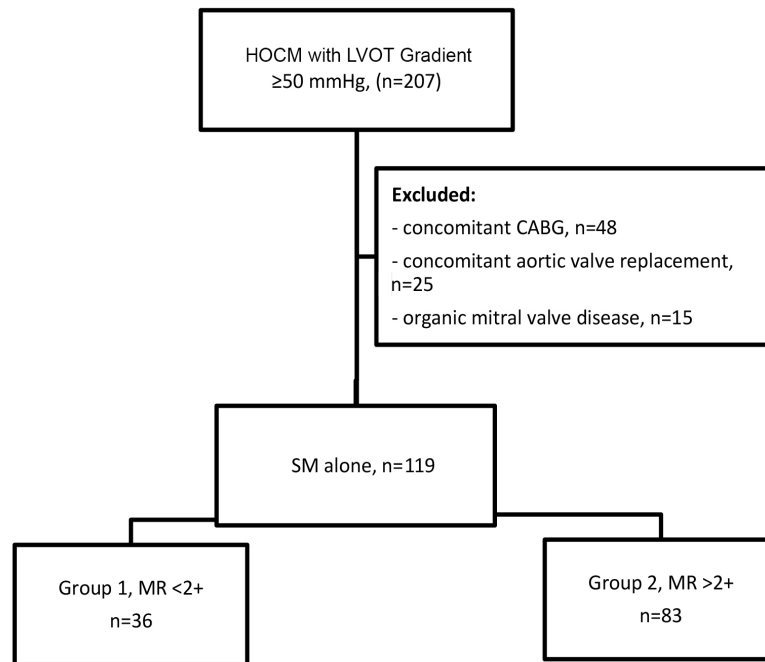


Figure 1. Study Design

HOCM: Hypertrophic obstructive cardiomyopathy, SM: Septal myectomy, CABG: Coronary artery bypass grafting, MR: Mitral regurgitation, LVOT: Left ventricular outflow tract

Patient Characteristics

The clinical and demographic characteristics of the patients along with preoperative echocardiogram findings are presented in Table 1. The age of patients was higher in group 2 than in group 1 (56.5 ± 12.7 years vs. 50.4 ± 13.4 years, $p=0.02$). Most patients in both groups had New York Heart Association functional class II-III heart failure. Patients with MR 2+ had a higher LVOT gradient (73 [57;99] mmHg vs. 54 [50;68] mmHg, $p<0.001$), whereas no significant differences were found in septal thickness (23.6 ± 5.1 mm vs. 23.9 ± 4.9 mm, $p=0.79$). In group 2, 51 patients (61%) had MR 2+, and 32 patients (39%) had MR 3+. Group 2 also had a higher operative risk according to EuroSCORE II ($p=0.04$). The conducted study complies with the standards of the Declaration of Helsinki, is approved by the Independent Ethical Committee of the Federal State Budgetary Institution Federal Center For Cardiovascular Surgery Ministry of Health of the Russian Federation (Khabarovsk) (approval no: 39, date: 11.11.2023).

Endpoints

The primary endpoint was the severity of MR after SM. The secondary endpoints included the need for repeated aortic cross-clamping to correct MR postoperative complications, residual LVOT gradient, residual systolic SAM, and IVS thickness.

Operative Treatment

All surgeries were performed by two experienced surgeons via a transaortic approach. Separate bicaval venous cannulation was performed in patients with moderate to severe MR. The heart was arrested using antegrade crystalloid (Custodiol solution (Dr. Franz Kohler Chemie GmbH, Germany) or warm blood cardioplegia. A standard SM, as described by Morrow⁽¹⁴⁾, was performed. If diffuse IVS thickening was present, the excision was extended as distally as possible up to the base of the papillary muscles (Figure 2). The aorta was then closed in a double-layer fashion. After bypass, the anatomy and function of LVOT, LVOT gradient,

and MR grade were evaluated using transesophageal echocardiography. In cases of residual high gradient or severe MR, cardiopulmonary bypass (CPB) was resumed for correction.

Statistical Analysis

Statistical calculations were performed using the SPSS software, version 21 (SPSS, Chicago, IL, USA). Categorical variables were presented as numbers and percentages and

Table 1. Baseline characteristics

Parameter	Group 1 (MR <2+) n=36	Group 2 (MR <2+) n=83	p-value
Age (years), M \pm SD	50.4 \pm 13.4	56.5 \pm 12.7	0.02
Female gender, n (%)	16 (44.4)	45 (54.2)	0.33
BMI, kg/m ² , Me [IQR]	29.0 [24.8;34.7]	29.4 [26.6;33.1]	0.88
Family history of HOCM, n (%)	3 (8.3)	3 (3.6)	0.28
Syncope, n (%)	11 (30.6)	22 (26.5)	0.75
Angina, n (%)	16 (44.4)	59 (71.1)	0.01
NYHA functional class, n (%):			
I	5 (13.9)	4 (4.8)	0.24
II	21 (58.3)	44 (53.0)	
III	9 (25)	32 (39.0)	
IV	1 (2.8)	3 (3.6)	
Atrial fibrillation, n (%)	5 (13.8)	16 (19.2)	0.48
Ventricular arrhythmias, n (%)	4 (11.1)	12 (14.4)	0.62
ICD insertion, n (%)	2 (5.6)	1 (1.2)	0.17
Diabetes mellitus, n (%)	4 (11.1)	6 (7.2)	0.48
Hypertension, n (%)	27 (75)	68 (82.0)	0.34
COPD, n (%)	5 (13.8)	9 (10.8)	0.64
LVEF, %, Me [IQR]	64 [62;72]	69 [64;73]	0.02
LVEDV, mL, Me [IQR]	81 [72;107]	81 [70;101]	0.74
LVESV, mL, Me [IQR]	29 [21;38]	24 [20;33]	0.12
SPAP, mmHg, Me [IQR]	24 [18;29]	30 [21;35]	0.04
IVS thickness, mm, M \pm SD	23.9 \pm 4.9	23.6 \pm 5.1	0.79
LVOT gradient, mmHg, Me [IQR]	54 [50;68]	73 [57;99]	<0.01
SAM, n (%)	35 (97.2)	83 (100)	0.13
MR grade, n (%):			
1+	35 (100)	0	<0.01
2+	0	51 (61.4)	
3+	0	32 (38.6)	
4+	0	0	
EuroSCORE II, Me [IQR]	0.8 [0.56;0.80]	1.1 [0.75;1.5]	0.04

M \pm SD: Mean \pm standard deviation, BMI: Body mass index, Me [IQR]: Median interquartile range, HOCM: Hypertrophic obstructive cardiomyopathy, NYHA: New York Heart Association, ICD: Implantable cardioverter defibrillator, COPD: Chronic obstructive pulmonary disease, LVEF: Left ventricular ejection fraction, LVEDV: Left ventricular end-diastolic volume, LVESV: Left ventricular end-systolic volume, SPAP: Systolic pulmonary artery pressure, IVS: Interventricular septum, LVOT: Left ventricular outflow tract, SAM: Systolic anterior motion, MR: Mitral regurgitation

compared using a χ^2 test or Fisher's exact test. The normal distribution of continuous variables was evaluated using the Kolmogorov-Smirnov test. Continuous variables with normal distribution were presented as the mean \pm standard deviation and compared using t-test. Continuous variables with non-normal distribution were presented

as median [25th percentile-75th percentile] and compared using the non-paired Mann-Whitney U test. The statistical hypotheses were tested at a significance level of $p=0.05$, indicating that a difference was considered statistically significant if $p<0.05$. Univariate and multivariate logistic regression analysis was performed to identify risk factors

Table 2. Operative and postoperative data

Parameter	Group 1 (MR <2+) (n=36)	Group 2 (MR <2+) (n=83)	p-value
CBP time, min, Me [IQR]	49 [43.6;57.3]	58 [45;69]	0.03
Cross-clamp time, min, Me [IQR]	31.5 [25.3;39.8]	34 [26;47.3]	0.18
Hospital mortality, n (%)	0	1 (1.2)	0.51
VSD, n (%)	0	0	1
Repeated aortic cross-clamping, n (%)	1 (2.8)	4 (4.8)	0.61
Mitral valve repair, n (%)	1 (2.8)	2 (2.4)	0.91
Mitral valve replacement, n (%)	0	1 (1.2)	0.51
Stroke, n (%)	0	1 (1.2)	0.51
Bleeding, n (%)	2 (5.6)	1 (1.2)	0.17
Atrial fibrillation, n (%)	7 (19.4)	14 (16.8)	0.12
Renal impairment, n (%)	1 (2.8)	0	0.13
PPM implantation for heart block, n (%)	2 (5.6)	6 (7.2)	0.74
Duration of stay in the ICU, days, Me [IQR]	2 [2;2]	2 [2;3]	0.5
Duration of postoperative stay in hospital, days, M \pm SD	11.3 \pm 2.9	10.8 \pm 2.6	0.29

CBP: Cardiopulmonary bypass, VSD: Ventricular septal defect, PPM: Permanent pacemaker, ICU: Intensive care unit, Me [IQR]: Median interquartile range, M \pm SD: Mean \pm standard deviation

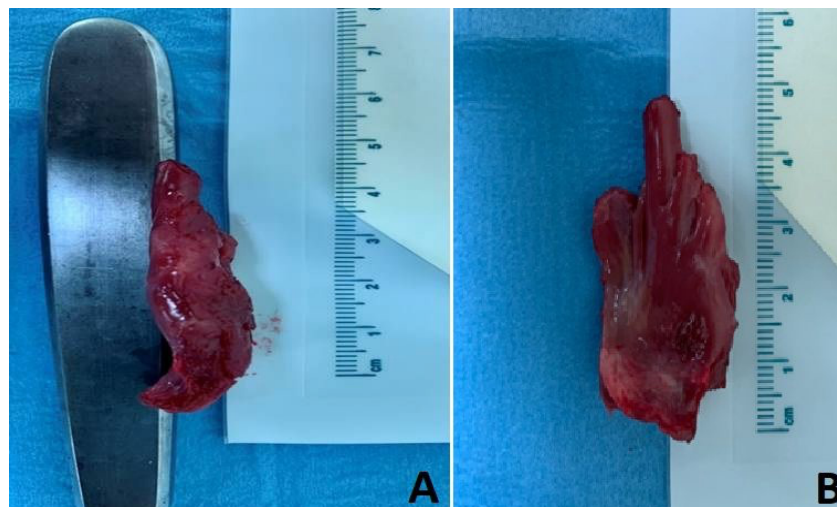


Figure 2. A) Segment of the interventricular septum excised as distally as possible (up to 5 cm)

for residual MR $\geq 2+$ after surgery. Data from the analysis are presented as ORs and 95% confidence intervals (OR; 95% CI).

Results

Surgical and Postoperative Periods

The mean CPB time was longer in the group with MR $>2+$ (58 [45;71] minutes or min. vs. 50 [44;57] minutes or min., $p=0.01$), with no difference in the cross-clamp time between the groups (32 [25;40] minutes or min. vs. 36 [26;48] minutes or min., $p=0.09$). One patient in group 1

(2.8%) and three patients in group 2 (3.6%) required repeated aortic cross-clamping to correct severe MR. In three cases, successful correction of MR was achieved by MV repair according to Calafiore; one patient from group 2 underwent MV replacement with a mechanical valve after an unsuccessful attempt at MV repair according to Calafiore. One patient in group 2 required repeat aortic cross-clamping and ascending aorta and hemiarch replacement due to aortic rupture. There were no cases of acute interventricular septal defect or repeated aortic cross-clamping to perform additional IVS resection due to a high residual LVOT gradient. One patient (1.3%) died in

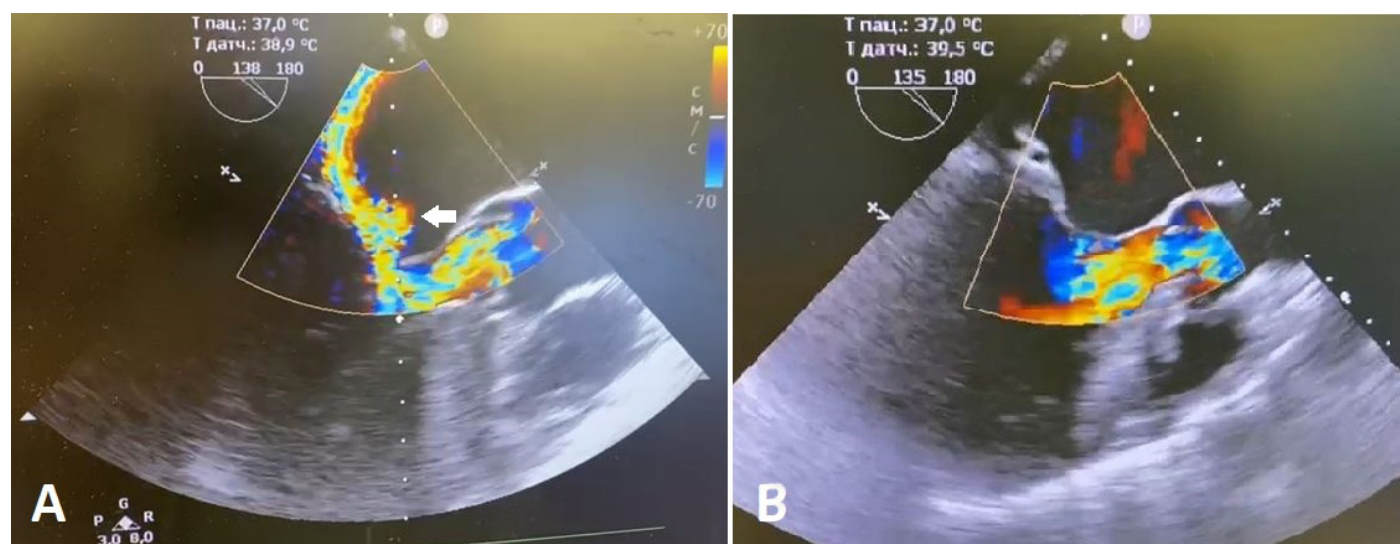


Figure 2. B) Mitral regurgitation before (A, white arrow) and after (B) septal myectomy

Table 3. Hemodynamic parameters before discharge

Variables	Group 1 (MR $<2+$) n=36	Group 2 (MR $<2+$) n=79	p-value
IVS thickness, Me [IQR]	12 [10;13]	13 [11;14]	0.36
LVOT gradient, Me [IQR]	11 [9;17]	11 [7;18]	0.93
Residual SAM, n (%)	2 (5.6)	7 (8.4)	0.58
Residual LVOT gradient >30 mmHg, n (%)	2 (5.6)	4 (4.8)	0.87
MR grade, n (%):			
1+	36 (100)	75 (91)	0.07
2+	0	7 (9)	
3+	0	0	
4+	0	0	

IVS: Interventricular septum, LVOT: Left ventricular outflow tract, SAM: Systolic anterior motion, MR: Mitral regurgitation, Me [IQR]: Median interquartile range, CI: Confidence interval, $M \pm SD$: Mean \pm standard deviation

Table 4. Risk factors for residual mitral regurgitation $\geq 2+$ after isolated septal myectomy

Risk factors for residual MR ≥ 2	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p	OR (95% CI)	p-value
IVS thickness after SM	0.981 (0.885-1.089)	0.722	1.065 (0.893-1.269)	0.483
LVOT gradient after SM	1.106 (0.957-1.279)	0.183	1.003 (0.975-1.032)	0.821
Residual SAM	16.640 (3.387-81.747)	0.001	13.994 (2.692-72.744)	0.02

MR: Mitral regurgitation, IVS: Interventricular septum, SM: Septal myectomy, SAM: Systolic anterior motion, LVOT: Left ventricular outflow tract, OR: Odds ratio, CI: Confidence interval

group 2 due to mesenteric thrombosis; there were no deaths in group 1. two patients (5.6%) in group 1 and six patients (7.2%) in group 2 required permanent pacemaker implantation due to complete atrioventricular block ($p=0.74$). The groups did not differ significantly in terms of the frequency of other postoperative complications or duration of intensive care unit or hospital stay (Table 2).

Postoperative Hemodynamics

According to transthoracic echocardiography and MRI (Table 3), the majority of patients in group 2 (91%, $n=75$) and all patients in group 1 had MR grades 0-1 at discharge (Figure 2). Residual MR grade 2+ was identified in 7 patients (9%) in group 2. There was a significant decrease in IVS thickness in both groups, with no significant differences between the groups (group 1: 12 [10;13] mm, group 2: 13 [11;14] mm, $p=0.36$). The LVOT gradient was 11 [9;17] mmHg in group 1 and 11 [7;18] mmHg in group 2 ($p=0.93$) (Figure 3). Two patients (5.6%) in group 1 and four patients (4.8%) in group 2 had residual LVOT gradient ≥ 30 mmHg ($p=0.87$). Residual SAM was identified in 2 patients (5.6%) in group 1 and 7 patients (8.4%) in group 2 ($p=0.58$). Univariate regression analysis identified residual SAM (OR: 16.640, 95% CI: 3.387-81.747, $p=0.001$) as a predictor of MR $\geq 2+$ after SM (Table 4). Multivariate regression analysis identified only residual SAM (OR: 13.994, 95% CI: 2.692-72.744, $p=0.02$) as a predictor of residual MR $\geq 2+$.

Discussion

In this study, we evaluated the clinical and hemodynamic results of isolated SM in patients with moderate and severe MR and compared them with patients with no or mild MR.

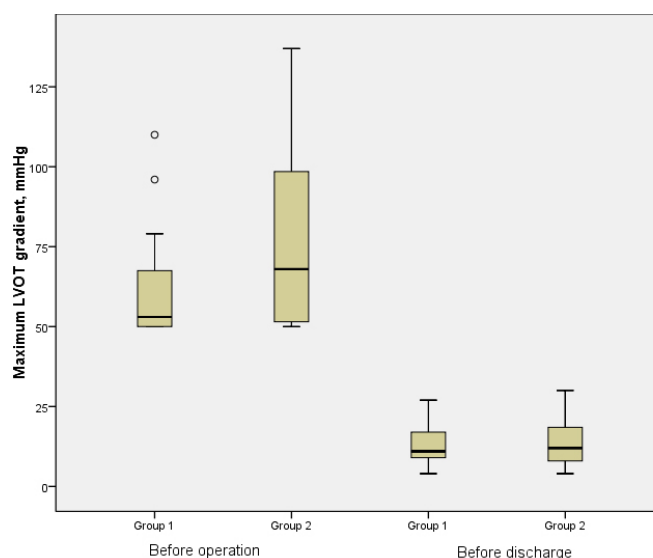


Figure 3. Maximum LVOT gradient before and after septal myectomy
LVOT: Left ventricular outflow tract

We used MR grade after surgery as the primary endpoint. The main finding of the study was that most patients with severe MR after isolated SM experienced a reduction in the severity of MR, with MR grade 2 persisting in only 9% of cases. The frequency of repeated aortic occlusion for unplanned MV intervention due to persistent or increasing severe MR was 3.4%; and MV replacement was performed in only one case (0.8%).

The need for MR correction among patients with HOCM remains a topic of debate.

The Mayo Clinic, which has the greatest experience in the surgical treatment of HOCM (over 3000 patients), believes that isolated SM adequately eliminates left

ventricular (LV) obstruction and SAM-induced MV regurgitation under two conditions. First, the MR was likely due to SAM without MV pathology and anomalies. Second, sufficient extended SM, including excision of the IVS toward the apex beyond the mitral-septal contact, should be performed. When these conditions are met, concomitant MV surgery is rarely required. The frequency of unplanned correction of MR due to insufficient depth and length of IVS excision was 2.8%. After isolated SM, the proportion of patients with MR >3+ decreased from 54.3% to 1.7%⁽⁴⁻⁶⁾.

Afanasyev et al.⁽¹⁵⁾ reported that 69% of patients with HOCM had moderate to severe MR before surgery, including those with independent MV pathology. MV annuloplasty due to MV pathology was performed in 8.6% of cases, and MV replacement was performed in 14.1% of cases. Residual MR >2+ was observed in 73 patients (12.8%), with the surgeon's individual experience (OR: 3.4, 95% CI: 1.5-7.7, $p=0.003$) and insufficient resection of the IVS (OR: 2.3, 95% CI: 1.4-3.8, $p=0.002$) identified as predictors by logistic regression analysis.

Proponents of a more aggressive approach to MR advocate for additional interventions on the MV, including MV replacement, edge-to-edge repair, anterior mitral leaflet plication, and secondary chordal resection. However, modern guidelines suggest that routine MV replacement should not be considered for patients with HOCM to eliminate LVOT obstruction, SAM, and MR because it is associated with increased early and long-term mortality risk⁽²⁾. Some authors have reported acceptable results of edge-to-edge SAM repair⁽¹⁰⁾. Nonetheless, the Alfieri stitch does not completely eliminate LVOT obstruction in cases of incomplete SM, may result in higher MV gradients, and could lead to mitral stenosis or MR in the long term. Anterior mitral leaflet plication, which was first proposed by Cooley⁽¹¹⁾ and McIntosh et al.⁽¹²⁾, is actively used in Cleveland (25% of all septal myectomies). This technique involves longitudinal plication of the anterior MV leaflet with several separate mattress stitches using 4-0 Prolene sutures and may be

beneficial for patients with HOCM and an elongated anterior MV leaflet.

Anomalies of the submittal structures can significantly contribute to the mechanism of LVOT obstruction, SAM, and MR, particularly in patients with lesser IVS thickness (<18 mm)^(10,16). These structures should be carefully evaluated for potential intervention, which may include: mobilization and excision of the accessory papillary muscle, excision of fibrous and muscular attachments between the mitral apparatus and the head of the papillary muscle, LV free wall, and IVS, and resection of the secondary chordae of the MV anterior leaflet. In our study, septal thickness did not influence the persistence of MR after surgery. Bogachev-Prokophiev et al.⁽⁹⁾, drawing on the experience of Ferrazzi et al.⁽⁸⁾, studied the effects of intervention performed on the submittal apparatus on postoperative gradient, residual MR, and SAM. All patients had moderate to severe MR at baseline. In the submittal intervention group compared with the isolated SM group, there was no residual MR (0% vs. 15%, $p=0.013$), SAM persisted less frequently (5% vs. 28%, $p=0.007$), and a lower LVOT gradient was observed (8 mmHg vs. 13 mmHg, $p=0.019$). Additionally, the need for repeated aortic cross-clamping was more common in the isolated SM group (17.5% vs. 2.5%, $p=0.031$). The authors concluded that, in most cases, extended SM is sufficient to achieve good results in patients with HOCM. However, when anomalies of the submittal structures are present, intervention may be the preferred approach.

The analysis of the secondary endpoints of this study (mortality, atrioventricular block, acute IVS defect, residual SAM, LVOT gradient >30 mmHg) demonstrated that our results were comparable to those obtained at centers with the greatest experience in surgical treatment of patients with HOCM. Mortality following SM was reported to be 0%-0.9% in the literature and 0.8% in our study population. The frequency of permanent pacemaker implantation was 0.9%-15% in the literature and 6.7% in our study; the frequency of acute IVS defect was 0%-5% in the literature and 0% in our study^(3,15,17). The most

experienced centers report residual SAM in 7-35% of cases and residual LVOT gradient >30 mmHg in 0%-11% of cases; in our study, residual SAM and residual LVOT gradient were reported in 7.6% and 5% of cases, respectively^(5,10,15). The surgeon's experience, depth, and length of IVS excision are commonly reported to be independent predictors of these adverse hemodynamic events^(5,15).

Study Limitations

This study is retrospective and based on our database, reflecting the experience of a single center. Both groups were represented by a small sample of patients. Long-term outcome studies and randomized trials are needed to select the optimal treatment for these patients.

Conclusion

In our study, among patients with moderate and severe MR, only 3.6% required repeated aortic cross-clamping and MV intervention. Before discharge, only 9% of the patients had moderate MR. Consequently, in most patients with HOCM and moderate/severe MR not due to organic MV lesions, isolated SM effectively relieves LVOT gradients, SAM of the MV, and associated MV regurgitation.

Ethics

Ethics Committee Approval: The conducted study complies with the standards of the Declaration of Helsinki, is approved by the Independent Ethical Committee of the Federal State Budgetary Institution Federal Center For Cardiovascular Surgery Ministry of Health of The Russian Federatio (Khabarovsk) (approval no: 39, date: 11.11.2023).

Informed Consent: This retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: Kobzev EE, Rosseykin EV, Desai V, Concept: Kobzev EE, Rosseykin EV, Desai

V, Design: Kobzev EE, Rosseykin EV, Desai V, Data Collection and/or Processing: Kobzev EE, Analysis and/or Interpretation: Kobzev EE, Literature Search: Kobzev EE, Writing: Kobzev EE, Rosseykin EV, Desai V.

Conflict of Interest: The author declare no conflicts of interest concerning the authorship or publication of this article.

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