Mid-Term Outcome of Mitral Valve Replacement During Septal Myectomy for Hypertrophic Obstructive Cardiomyopathy

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Abstract

Background

The mitral valve shows significant involvement in hypertrophic obstructive cardiomyopathy (HOCM). The mid-term outcomes of management of HOCM by prosthetic valve replacement with septal myectomy remain unclear. This study compared the prognosis of patients with and without prosthetic valve replacement.

Methods

From 01/2009 until 10/2015, 24 patients with HOCM underwent septal myectomy with or without valve repair/replacement were recruited. A total of 23 patients underwent echocardiographic evaluation before and after the operation. The follow-up duration ranged from 0.4 to 7 years (median 2.5 years). The Kaplan-Meier test was used to explore the association between prosthetic valve replacement and overall/disease-free survival among HOCM patients.

Results

A total of 9 patients underwent septal myectomy with/without mitral valve repair (MVr), and the other 15 patients underwent septal myectomy with mitral valve replacement (MVR). Six patients treated with MVR had unfavorable outcomes, including one peri-operative and three late deaths; one patient suffered from aborted sudden death, and one patient was treated for prosthetic valve endocarditis. Prosthetic valve replacement was associated with poor disease-free survival ($p = 0.025$).

Conclusions

Septal myectomy with or without-MVr was associated with a better outcome than septal myectomy with MVR in HOCM patients. The differences in prognosis were caused by more complicated left ventricular outflow tract structures and more prosthetic valve complications among patients undergoing MVR.

Background

Hypertrophic obstructive cardiomyopathy (HOCM) is a common cardiovascular disease that leads to symptomatic left ventricular outflow tract (LVOT) obstruction, including dyspnea, chest pain and syncope, resulting in heart failure. The obstruction can be caused by a hypertrophic ventricular septum and/or systolic anterior movement (SAM) of the mitral valve leaflets (1, 2). Therefore, HOCM often occurs with mitral valve disease, with most patients exhibiting valve prolapse and regurgitation.

Accordingly, the treatment aim is to decrease the left ventricular outflow tract (LVOT) gradient either by septal myectomy or alcohol septal ablation (3). Septal myectomy is currently the preferred treatment for HOCM patients with an LVOT obstruction whose symptoms are refractory to maximal medical therapy, and it is associated with a better prognosis (4). SAM can be managed by mitral valve repair or replacement, but the latter cause long-term valve and left ventricular dysfunction (5–8).

However, because of mixed etiologies, inadequate study and limited sample sizes, the published articles generally do not report a long-term outcome for HOCM patients treated with or without artificial valve replacement. Hence, the purpose of this study was to assess the effect of valve replacement on mid-term outcomes in patients undergoing septal myectomy for HOCM.

Methods

Patients

This retrospective observational study was approved by the Institutional Review Board of the First Affiliated Hospital of Sun Yat-sen University (2018-101). At the First Affiliated Hospital of Sun Yat-Sen University from 01/2009 to 10/2015, 24 patients with severe medically refractory symptoms from HOCM, as diagnosed by echocardiogram, underwent septal myectomy. Preoperative, operative, and postoperative data were obtained from the database and from reviewing medical records. The preoperative and postoperative echocardiograms were analyzed. HOCM was defined by the presence of symptoms with a peak LVOT gradient of >50 mmHg with provocation or at rest. Prior to the surgery and after extensive discussion of treatment options, including limitations and risks, written informed consent was obtained for all procedures. The investigation conformed with the principles outlined in the Declaration of Helsinki and local legal requirements. The patients were followed up by telephone interview and by reviewing the patients' clinical records, including echocardiographic examinations.

Procedure

The septal myectomy procedure, also known as the Morrow operation or extended septal myectomy, was previously described in detail by Bin CUI[2]. Surgery was performed via a median sternotomy with cannulation and cardiopulmonary bypass. The classical Morrow procedure was performed to resect the hypertrophic interventricular septum from 2 to 3 mm rightward to the midpoint of the right coronary sinus to 10-12 mm toward the left coronary sinus. Typically, the resection was extended to the bottom of the papillary muscle of the anterior mitral leaflet. For some patients, the resection was extended distally beyond the level of the mitral anterior papillary muscles toward the apex, and the hypertrophic septal muscle below the membranous septum may also be resected. Intraoperative TEE evaluation was performed immediately after the patients were weaned from CPB.

Statistics

Continuous values are presented as the mean ± standard deviation. Paired t-tests were used to compare continuous preoperative and postoperative data. One-way ANOVA was used to compare data between patients treated with/without valve replacement. Chi square and Fisher's exact tests were used to compare categorical preoperative and postoperative data. Deaths and cumulative events were calculated using the Kaplan-Meier method, with all-events or censored events measured from the time of the operation. The significant differences in events between groups were assessed with the log-rank test. Statistical significance was indicated by a p value <0.05.

Results

A total of 24 patients with a mean age of 55 ± 12 years who underwent septal myectomy with or without valve surgery were identified and followed for an average 30 months. The baseline characteristics are shown in Table 1. Among these patients, 5 underwent isolated septal myectomy, 4 underwent mitral valve repair (MVr) with an annuloplasty ring, 14 underwent mitral valve replacement (MVR), and 1 underwent both aortic and mitral valve replacement.

Table 1
Demographic and clinical characteristics

Variable	n (%)
Male	13 (54%)
Operation	
Septal Myectomy	5 (21%)
Myectomy + Mitral Valve Replacement	14 (58%)
Myectomy + Mitral Valve Repair	4 (17%)
Myectomy + Aotric + Mitral valve replacement	1 (4%)
NYHA Function Class	
II	9 (38%)
III	14 (58%)
IV	1 (4%)
Atrial Fibrillation	3 (13%)
Chronic kidney disease	2 (8%)
Infective Endocarditis	1 (4%)
Pre-operative Stroke	1 (4%)
Follow-up	
Perioperative Death	1 (4%)
Die from acute heart failure	2 (8%)
Die from Infective Endocarditis	1 (4%)
Artificial Valve Endocarditis	1 (4%)
Aborted Sudden Death	1 (4%)
NYHA: New York Heart Association	

Among 24 patients, 6 patients had unfavorable outcomes, including 1 peri-operative death, and 3 late deaths during follow-up (1 with a prosthetic valve infection that was refractory to treatments and 2 with acute heart failure several months later). One patient who suffered from prosthetic valve infection was successfully treated and stayed alive. Another patient with a previous history of aborted sudden death experienced another attack one year after the operation.

The pre- and postoperative data are shown in Table 2. The patient who died perioperatively was not included. Before septal myectomy, 14 (58%) patients were classified as New York Heart Association

(NYHA) functional class III/IV. After the surgery, the heart functions significantly improved, and no patients remained classified as NYHA class III/IV ($P < 0.001$). There was also a decrease in the proportion of patients with SAM and moderate-to-severe mitral regurgitation, which occurred in 17 patients (77%) before surgery and 2 patients (9%) after surgery. As expected, septal myectomy resulted in a significant reduction in ventricular septal thickness (from 25 ± 6 mm to 17 ± 4 mm, $p < 0.001$). The LVOT gradient also significantly decreased from 93 ± 39 mmHg to 24 ± 21 mmHg ($p < 0.001$). The size of the left ventricle decreased from 46 ± 8 mm to 43 ± 6 mm($P = 0.01$). Ejection fraction and pulmonary pressure were also significantly decreased.

Table 2
Pre- and postoperative comparisons

Variable	Pre-operative (n = 23)	Post-operative (n = 23)	P value
NYHA heart function III-IV	14 (61%)	0 (0%)	< 0.001*
Mitral Valve SAM	10 (43%)	1 (4%)	0.002*
Mitral regurgitation (> grade II)	17 (71%)	0 (0%)	< 0.001*
LVOT gradient (mmHg)	95 ± 40	24 ± 23	< 0.001*
The thickest of VS (mm)	24 ± 6	17 ± 4	< 0.001*
Size of LV (mm)	46 ± 7	42 ± 5	0.006*
Size of LA (mm)	44 ± 7	43 ± 7	0.706
EF (%)	68 ± 8	62 ± 8	0.006*
Pulmonary Artery Pressure (mmHg)	28 ± 14	19 ± 12	0.008*
Data are mean ± SD for continuous data or number (percent) for categorical data.			
SAM: Systolic Anterior Movement; LVOT: Left Ventricular Outflow Tract; VS: Ventricular Septum; LV: Left Ventricle; LA: left atrium; EF: Ejection Fraction.			

We further compared the preoperative clinical characteristics in patients treated with or without artificial valve replacement (Table 3). There were no significant differences in sex, heart function, SAM, mitral regurgitation and echo data between groups except for of ventricular septal thickness (26 ± 6 mm in valve replacement group vs. 18 ± 5 mm in the no valve replacement group).

Table 3
Demographic and clinical characteristics between groups

Variable	Valve Replacement (n = 15)	No valve Replacement (n = 9)	P value
Male	8 (53%)	5 (56%)	0.625
NYHA Function Class			
II	6 (40%)	3 (38%)	0.547
III-IV	9 (60%)	6 (67%)	
SAM	8 (53%)	8 (89%)	0.087
Mitral regurgitation (> grade II)	12 (80%)	6 (67%)	0.397
CPB time (min)	206 ± 80	165 ± 94	0.271
Cross clamp time (min)	61 ± 40	50 ± 34	0.499
Overall Survival	11 (73%)	0 (0%)	0.128
Die perioperatively	1 (7%)	0 (0%)	
Die from acute heart failure	2 (13%)	0 (0%)	
Die from Infective Endocarditis	1 (7%)	0 (0%)	
Artificial valve Endocarditis	1 (7%)	0 (0%)	
Aborted Sudden Death	1 (7%)	0 (0%)	
Disease Free Survival	9 (67%)	0 (0%)	0.037*
Echo data			
LVOT gradient (mmHg)	89 ± 42	105 ± 33	0.348
Thickness of Ventricular Septum (basal segment, mm)	26 ± 6	18 ± 4	0.007*
Size of LV (mm)	47 ± 7	43 ± 7	0.140
Size of LA (mm)	44 ± 8	43 ± 7	0.674
EF	67 ± 9	68 ± 5	0.753
Pulmonary Pressure (mmHg)	27 ± 15	29 ± 12	0.738

NYHA: New York Heart Association; SAM: Systolic Anterior Movement; CPB: Cardiopulmonary Bypass; LVOT: Left Ventricular Outflow Tract; LV: Left Ventricle; LA: left atrium; EF: Ejection Fraction

The degree of mitral regurgitation and SAM among patients treated without MVR was tracked before and after the surgery (Fig. 1a and b). At the time of discharge, mitral regurgitation had improved to grade 1 or 0 in 8 patients (89%). One patient still had grade 2 mitral regurgitation. During the follow-up, a further decrease or increase in mitral regurgitation was observed in 2 patients. Minor SAM was observed in only 1 patient after the operation and remained unchanged in the follow-up.

All 6 patients with unfavorable outcomes in the follow-up had undergone valve replacement surgery. There was no difference in overall survival between the MVR and no MVR groups (P = 0.1, log-rank test). Overall and disease-free survivals was further calculated using the Kaplan-Meier plot (Fig. 2). Based on the log-rank test, there was a significant difference in disease-free survival (p = 0.025). Because the mortality rate was zero in the no valve replacement group, the multivariate Cox regression model was not used to assess whether valve replacement was an independent prognostic factor for disease-free survival.

Discussion

Our study provided evidence that surgical septal myectomy had a satisfactory peri-operative outcome with improved heart function and decreased LVOT pressure, ventricular septal thickness, left ventricular size and pulmonary artery pressure. In the follow-up, patients with artificial valve replacement had lower disease-free survival and overall survival. In addition to the 3 patients who died of acute or chronic heart failure, 25% of deaths (1 in 4) resulted from artificial valve endocarditis. Another patient with prosthetic valve endocarditis survived after treatment, indicating that artificial valve dysfunction also plays an important role in long-term outcomes. Isolated surgical septal myectomy was associated with excellent prognosis with zero mortality, which was concordant with previous studies (9).

According to recent studies, the mitral leaflets of patients with HOCM, especially the posterior mitral leaflet, are longer and exhibit a greater area than those of normal controls, leading to varying degrees of mitral regurgitation (10–12). The rapid ejection of blood flow through the LVOT initiates a drag force on the mitral valve, which causes an anterior displacement of the mitral valve apparatus (2, 13). On the another hand, the increased length of the anterior or posterior mitral valve leaflet may be pushed into the LVOT by rapid blood flow (11.14). Although SAM may not be alleviated completely, most cases can be managed by isolated septal myectomy. Mild SAM will not cause prominent activity restriction, which is in line with our results (2). Apart from SAM, residual mitral regurgitation can be observed after the LVOT obstruction is adequately relieved and may be caused by mitral valve prolapse, elongated leaflets, annular calcification, papillary muscle thickness, etc (11, 15, 16). In those cases, mitral valve repair (MVr) or replacement (MVR) should be performed. However, the repair is relatively hard because of valve structure distortion and residual LVOT thickness. In addition, the thickened myocardium is more vulnerable to another aorta clamping attempt if the repair fails. Our research demonstrated that a thickened ventricular septum may lead surgeons to choose valve replacement. As a result, MVR may be advocated by some surgeons to achieve a better short-term outcome.

In our study, 13 out 17 patients (76.4%) with concurrent mitral valve disease received MVR. According to an early study in 2011, most patients (82.8%) with a HOCM diagnosis underwent MVR for the correction of mitral valve pathology in the USA, indicating that MVr is underused among such patients (17). However, in our center, most patients had prolonged courses of disease before the surgery and relatively thin mitral leaflets, which may lead to a more challenging mitral valve repair. The peri-operative mortality rate for patients treated with MVr is zero, and for those treated with MVR is 11.18%, which are consistent with our research. MVr, rather than MVR,is now regarded as a better procedure for patients with degenerative diseases, unless ischemic heart diseases are present (18). The risk-adjusted survival data show improved mid- and long-term survival for MVr with better duration, preservation of left ventricular systolic/diastolic functions and freedom from prosthetic valve-related complications, especially infective endocarditis, and hemorrhage (19–22), which occurs only in patients with extremely complex disease, including anterior or bileaflet prolapse, valve calcification and an enlarged LA (23). Our results showed several cases of acute heart failure and aborted sudden death several months after MVR, indicating that MVr play may an important role in maintaining left ventricular function. Longer anterior or posterior mitral leaflets with prolapse are commonly observed in HOCM patients, whereas annular calcification is relatively rare. Despite worse mitral valve structure in patients undergoing MVR, MVr should be performed in a majority of patients for a better prognosis. Many MVr techniques can be performed, including leaflet detachment, extension, retention (11) and annuloplasty (24–25). From our results, residual regurgitation or SAM after MVr was acceptable, because they did not cause obvious activity restriction and reoperation among patients.

Our research has several limitations. This was not a randomized trial and included MVR patients suffering from more complicated diseases, thus resulting in relatively worse prognosis in MVR patients. In addition, the sample size is relatively small. The absence of mortality in the MVr group caused the hazard ratio in the Cox regression model to be extremely high, which restricted its use.

In conclusion, septal myectomy is an appropriate technique for managing HOCM. Septal myectomy with or without MVr was associated with a better outcome than septal myectomy with MVR in HOCM patients. The differences in prognosis were not only due to poorer mitral valve and septum structure among patients undergoing MVR but also due to more prosthetic valve complications. Treatment with MVr should be the first choice among HOCM patients with concomitant mitral valve dysfunction unless they have complicated diseases.

Declarations

Ethics approval and consent to participate

This retrospective observational study was approved by the Institutional Review Board of the First Affiliated Hospital of Sun Yat-sen University (2018-101). All participants provided written consent before entering the study.

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Not applicable

Consent for publication

Not applicable.

Availability of data and materials

The datasets used during the current study are available from the correspond- ing author on reasonable request.

Competing interests

All authors declare that they have no competing interests.

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Figures

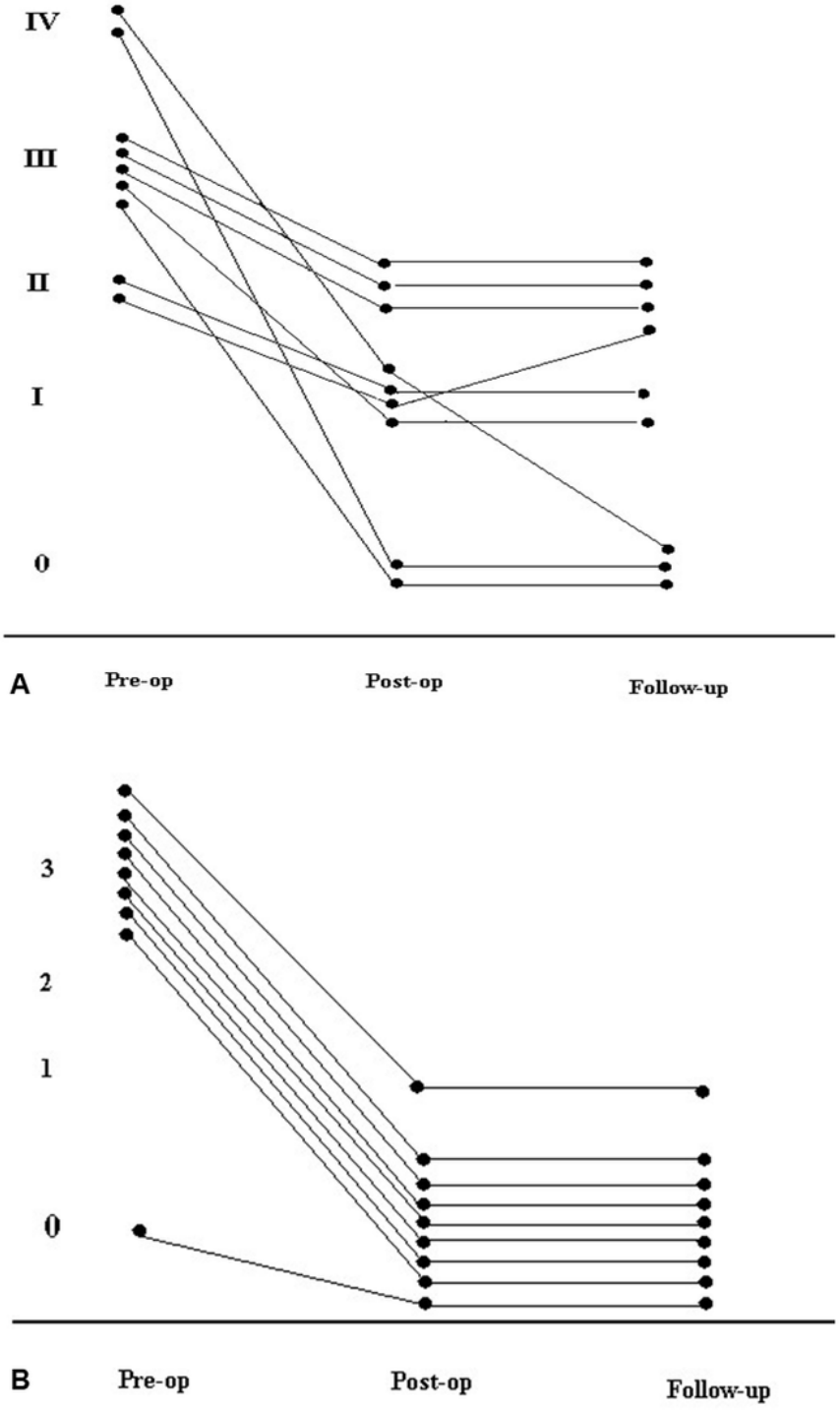

Figure 1

Time course of mitral regurgitation and SAM after septal myectomy with or without MVP before the operation, before discharge and during follow-up. The degree of mitral regurgitation (1A), and the degree of SAM (1B).

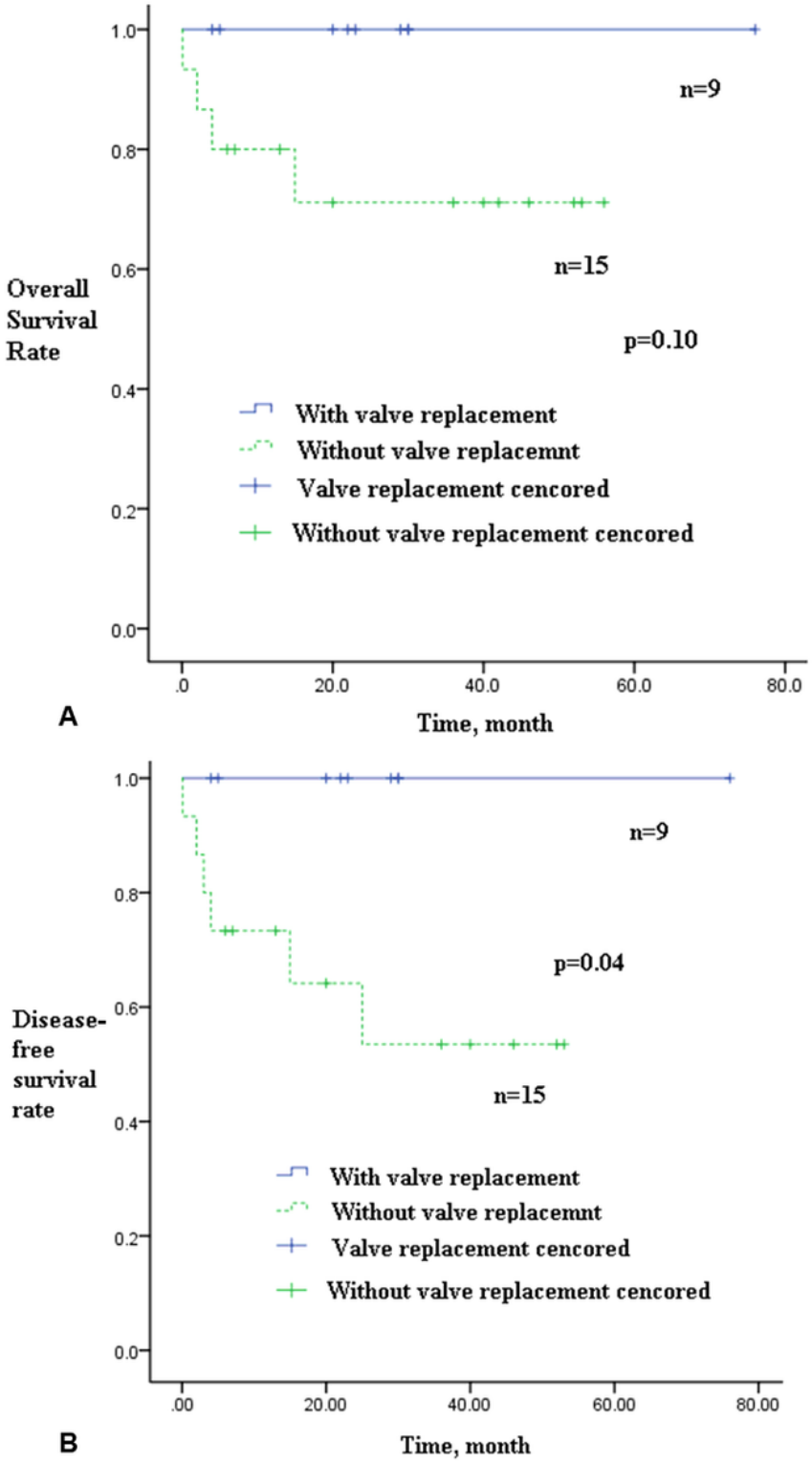

Figure 2

Kaplan-Meier survival curves for overall (A) and disease-free survival (B) in HOCM patients treated with or without prosthetic valve replacement. (Log-rank test, overall survival, p=0.10; and disease-free survival, p=0.025).