Midterm Outcome of Septal Myectomy for Hypertrophic Obstructive Cardiomyopathy (HOCM): A Single-Center Observational Study

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ABSTRACT

Background: For years, septal myectomy has been considered the best available treatment for hypertrophic cardiomyopathy. In Bangladesh, however, this technique is only nascent. We present a case series of septal myectomy with outcomes after 1 to 6 years at the National Heart Foundation Hospital & Research Institute.

Methods: For this study, 21 patients who underwent septal myectomy from 2014 to 2019 were monitored retrospectively. Evidence was collected from the hospital database and followed up via telephone conversations using a structured questionnaire. Patients’ preoperative, postoperative, and follow-up clinical data were collected and analyzed.

Results: The results reveal that after septal myectomy, there were significant improvements in terms of left ventricular outflow gradient ($P \leq .01$), left ventricular ejection fraction ($P = .001$), pulmonary arterial systolic pressure ($P \leq .01$), mitral regurgitation ($P \leq .01$), systolic anterior motion ($P \leq .01$), and New York Heart Association class ($P \leq .01$).

Conclusion: This study suggests that septal myectomy be offered to symptomatic hypertrophic obstructive cardiomyopathy patients, as its survival benefits and symptoms relief are excellent. This study suggests that septal myectomy that dynamic obstruction at the left ventricular outflow tract is the major hemodynamic problem. We hope that with appropriate measures, new myectomy programs in our country can provide extended longevity and restore the quality of life.

INTRODUCTION

Hypertrophic cardiomyopathy is considered one of the most common forms of genetic heart disease, occurring in >1 in 500 [Semsarian 2015]. The etiology is related to genetic mutations of the sarcomere, resulting in hypertrophy of the myocardium. Eventually, most patients develop dynamic left ventricular outflow tract obstruction due to septal hypertrophy, as well as systolic anterior motion (SAM) of the mitral valve, possibly due to the Venturi effect or anatomic differences in papillary muscle position and valve leaflets. Secondary mitral regurgitation may also develop [Maron 2006].

Common symptoms are exertional dyspnea, angina, and syncope. Devastating consequences such as progressive heart failure and sudden cardiac death, primarily occur due to electrophysiological abnormality from scarring. Fibrosis of hypertrophied myocardium is often seen as well. Exertional dyspnea and fatigue symptoms can be produced by severe diastolic dysfunction in patients with hypertrophic obstructive cardiomyopathy (HOCM) without left ventricular outflow tract (LVOT) obstruction [Abozguia 2010]. The initial stage of the disease can be managed by medical therapy; however, limiting symptoms demand septal reduction therapies [Rick 2016]. Medications used include high-dose β-blockers, verapamil, disopyramide [Maron 2003; Maron 2002; Spirito 1997], and low-dose diuretics in the presence of congestive heart failure. Even in highly symptomatic cases, most patients are managed pharmacologically. Despite relevant medication adjustment, symptom relief can be incomplete, transient, and accompanied by intolerable drug-related adverse effects [Schaff 2012].

Surgery is indicated for patients with persistent symptoms refractory to medical treatment and severe LVOT obstruction with a resting gradient >30 mmHg [Schaff 2012]. In individual patients, there is often uncertainty about the importance of minimal resting gradients in the pathophysiology of limiting symptoms. However, it is now recognized that in a sizable proportion of patients, those with minimal LVOT gradients at rest will have larger gradients provoked after exercise, Valsalva maneuver, administration of amyl nitrite, or isoproterenol infusion [Vaglio 2008].

The question is whether septal reduction for relief of the inducible LVOT obstruction will lead to clinical improvement [Schaff 2012], as patients with labile LVOT obstruction should be more responsive to medical treatment than patients with severe resting outflow tract gradients. Analysis has shown...
that patients with HOCM and preoperative latent obstruction have excellent survival and functional improvement after transaortic myectomy. Operative risks are low for patients with latent obstruction, and subsequent survival was similar to that of patients with severe resting obstruction. Undeniably, 10-year survival of patients with preoperative latent obstruction, including patients with concomitant procedures, was identical to that of an age-matched group. This finding, along with comparable improvements in functional status after surgery, suggests that the major contributor to symptoms in patients with latent obstruction is dynamic outflow gradient, rather than severe diastolic dysfunction [Schaff 2012]. Alcohol septal ablation improved 76% of symptoms over 4 years. However, in-hospital complication rates are higher with alcohol ablation than with myectomy, leaving unanswered the question of an enhanced propensity for ventricular arrhythmia [Sorajja 2008]. Furthermore, for patients <65 years old, symptom relief is better after myectomy, proving that surgical myectomy should be the preferred technique for septal reduction in patients who are in good general health and have no contraindications for surgery [Schaff 2012]. Postoperative longitudinal studies show sustained clinical improvement in 85% to 90% of patients, who become asymptomatic (or only mildly symptomatic) on average for 8 years (and up to 25 years) after myectomy [Maron 2004; Woo 2005; Ommen 2005; Maron 2005; Dearani 2007; Nishimura 2010]. There are some comparative observational and nonrandomized studies [Dearani 2007; Nishimura 2010; Maron 2007; ten Cate 2010; Sorajja 2008; Firoozi 2002; Merrill 2000; Qin 2001], together with a recent meta-analysis [Agarwal 2010], proves that surgery can provide the most consistent, complete, and rapid relief of symptoms (particularly in patients >65 years). Furthermore surgery is associated with lower postintervention outflow gradients and fewer procedural complications and reinterventions [Maron 2011].

Therefore, for the last 50 years, septal myectomy among the septal reduction therapies has been considered the gold standard treatment for patients with HOCM and drug-refractory heart failure [Firoozi 2002]. Relief of LVOT obstruction by transaortic septal myectomy improves symptoms in >85% of patients with severe resting obstruction [McCully 1996]. This technique provides permanent amelioration of obstruction (and relief of mitral regurgitation) at rest and it restores functional capacity with an acceptable quality of life at any age, exceeding what is achievable with chronic administration of cardioactive drugs [Maron 2003]. These benefits can be demonstrated subjectively by patient history and objectively by increased treadmill time, maximum workload, peak oxygen consumption, and improved myocardial oxygen demand, metabolism, and coronary flow [Maron 2003; Firoozi 2002; Ommen 1999]. Heart failure from obstructive HOCM, therefore, can be regarded as surgically correctable. Septal myectomy effectively relieves LVOT obstruction and cardiac symptoms in adults and children with obstructive HOCM.

The prevalence of HOCM patients in Bangladesh is not known. Malek et al. [2014] performed a study with 3648 patients and found that 4.06% had HOCM. That is a substantial number of people, and it is a matter of great regret that only a few of them got appropriate medical attention and care because of poor diagnosis and referrals. In Bangladesh, surgical septal myectomy is still an infrequent procedure and is performed with a satisfactory outcome mainly at the National Heart Foundation Hospital & Research Institute. Through this study, we share experiences and observations based on outcomes of the patients who underwent septal myectomy in this institution.

**METHODS**

In total, 23 myectomies were performed at the National Heart Foundation Hospital & Research Institute between July 2016 and June 2019. Of these 23, this retrospective cohort study examined 21 patients (one patient passed away on day 1 and 1 patient was lost to follow-up). All patients admitted to the Cardiac Surgery Department to undergo septal myectomy were included in this study, which was conducted according to ethical guidelines. Patients who required concomitant cardiac surgical procedures were not excluded. After admission,
Table 1. Demographic variables (N = 21)

| Characteristic | n (%)         | Mean ± Standard Deviation |
|----------------|---------------|---------------------------|
| Age (y)        |               |                           |
| 25 to 40       | 9 (42.86)     | 39.76 ± 14.003            |
| 40 to 60       | 5 (23.81)     |                           |
| >60            | 2 (9.52)      |                           |
| Male           | 14 (66.7)     |                           |
| Female         | 7 (33.3)      |                           |
| Height (cm)    |               | 158.24 ± 11.054           |
| <150           | 2 (9.52)      |                           |
| >150           | 19 (90.47)    |                           |
| Weight (kg)    |               | 61.71 ± 11.376            |
| >50            | 17 (80.92)    |                           |
| <50            | 4 (19.05)     |                           |
| BMI (kg/m²)    |               | 24.67 ± 4.258             |
| <20            | 19 (90.47)    |                           |
| >20            | 2 (9.52)      |                           |

all patients went through routine preoperative preparation, including color Doppler echocardiography, which provides the best estimation of septal thickness and is critical in planning the extent of the surgical resection. Statistical analysis of preoperative, intraoperative, and postoperative variables was done. After weaning from cardiopulmonary bypass, transesophageal echocardiography (TEE) was performed before initiation of cardiopulmonary bypass to assess ventricular septal thickening, mitral valve morphology, and degree of mitral regurgitation and to measure the left ventricular (LV) outflow tract gradient. The left ventricle was vented through the right upper pulmonary vein. After clamping of the distal ascending aorta, the heart was arrested with antegrade cold cardioplegia. The aorta was opened through an oblique incision extending up to the noncoronary sinus. After gentle retraction of the aortic leaflets, the hypertrophied septum was visualized, and pressing the right ventricular free wall improved the view further. The first incision was made in the septum, 5 mm left of the nadir of the right coronary cusp, and a second incision was made just before the commissure of left coronary cusp and noncoronary cusp. These 2 incisions were connected with a transverse incision, and pieces of septum were excised. Further excision of muscle bulk was done to increase the cross-sectional area of the left ventricular outflow tract.

After weaning from cardiopulmonary bypass, TEE confirmed satisfactory relief of outflow tract obstruction and resolution of mitral regurgitation. Indications to resume CPB and perform additional muscular resection or mitral valve intervention included residual mitral–septal contact with gradient >30 mmHg or ≥2 mitral regurgitation.

Statistical Analysis

Continuous and categorical data were expressed as mean (± standard deviation) and n (%), respectively. Comparisons of characteristics between groups were made with unpaired Student’s t test or 1-way ANOVA, where appropriate, for continuous and categorical data. A P value of <.05 was considered statistically significant. Study end points were all-cause mortality and HOCM-related mortality. Statistical analysis was performed with SPSS, version 20.

RESULTS

The mean age of patients was 37.857 ± 12.302 years (range 23 to 67), with 9 patients (42.86%) <40 years old and 2 (9.5%) 40 to 60; 14 patients (66.7%) were male; and 19 patients (90%) had a body mass index <20 kg/m². One patient had diabetes mellitus, and 10 patients had associated mitral or aortic valve pathology. Twelve patients underwent isolated myectomy, and others needed ≥1 additional procedure. Only 1 patient required mitral valve replacement for structural mitral valve disease along with septal myectomy.

There were no statistically significant differences between pre and postoperative hemoglobin concentration (P = .478) or serum creatinine (P = .691). Maximum septal thickness decreased from 20.67 ± 3.86 mm preoperatively to 16.52 ± 2.42 mm a month following surgery which was statistically significant (P < .001), and the value was similar in the follow-up period (15.02 ± 1.94 mm). There was a satisfactory improvement of left ventricular outflow gradients after surgery (preoperative, 81.57 ± 17.05; postoperative, 18.95 ± 7.9 mmHg), which was statistically significant (P < .001). During follow-up, the most recent echocardiogram showed that it decreased further (8.87 ± 2.54), which was statistically significant (P ≤ .001).

Heart failure symptoms consistent with New York Heart
Association (NYHA) class III/II were present preoperatively in 11 patients (class III, 3; class II, 8; mean 2.95 ± 0.38) based on personal functional capacity deficits, including exertional dyspnea or chest pain during daily work. No patient had NYHA class IV symptoms. During follow-up, all patients reached NYHA class I, which was statistically significant ($P \leq .001$).

Pulmonary artery systolic pressure (PASP) improved (preoperative, 39.05 ± 4.34; postoperative, 34.29 ± 4.78), and improvement persisted during follow-up (21.86 ± 4.98) and was statistically significant ($P \leq .001$). Left ventricular ejection fraction (LVEF) was similar in all groups preoperatively (64.86 ± 5.17), after myectomy (64.43 ± 4.42), and at follow-up (65.62 ± 4.33); no significant change was noted. One patient found to have severe mitral regurgitation (MR) (3.14 ± 0.73), due to rheumatic structural changes that required mitral valve replacement. Eight patients with preoperative moderate mitral regurgitation needed no intervention and had no or mild mitral regurgitation postoperatively. Sixteen patients had grade IV SAM, and three patients had grade III SAM; in immediate postoperative Cardiac Echo two patients had grade I SAM; at follow-up, none of the patients had no SAM.

Left atrial size decreased from 39.90 ± 5.52 mm preoperatively to 36.95 ± 5.48 mm postoperatively, with a further reduction at follow-up (30.19 ± 5.47 mm) that was statistically significant ($P \leq .01$). LV diameter (internal diameter end diastole [LVIDd] and systole [LVIDs]) improved, from 41.10 ± 7.27 and 26.33 ± 4.60, respectively, before surgery to 42.14 ± 6.42 and 26.67 ± 4.39 after surgery. One patient required a permanent pacemaker for complete heart block in the postoperative period. Iatrogenic ventricular septal defect (VSD) was identified in 1 patient on perioperative TEE and was repaired. During follow-up, no patient underwent repeat surgical myectomy for persistent outflow tract obstruction. Study mean CPB time was 113.62 ± 40.38 minutes, and aortic cross-clamp time was 75.95 ± 34.01 minutes.

**DISCUSSION**

On January 2014, a myectomy program was introduced at our institute, comprising one surgeon trained at the Mayo Clinic under their myectomy program, dedicated local surgeons, cardiologist, intensivist and anesthesiologist. The goal of the program was to increase awareness among patients and physicians about diagnosis, appropriate treatment, and required follow-up. The team set up a protocol of follow-up after satisfactory septal myectomy, which is 1, 3, and 6 months after surgery and yearly follow-up thereafter by color Doppler echocardiogram. So far we have operated on 23 patients and have followed up 21 patients under our protocol. More patients are waiting for surgery in our program.

Septal myectomy is performed mainly for symptom relief but also provides an improvement in survival benefits. Severe resting LVOT obstruction seems to increase mortality for patients with HOCM [Maron 2003; Rastegar 2017]. During this series, there was an satisfactory improvement of LV outflow gradients after surgery, which were statistically significant ($P < .01$). During follow-up, LV outflow gradients improved further. Omnen et al [2005] reported that late survival of patients with HOCM

| Table 2. Preoperative, immediate post operative and follow up variables* |
|-----------------|-----------------|-----------------|-----------------|---|
|                 | Preoperative    | Postoperative   | Follow-Up       | P  |
| Hemoglobin      | 13.03 ± 1.48    | 12.63 ± 1.29    | 12.55 ± 1.32    | .478|
| Serum creatinine| 1.005 ± 0.26    | 1.052 ± 0.24    | 1.062 ± 0.19    | .691|
| PPG             | 81.57 ± 17.05   | 18.95 ± 7.90    | 8.87 ± 2.54     | <.001|
| IVST            | 20.67 ± 3.86    | 16.52 ± 2.42    | 15.02 ± 1.94    | <.001|
| LVPWd           | 13.67 ± 3.17    | 12.38 ± 2.87    | 11.31 ± 2.15    | .037|
| LA size         | 39.90 ± 5.52    | 36.95 ± 5.48    | 30.19 ± 5.47    | <.001|
| LVIDd           | 41.10 ± 7.27    | 45.10 ± 5.43    | 45.67 ± 50      | .088|
| LVIDs           | 26.33 ± 4.60    | 29.24 ± 4.94    | 32.10 ± 4.21    | .089|
| Ejection fraction| 64.86 ± 5.17  | 64.43 ± 4.42    | 65.62 ± 4.33    | .705|
| PASP            | 39.05 ± 4.54    | 34.29 ± 4.78    | 21.86 ± 4.98    | <.001|
| MR              | 3.14 ± 0.73     | 0.95 ± 0.50     | 0.76 ± 0.44     | <.001|
| SAM             | 3.67 ± 0.66     | 0.10 ± 0.30     | 0.0             | <.001|
| NYHA            | 2.95 ± 0.38     | 1               | 1               | <.001|

*Data are mean ± standard deviation.

IVST, interventricular septal thickness; LA, left atrium; LVPWd, left ventricular posterior wall dimension; PPG, Peak pressure gradient; LVIDd, Left ventricular internal diameter in diastole; LVIDs, Left ventricular internal diameter in systole; PASP, Pulmonary artery systolic pressure; MR, Mitral regurgitation; SAM, Systolic anterior motion; NYHA, New York Heart Association.
who had septal myectomy was similar to survival of patients with HOCM without obstruction, and patients with myectomy had improved HOCM-related mortality and freedom from sudden cardiac death compared with nonoperated patients with HOCM with obstruction. More recently, Sorajja et al. [2009] found that even in the absence of severe cardiac symptoms, the magnitude of resting LVOT gradient is directly and independently associated with increased risk of adverse clinical outcome.

Maron et al. [2003] reported that risk of death from HOCM increased by 2-fold in patients with outflow tract obstruction (a basal gradient of ≥30 mmHg) compared with patients without obstruction, plus risk of progression to NYHA class III or IV or death from heart failure, or 4-fold increased risk of stroke [Maron 2011]. This study shows a reduction of preoperative NYHA class III/IV to class I in all patients (P ≤ .001). Dearani et al. [2007] showed that symptomatic improvement with myectomy was gratifying: 90% of patients improved by ≥1 NYHA class, and improvements persisted in most according to later follow-up.

Gradient reduction results in basal septal thinning, with resultant enlargement of the LVOT area (and redirection of forward flow with loss of drag and Venturi effects on the mitral valve) [Sherrid 2003; Shah 1972; Sherrid 1993]. Consequently, SAM of the mitral valve and mitral–septal contact are abolished [Shah 1972; Maron 1983; Franke 1998]. Mitral regurgitation is usually eliminated without the need for additional mitral valve surgery [Yu 2000]; left atrial size (and possibly the long-term risk for atrial fibrillation) is reduced [Wigle 1985; Watson 1977; Wigle 1995]; and left ventricular systolic wall stress with left ventricular end-diastolic pressures are normalized [Maron 2003; Yu 2000; Wigle 1985; Wigle 1995; Ommen 2005].

In this series, maximum septal thickness in the patient population was significantly reduced after surgery (P < .001) and was similar during the follow-up period. In terms of cardiac dimensions, left atrial size decreased significantly, with a further reduction during follow-up (P ≤ .01). LV diameter (LVIDd and LVIDs) was similar before and after surgery. LVEF was similar in all groups at all times (no significant difference).

Diastolic dysfunction is a primary pathophysiologic mechanism in HOCM; increases in left ventricular end-diastolic pressure and left atrial and pulmonary venous pressures may lead to symptoms of effort dyspnea and limited aerobic capacity. When diastolic dysfunction progresses, LV filling becomes more dependent on atrial contraction and atrial arrhythmias, especially atrial fibrillation. This may precipitate an acute and profound decrease in cardiac output, plus worsening of symptoms. Symptomatic patients with minimal resting LVOT gradients often create uncertainty over the hemodynamic importance of obstruction and the role of septal reduction therapy [Schaff 2012]. Patients with obstructive HOCM who have low resting gradients and latent obstruction may have limiting symptoms similar in character and severity to those of patients with more severe resting gradients. Septal myectomy should be offered to these patients, as survival and symptom relief are excellent, suggesting that dynamic obstruction is the major hemodynamic problem rather than diastolic dysfunction [Schaff 2012].

Other than myectomy, the identification and management of various associated anomalies are necessary for the success of the procedure. According to Wang et al. [2016], >80% of patients had various intraventricular anomalies such as an aberrant papillary muscle. In regard to mitral regurgitation, SAM of the anterior leaflet of the mitral valve is a unique pathophysiological feature of HOCM, and SAM causes LVOT obstruction and mitral valve regurgitation. Most patients with HOCM have mitral regurgitation related to SAM of the mitral valve, which is relieved through an adequate myectomy [Hong 2016]. Concomitant mitral valve surgery is rarely necessary unless intrinsic mitral valve disease is present. When mitral valve procedures are required, repair is preferred over replacement [Kim 2018]. Among our study population, 16 patients (76.2%) had grade IV SAM before surgery, and 3 (14.3%) had grade III SAM; during follow-up, no patient had SAM by echocardiogram. Only 1 patient, who had severe mitral regurgitation due to rheumatic structural changes, required mitral valve replacement, and 8 patients with preoperative moderate mitral regurgitation required no intervention, with no or mild mitral regurgitation postoperatively.

From the study group, 1 patient required postoperative permanent pacemaker implantation for complete heart block. Iatrogenic VSD occurred with 1 patient and was repaired after completion of myectomy. During follow-up, none of the patients underwent repeat surgical myectomy for persistent or recurrent outflow tract gradient.

There is a significant learning curve with this procedure [Said 2013] to avoid major technical complications such as complete heart block, ventricular septal defect, injury to the aortic or mitral valves, and incomplete resection. A frequent cause of incomplete muscle resection is losing the resection plane and axis during myectomy. To avoid losing the resection plane, it is helpful to cut the depth of the muscle to be resected along the longitudinal axis using a cutter knife. With this incision as a reference point, an extended septal myectomy can be easily performed [Kim 2018].

It is important to note that despite the removal of the obstructive component of the septum, these patients can have significant diastolic dysfunction resulting from underlying hypertrophic cardiomyopathy. They do well with maintenance of atrial-ventricular synchrony, avoidance of inotropes and afterload-reducing agents, and maintenance of adequate preload. Some surgeons routinely use aspirin and β-blockers for the prevention of atrial fibrillation [Ralph-Edwards 2017]. From our study group, 1 patient had preoperative atrial fibrillation that was successfully treated with β-blockers and amiodarone.

With very low surgical mortality in experienced centers, septal myectomy reliably abolishes impedance to LV outflow and heart failure-related symptoms, restores quality of life, and is significantly associated with long-term survival similar to that in the general population [Maron 2011]. Contemporary surgical series and an initiative from Tufts Medical Center underscore the vital transformation of septal myectomy from a highly morbid operation [Schulte 1993] to one of the safest open-heart procedures, currently with low
operative mortality of <1% at experienced centers [Ommen 2005; Smedira 2008; Ball 2011; Desai 2013; Sedehi 2015; Liebregts 2015; Maron 2015]. Among all 23 patients operated at our center, 1 patient (4.35%) died on day 1 because of acute renal shut down, and another patient was lost to follow-up. Mortality is overestimated, as the study has a smaller sample size. Deaths within 30 days or during the index hospitalization after myectomy were considered operative deaths and were included in both end points. HOCM mortality included sudden cardiac death (unexpected within 1 hour of witnessed collapse or nocturnally) or heart failure death (in the context of progressive cardiac decompensation).

Late survival of patients who underwent myectomy for obstructive HOCM exceeded that of patients who did not undergo surgery [Maron 2004; Ommen 2005]. Furthermore, myectomy might be associated with reduced long-term risk of sudden cardiac death [Ommen 2005].

Limitations

This study was conducted with a small group of patients. A larger multicenter study would provide a better overview of the surgery’s outcome in the population of Bangladesh.

Conclusions

Because of the limitation of cardiac facilities (such as color Doppler echocardiography and expert cardiology opinions), very few patients are diagnosed and fewer patients are referred to us. Both the physicians and patients are less aware of the availability of the treatment in our country, and this is the reason patient numbers in our study are small. However, septal myectomy should be offered to all HOCM symptomatic patients, as its survival and symptom relief are excellent, suggesting that dynamic obstruction is the major hemodynamic problem. Over a short duration of time with a small patient population with obstructive HOCM, the National Heart Foundation Hospital & Research Institute has shown excellent results, comparable to those of surgical centers having longer experience in myectomy. Thus, myectomy can be safely performed outside of large US/European referral centers. Through this initiative, the natural history of many HOCM patients has benefited substantially, including the successful relief of outflow obstruction, extended longevity, and restored quality of life.

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