A Surgical Experience of Symptomatic Sigmoid Septum: Drastic Exacerbation of Mitral Regurgitation after Sufficient Ventricular Septal Myectomy

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A 74-year-old woman presented with progressive dyspnea on exertion. Transthoracic echocardiography (TTE) demonstrated significant left ventricular outflow tract (LVOT) obstruction with a pressure gradient of 100 mmHg caused by a sigmoid septum (SS). Mitral regurgitation (MR) of a mild to moderate degree occurred due to systolic anterior motion (SAM) of the anterior mitral leaflet (AML), with no intrinsic mitral valve (MV) abnormality. Myectomy of the hypertrophied septal bulge ameliorated the pressure gradient to 8 mmHg with similar MR. However, just before the sternal closure, hemodynamic status deteriorated drastically to ventricular fibrillation. MR exacerbated to a severe degree with an uncertain etiology; thus, a mechanical prosthetic valve was implanted. The postoperative course was complicated by prolonged mechanical ventilation due to massive pulmonary edema and complete atrioventricular block (CAVB) requiring permanent pacemaker implantation. One year postoperatively, the patient is asymptomatic and TTE revealed no residual pressure gradient with an iatrogenic ventricular septal defect (VSD). This case, the first published surgical experience of SS, may indicate that secondary MR, which is usually relieved by sufficient myectomy in hypertrophic cardiomyopathy (HCM), can exacerbate markedly, and that myectomy might not be advisable in SS. The therapeutic strategy must be considered carefully before embarking on surgical intervention.

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prognosis. However, it can be symptomatic with marked limitation of exercise tolerance, albeit rarely, by causing LVOT obstruction (LVOTO) accompanied by systolic anterior motion (SAM) of the anterior mitral leaflet (AML) and subsequent mitral regurgitation (MR), even in the absence of classical features of HCM. The degree of LVOTO increases with provocation (e.g., exercise or valsalva maneuver), and corresponds closely with the appearance of symptoms. The mechanism of obstruction is thought to be similar to that in HCM. Complex interactions between the Venturi effect caused by flow acceleration around a hypertrophied septum and the drag effect caused by altered flow vectors within the LV to push the mitral valve (MV) into that LVOT are thought to be involved. Preserved and often hyper-contractile systolic function with a reduced LV cavity size might also have contributed.

Management of symptomatic LVOTO in SS has not been well established. Negative inotropes are effective and the first choice in HCM, but the role of these agents in SS is uncertain, with the literature mostly limited to isolated case reports. In the largest study of drug treatment for SS, performed retrospectively in 9 patients, Ranasinghe, et al. found 4 patients with a response to a β-blocker alone, and 3 who responded to subsequent administration of disopyramide, with effective reduction or amelioration of LVOTO leading to significant symptomatic improvement with no serious side effects. Several case reports have shown that cibenzoline is also effective for symptomatic SS. These negative inotropes seem to exert an effect over months by reducing left ventricular afterload and ejection acceleration, which indicates the importance of LV contractility in development of LVOTO in SS.

Case Report

A 74-year-old woman was referred to our hospital because of progressive dyspnea on exertion for 4 months. She was receiving medication for hypertension with 5 mg carvedilol and 5 mg amlodipine. Her medical and familial history were unremarkable. She was in New York Heart Association (NYHA) class III, but a physical examination showed only a grade 4/6 systolic ejection murmur at the third left sternal border. Electrocardiography showed a regular sinus rhythm and left ventricular hypertrophy with strain pattern ST-T changes in V5 and V6. Chest roentgenography revealed a cardiothoracic ratio of 56% with a clear lung field. Blood laboratory test results showed only an elevated brain natriuretic peptide level (84.6 pg/ml). Transthoracic echocardiography (TTE) showed focal hypertrophy of the upper left ventricular septum of thickness up to 16 mm (Fig. 1A). No marked ventricular hypertrophy was observed in other parts, a finding that was incompatible with typical HCM, but consistent with SS (Fig. 1B). Significant LVOTO with a pressure gradient of 100 mmHg at rest subsequent to the mitral-septal contact was measured. Left ventricular...
function was normal to hyperkinetic with a relatively small lumen. The left ventricular dimensions were an end-diastolic diameter of 41 mm, end-systolic diameter of 22 mm, fractional shortening of 46%, posterior wall thickness of 11 mm, and interventricular septum wall thickness of 9 mm. Mild to moderate MR caused by SAM with no intrinsic MV abnormality was observed (Fig. 1C). Both papillary muscles (PMs) were mildly hypertrophic, especially in systole, but otherwise their location and shape were normal with no apparent accessory muscles. Cardiac catheterization confirmed the echocardiographic findings with a pressure gradient of 113 mmHg at rest, accompanied by postextrasystolic potentiation. MR was mild without pulmonary hypertension and coronary arteries were intact.

LVOTO due to SS, not HCM, evidently burdened the patient. She was offered maximal drug therapy with increased or exchanged β-blockers and subsequent administration of antiarrhythmics, percutaneous transluminal septal myocardial ablation, or surgical myectomy. After written consent, the patient chose to undergo myectomy with the hope of achieving faster symptomatic relief. Surgery was thus planned to alleviate the LVOTO by resecting the subaortic septal bulge in accordance with the Morrow procedure in HCM.

Exposure was obtained through a median sternotomy. The pressure gradient between the right radial artery and the LV was measured simultaneously as 60 mmHg, which was potentiated to 135 mmHg after premature ventricular beat. Transesophageal echocardiography (TEE) showed mild MR with no intrinsic abnormality of the MV and PMs. Cardiopulmonary bypass (CPB) was instituted between the ascending aorta and the venae cavae. Under cardioplegic cardiac arrest, the aorta was incised transversely. The hypertrophied subaortic septal bulge was resected en block (22 × 21 × 5 mm) through the aortic valve based on the Morrow procedure (Fig. 2A). The pressure gradient across the LVOT was reevaluated as 8 mmHg, and 18 mmHg at provoked extrasystole, after uneventful weaning from the CPB without inotropic agents. MR remained mild. The reduced pressure gradient with unchanged MR indicated successful myectomy. However, just before the sternal closure, about 40 minutes after cessation of CPB, the hemodynamic condition deteriorated drastically to ventricular fibrillation in a few minutes. Electrical cardioversion could be achieved only after resumption of CPB, and TEE revealed exacerbated MR probably without significant residual LVOTO. TEE could not establish the exact etiology of the worsened MR, which was still massive with an elevated mean left atrial pressure of 22 mmHg under total CPB. The exacerbated MR, which probably led to the circulatory collapse, required management. Through right-sided left atriotomy under re-cardioplegic cardiac arrest, the MV was inspected but seemed intact, except for a slightly shrunk posterior mitral leaflet. The etiology of the massive MR could still not be established, even macroscopically, which led us to choose MV replacement, rather than MV repair. After removal of the AML, a mechanical MV...
prosthesis, which seemed more appropriate than a biological one in this small LV, was implanted. Weaning from the second CPB was uneventful and the operation ended under stable circulatory conditions, despite insufficient oxygenation with intermittent foamy sputum.

The postoperative course was complicated. Chest roentgenography immediately after the operation revealed regional infiltration in the right upper pulmonary field, which was compatible with acute pulmonary edema subsequent to the intraoperative circulatory collapse. Respiratory failure continued with persistent foamy sputum, and the patient needed mechanical ventilation for 3 days and oxygen administration for 5 more days, because dyspnea exacerbating on exertion persisted with orthopnea and wet cough. Her hemodynamic status was relatively stable, except for complete atrioventricular block (CAVB), which required continuous external cardiac pacing. Low grade fever of unknown origin with elevated inflammatory reactions persisted for 10 days, even under treatment with sufficient antibiotic agents, and this prevented internal pacemaker implantation as late as 2 weeks after surgery. After the pacemaker implantation, the general condition improved rapidly, and the patient was discharged from hospital 30 days postoperatively. A specimen of the resected septum showed fibrosis of the endocardium and myocardium with only slight myocardial disarray, which was not compatible with HCM (Fig. 2B).

Exertional dyspnea persisted, but subsided in a few months after discharge. One year after surgery, TTE demonstrated no residual pressure gradient and a good prosthetic valve and cardiac function, and also revealed an iatrogenic ventricular septal defect (VSD) (Fig. 3A and 3B). The patient is currently asymptomatic in NYHA class I, but is burdened with certain risks of prosthetic valve-, pacemaker- and anticoagulation-related morbidities. The VSD also requires repair, but she currently refuses to undergo further surgery.

Discussion

Surgery for LVOTO in cases of symptomatic SS has not been reported to our knowledge, although this approach is well established for HCM. Transaortic ventricular septal myectomy (the Morrow procedure) is the fundamental surgical method and has an excellent outcome in HCM. Controversy still exists as to whether myectomy alone is sufficient for eliminating MR because almost every patient who undergoes myectomy has some degree of secondary or functional MR, which is caused by SAM of the AML without structural MV abnormality. The degree of MR is proportional to that of LVOTO; thus, myectomy, which enlarges the LVOT directly by resecting the septum, usually leads to spontaneous resolution of MR without additional valve surgery. Inappropriate myectomy may result in residual LVOTO and MR, but even in these situations re-myectomy alone should be considered preferentially to mitral surgery. Even in a case in which structural
abnormalities contribute to MR, where concomitant mitral surgery may also be required.\textsuperscript{10,13} Myectomy alone is occasionally effective for at least partial alleviation of MR.\textsuperscript{11}

Certain limitations have been documented in the Morrow procedure, with a failure rate between 5 and 20%.\textsuperscript{10,16} There is a technical difficulty in obtaining an adequate surgical view through aortotomy, with no reliable method to monitor the extent of resection during cardiac arrest, which may result in too little resection with persistent LVOTO or too much resection with postoperative CAVB and VSD.\textsuperscript{9} Other limitations are related to the direct action of this procedure, which is merely a physical enlargement of the LVOT. The reduced cross-sectional area of the LVOT is not the only determinant of LVOTO, and multiple interrelated factors, such as heterogeneity of the hypertrophied septum, structural abnormality of the MV, and anatomical variants of the PM also interact in the pathophysiology.\textsuperscript{6–10,16,17}

An optimal surgical outcome with sufficient relief of both LVOTO and MR requires the following factors to be addressed,\textsuperscript{10} and thus the Morrow procedure has been modified and additional procedures have been proposed for this purpose. First, extended myectomy (about a 7-cm resection) has been recommended, in which the septal bulge is more extensively resected than in the classical Morrow procedure (about a 3-cm resection) to the base of the PMs.\textsuperscript{8–10,12,16,17} This can relieve SAM more effectively by pushing the AML more posteriorly and redirecting the blood flow within the LV away from the MV. This approach can also prevent midventricular obstruction, which may cause recurrent LVOTO, even after successful relief of SAM.\textsuperscript{6,8,9,15} Second, horizontal plication of the AML in addition to extended myectomy via aortotomy has also been reported in selected patients with a redundant AML or mitral chordae. This can directly alleviate MR by preventing excursion of the AML into the LVOT.\textsuperscript{8,9,16} Third, reorientation of the PMs, which realigns the PMs away from the LVOT toward the MV by placing several mattress sutures between the PMs and LV, has been proposed for patients with displaced or hypermobile PMs.\textsuperscript{12,18} Mobilization and partial excision of PMs with the aim of separating hypertrophied or malattached PMs from the ventricular wall and from each other have also been described. These procedures can redirect the blood flow away from MV leaflets to suppress MR.\textsuperscript{8,9,17}

The etiology of the exacerbated MR in this case remains uncertain, but we assume that the PMs might have been involved. Even in SS, myectomy can resolve MR because the mechanism of LVOTO is thought to be similar to that in HCM.\textsuperscript{9} However, MR deteriorated so drastically as to reach circulatory collapse despite sufficient relief of LVOTO, which is a relatively rare development, even in the HCM literature. Worsened MR or additional mitral surgery without structural MV abnormality after sufficient isolated myectomy has seldom been described in HCM.\textsuperscript{7,13} In SS, miscellaneous factors, such as the contractility of the LV, might not be assignable in the development of LVOTO.\textsuperscript{1–3} In this case, echocardiography and direct inspection during the resumed CPB did not reveal an intrinsic abnormality or iatrogenic injury subsequent to myectomy in the MV, for which surgical intervention needed to be considered: e.g., calcification of the mitral annulus restricting leaflet motion, degenerative or myxomatous changes, prolapsed leaflet, or ruptured chordae.\textsuperscript{8,9,12,19} The size and shape of the resected AML seemed normal and a microscopic examination revealed only mild fibroelastic changes. The shrunk posterior mitral leaflet, which can lead to decreased mobility and an interleaflet gap that promotes MR,\textsuperscript{12} might have contributed to the pathology, but this change was only slight.

PMs can cause LVOTO in HCM, particularly in patients with minimal or no basal septal hypertrophy,\textsuperscript{12,17,18} and several anatomical variants of PMs have been identified in terms of number, location, mobility and attachment.\textsuperscript{10} PMs may still have an important effect after myectomy by redirecting blood flow to catch the AML and by drawing the MV into the LVOT.\textsuperscript{8,12,15,16} Preoperative TTE frequently fails to detect a PM abnormality,\textsuperscript{12} but a retrospective review in this case showed at least mildly hypertrophied and hypermobile PMs, which might have contributed to LVOTO independent of basal septal thickness.\textsuperscript{18} We did not inspect the PMs thoroughly during surgery because exacerbated MR forced performance of MV replacement. A more detailed assessment before surgery with multimodal imaging including cardiac magnetic resonance imaging (MRI),\textsuperscript{10,12} and a more careful perioperative examination, even after myectomy, might have resulted in another outcome through additional interventions for the PMs, as described above. Kwon, et al. reported good outcomes after PM reorientation with or without myectomy in patients with minimal or normal septal thickness and hypermobile PMs, similarly to our patient.\textsuperscript{18}

MV replacement alone without myectomy as an initial procedure might have been optimal in this case, although
only mild to moderate MR was functionally present preoperatively, for which mitral surgery would usually not be indicated. MV replacement with removal of the AML relieves LVOTO and can usually be performed without the surgical complications described below. For functional MR in HCM, MV replacement is generally not recommended because of possible complications related to the substitute valve and anticoagulation. The relatively small LV cavity with hypertrophied muscles has another technical concern of ventricular perforation, especially with a biologic prosthesis, and therefore, we chose a mechanical valve despite the age of the patient. MV replacement is often avoided in HCM because many patients undergo surgery at a relatively young age. However, patients above 70 years old or those with a minimally hypertrophied septum are regarded as a subgroup, in which initial MV replacement can be justified as a safer alternative than myectomy.

Postoperative massive pulmonary edema, CAVB, and VSD might have been avoided by different choices in the procedure. First, pulmonary edema was probably induced by the circulatory collapse before resumption of CPB, rather than by the invasiveness associated with the repeated CPB and additional MV replacement. A requirement for resumption of CPB for residual LVOTO or MR occurs at a rate of 20% in myectomy, and concomitant mitral surgery is also performed commonly and safely in 11% to 20% of patients with HCM. If MV replacement had been performed before the circulatory collapse, postoperative LVOTO and MR might occur at a rate of 20% in myectomy, and concomitant mitral surgery is also performed commonly and safely in 11% to 20% of patients with HCM. Second, CAVB and VSD developed because the resection was too extensive, although this was the normal size used in HCM and was performed by an experienced surgeon (K.M.) with over 100 cases. As much resection as possible is generally favorable because residual LVOTO subsequent to inadequate resection directly affects the surgical outcome and is the most frequent cause of re-operation. However, postoperative CAVB and VSD, which cause further complications and require additional interventions, are not justified. The septum at which resection is usually performed in myectomy tends to be relatively thin, even in HCM; thus, a minimally hypertrophied septum of less than 18 mm is regarded as a relative contraindication for myectomy. Our case was, not HCM, but SS, with only a localized septal hypertrophy of thickness up to 16 mm. Also, the current understanding of the pathophysiology of LVOTO suggests that resection of the subaortic septal bulge plays a smaller role than previously thought in relieving SAM.

Thus, less resection than we performed might have also achieved adequate relief of LVOTO while avoiding CAVB and VSD, since Cavalcante, et al. have shown that mini-myectomy (less than 5 mm resection) in patients without significant septal hypertrophy can resolve both LVOTO and SAM safely in combination with PM reorientation.

MV repair, rather than MV replacement with a prosthetic valve, could not be applied in this case, although this procedure is often in combined with myectomy to give a good outcome. In our case, there was no structural abnormality in the mitral leaflets and chordae to be repaired, and possible residual MR after MV repair might have required a third CPB period. MV repair may also simultaneously predispose the patient to persistent SAM and residual LVOTO by displacing the MV anteriorly, especially with an annuloplasty band, and for these reasons we chose MV replacement.

Percutaneous transluminal septal myocardial ablation, which is an alternative option for HCM patients who are not suitable for myectomy, may have been another therapeutic option in our case, since Viera, et al. reported a successful outcome in a patient with symptomatic drug-refractory SS.

**Conclusions**

This report is the first published surgical experience in a case of SS, to our knowledge, and may indicate that the Morrow procedure cannot be simply applied to SS. Thus, maximal pharmacological therapy with β-blockers and other antiarrhythmics should first be used even in asymptomatic SS. If drug therapy fails, surgery might be considered, but a detailed assessment of the pathophysiology of the LVOTO, including the MV and PMs, should be performed before and during surgery. MV replacement might be the safest procedure to choose in these cases.

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**Disclosure Statement**

We declare that we have no conflicts of interest to disclose.
References