Apical myectomy for patients with hypertrophic cardiomyopathy and advanced heart failure

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ABSTRACT

Objective: In patients with apical hypertrophic cardiomyopathy, extensive apical hypertrophy may reduce left ventricular end-diastolic volume and contribute to diastolic dysfunction, angina, and ventricular arrhythmias. Transapical myectomy to augment left ventricular cavity size can increase stroke volume and decrease left ventricular end-diastolic pressure. In this study, we describe early outcomes of patients with apical hypertrophic cardiomyopathy after transapical myectomy and compare survival with that of patients with hypertrophic cardiomyopathy listed for heart transplantation.

Methods: Between September 1993 and March 2017, 113 symptomatic patients with apical hypertrophic cardiomyopathy underwent transapical myectomy. Clinical information, echocardiographic data, and follow-up were reviewed. With the use of a national database, survival was compared with that of patients with hypertrophic cardiomyopathy listed for heart transplantation.

Results: In the surgical cohort, median (interquartile range) age was 50.8 (39.3-60.7) years, and 49 (43%) were male. Preoperatively, 108 patients (96%) were in New York Heart Association class III/IV. All patients underwent transapical myectomy. There were 4 (4%) deaths within 30 days of operation. At last follow-up, 76% of patients reported improvement in symptoms, and 3 patients (3%) subsequently underwent cardiac transplantation for recurrent heart failure. The estimated 1-, 5-, and 10-year survivals were 96%, 87%, and 74%, respectively. Survival appeared superior to patients with hypertrophic cardiomyopathy listed for heart transplant.

Conclusions: Apical myectomy is beneficial in severely symptomatic patients with apical hypertrophic cardiomyopathy. Early risk of the procedure is low, and approximately 76% maintain clinical improvement with resolution of symptoms. Long-term survival appears better than for patients listed for heart transplantation. (J Thorac Cardiovasc Surg 2020;159:145-52)

Apical hypertrophic cardiomyopathy (HCM) is a phenotypic variant of HCM, in which hypertrophy is especially prominent at the apex of the left ventricle (LV) (Figure 1). It is considered relatively uncommon in Western countries (1%-10% of all patients with HCM), but may occur more frequently in Asian populations, in whom it is reported in as many as 40% of patients with HCM.3,5
Sakamoto and colleagues first described apical HCM in a Japanese patient in 1976, and initial studies of the clinical outcome described a relatively benign disease course and good overall prognosis. However, recent investigations suggest that apical HCM can be associated with debilitating symptoms, including fatigue, angina, and severe dyspnea. Furthermore, serious adverse outcomes have been described, such as ventricular arrhythmias, stroke, heart failure, and sudden cardiac death. Indeed, survival of patients with apical HCM is significantly worse than in an age- and sex-matched population without HCM.

Medical therapy of apical HCM includes nonvasodilatory beta-blockers and non–dihydropyridine calcium channel blockade, but in many patients, pharmacologic therapy does not dramatically relieve symptoms. Until recently, heart transplantation provided the only surgical option for patients with severely symptomatic apical HCM. However, transapical myectomy to enlarge the LV cavity can improve diastolic dysfunction and associated symptoms. Previously, we reported the first 44 patients with apical HCM who underwent transapical myectomy for enlargement of the ventricular cavity at our institution. The present study updates and extends this experience of surgically managing patients with apical HCM and contrasts survival in patients receiving apical myectomy with that in patients with HCM who are listed for heart transplantation.

**MATERIALS AND METHODS**

**Study Patients**

After approval from the Institutional Review Board, we reviewed 113 consecutive adult patients who underwent transapical myectomy between September 1993 and March 2017 at the Mayo Clinic, Rochester, Minnesota. All patients with apical HCM in whom operation was performed to augment LV cavity size were included, but we excluded patients who had transapical septal myectomy for relief of midventricular obstruction. Preoperatively, all patients remained limited with diastolic heart failure despite best medical treatment, and the option of transplantation was discussed with those who had New York Heart Association (NYHA) class III or IV symptoms.

**Abbreviations and Acronyms**

- HCM = hypertrophic cardiomyopathy
- IQR = interquartile range
- LV = left ventricular
- MRI = magnetic resonance imaging
- NDI = National Death Index
- NYHA = New York Heart Association
- SRTR = Scientific Registry of Transplant Recipients
- TTE = transthoracic echocardiography

**Diagnosis of Apical Hypertrophic Cardiomyopathy and Patient Selection**

Diagnosis of apical HCM and patient selection for myectomy have evolved over this 24-year experience. The apical distribution of ventricular hypertrophy can be confirmed by multiple imaging techniques including transthoracic echocardiography (TTE) and cardiac magnetic resonance imaging (MRI) (Figure 1). Typical phenotypic characteristics include an apical wall thickness 15 mm or greater, apical displacement of the anterolateral and posteroendocardial papillary muscles, and asymmetric septal hypertrophy mainly confined to the apex of the LV. If concomitant subaortic or midventricular obstruction is present, resting and provoked gradients are also measured on TTE. If an apical aneurysm is suspected, echocardiographic contrast administration or cardiac MRI can clarify apical anatomy.

Patients who benefit from apical myectomy to augment LV chamber size are those with diastolic heart failure and small LV end-diastolic volume. In our initial experience, we routinely performed left heart catheterization to measure LV pressure and to visualize the LV chamber with contrast ventriculography. Currently, we prefer cardiac MRI for visualizing LV morphology and quantifying LV volume. Candidates for apical myectomy will usually have LV end-diastolic volume less than 50 mL/m² and LV stroke volume less than 30 mL/m², although these indices are age- and sex-specific, and should be evaluated on an individual basis.

**Operative Details**

To enlarge the LV cavity, septal myectomy is performed via a transapical incision (Video 1), and our technique has been described in detail. In brief, operation is performed through a standard median sternotomy and the LV is assessed using intraoperative transesophageal echocardiography. It is important to examine carefully for subaortic obstruction with systolic anterior motion of the mitral valve. A minority of patients will have some degree of concomitant LV outflow tract obstruction that will require additional transaortic septal myectomy.

The heart is arrested using antegrade cardioplegia, and the apex of the heart is delivered anteriorly. The left ventriculotomy is made lateral to and far enough from the left anterior descending coronary artery so that closure will not compromise the vessel.

We then identify and protect the anterolateral and posteroendocardial papillary muscles, and begin the myectomy on the ventricular septum to enlarge the LV cavity. If prominent papillary muscles are present, these may be shaved to further increase LV volume. The myectomy is extended proximally, beyond the midventricular level. Adequacy of muscle excision is judged visually and by palpation. If an apical aneurysm is identified on preoperative TTE or intraoperative inspection, the outpouching is resected completely. The ventriculotomy is closed using a 2-layer approximation over strips of Teflon felt.

**Data Collection and Follow-up**

Data were collected from our prospectively maintained cardiovascular surgery database, from follow-up questionnaires, and from chart review of electronic medical records. Follow-up questionnaires were sent to all patients at 1, 3, 5, 10, 15, and 20 years postoperatively. Postoperative health status was determined with the following questions: “Please rate your general state of health before your surgery (1 = excellent, 2 = very good, 3 = good, 4 = fair, 5 = poor)” and “Please rate your general state of health since your surgery (1 = excellent, 2 = very good, 3 = good, 4 = fair, 5 = poor).” Vital status was determined using the Mayo Clinic electronic medical records, the national death and location database (Accurint, LexisNexis for Mayo Clinic patients), and correspondence with family members and physicians.

Follow-up information regarding survival is complete for the entire patient cohort. However, functional outcomes were obtained in 62 patients; questionnaires were completed by 41 patients.
National Death Index

Information on vital status was verified using records from the National Death Index (NDI). The NDI is a centralized database that collects information on causes of death compiled from US vital statistics offices. Mortality data are provided by each US state to the National Center for Health Statistics. Cause of death is coded according to the International Classification of Diseases 9th or 10th Revision.

Scientific Registry of Transplant Recipients

This study used data from the Scientific Registry of Transplant Recipients (SRTR). The SRTR data system includes data on all donor, wait-listed candidates, and transplant recipients in the United States, submitted by the members of the Organ Procurement and Transplantation Network. The Health Resources and Services Administration, US Department of Health and Human Services provides oversight to the activities of the Organ Procurement and Transplantation Network and SRTR contractors.

Informal comparison was made of survival in the apical HCM cohort versus SRTR cohort with HCM listed for heart transplant. From January 2004 to August 2017, 1235 adult patients with a diagnosis of HCM were waitlisted for heart or heart-lung transplantation within SRTR. Duplicate listings (n = 54) were removed, and patients who died on the same day as their listing date (n = 3) were excluded from analysis. Therefore, the waitlist cohort included 1178 unique adult patients identified through this national database. Of these, 878 (75%) underwent transplantation.

Statistical Analysis

Categoric data are presented as frequencies and percentages, and continuous variables are expressed as medians and interquartile range (IQR). To adjust for the age and sex differences of the transplant waitlist/transplant cohort and the myectomy cohort (for those with NYHA class III or IV), the data were reweighted to the empirical distribution of the cohort. Survival analyses were carried out on the unweighted and the
An analysis of Clinical outcomes in patients with Hypertrophic Cardiomyopathy (HCM) was carried out in R statistical software (version 3.4.2, Vienna, Austria).

### Preoperative Echocardiography

All patients underwent transthoracic Doppler echocardiography before surgery, and preoperative TTE data are presented in Table 1. The median (IQR) ejection fraction was 70.5 (66.0-75.0). Median LV end-diastolic diameter was 44.0 (39.0-50.0) mm, and LV end-systolic diameter was 25.0 (22.0-29.5) mm. Apical HCM distribution was observed on TTE in all patients; concomitant subaortic obstruction was present in 23 patients (20%), midventricular obstruction was present in 26 patients (23%), and apical aneurysms were present in 25 patients (22%).

### Operative Details and Postoperative Complications

All patients underwent transapical myectomy to enlarge the ventricular cavity. In 23 patients (20%) with complex long-segment septal hypertrophy involving both subaortic area and LV apex, combined transaortic and transapical incisions were made to excise septal muscle. Apical aneurysms were repaired in 25 patients (22%).

During the early postoperative period, there were 4 (4%) 30-day mortalities, and 6 patients (5%) required reoperation for bleeding. Postoperative atrial fibrillation was observed in 28 patients (25%), but there were no surgical site infections or pacemaker insertions after surgery. There were no operative deaths in patients with concomitant subaortic obstruction; 1 patient who died postprocedure had midventricular obstruction, and 2 patients had apical aneurysms. Early mortality rates improved as our experience increased; in the first decade, 30-day mortality was 8% and decreased to 5% in the second decade, and there have been no 30-day mortalities in 35 patients undergoing operation since 2013 (Figure 2).

### Late Outcomes

There were 19 late deaths for overall estimated 1-, 5-, and 10-year survivals of 96%, 87%, and 74%, respectively. By using data from the NDI, causes of mortality could be determined in 18 of these patients. Nine patients (50%) died of HCM, and the remaining 9 patients (50%) died of unrelated causes. During follow-up, 3 patients (3%) underwent cardiac transplantation and 1 patient (1%) required LV assist device implantation for heart failure. Details on functional status were ascertained through follow-up visits, as well as survey responses; data were available in 62 patients (55%) at a median follow-up of 3.6 (1.1-8.1) years.
Preoperatively, 59 patients (95\%) were in NYHA III or IV, and postoperatively this decreased to 28 patients (45\%). More specific data from follow-up questionnaires were available in 41 patients (36\%) at a median follow-up of 5.2 (3.2-10.1) years; in these patients, 31 (76\%) reported improvement in general health compared with their preoperative condition, 9 (22\%) stated that their general health had stayed the same, and only 1 (2\%) reported worsening health status (Figure 3).

Comparison With Cardiac Transplantation

To provide perspective on survival of patients undergoing apical myectomy, we contrasted survival of patients with NYHA class III or IV symptoms (n = 108) with that of patients with HCM listed for heart transplantation. Patients in our surgical cohort were older than those listed for transplant (P = .001) and less likely to be male (P = .006). Survival of patients receiving apical myectomy appeared superior to those listed for transplant in both the unweighted and age- and sex-weighted data (Figure 4, A and B). In further analysis, survival of patients who received heart transplant seemed similar to survival of patients receiving apical myectomy (unweighted data in Figure 4, C, age- and sex-weighted data in Figure 4, D).

DISCUSSION

Historically, apical HCM has been considered a benign condition, but recent data suggest that apical HCM can be associated with a variety of debilitating symptoms, as well as life-threatening complications.\textsuperscript{9} Medical management is often inadequate, and heart transplantation is the only option for many patients with advanced symptoms.\textsuperscript{7,17,19} In the present surgical series of 113 patients with apical phenotype of HCM, small LV diastolic volume appeared to contribute to preoperative diastolic heart failure. More than 95\% of patients had NYHA class III or IV dyspnea, and the extent of heart failure is considerably higher than previously reported in nonsurgical cohorts.\textsuperscript{8,20,21} The present study confirms that surgical management with transapical myectomy to enlarge the LV cavity has acceptable early mortality and decreases symptoms related to diastolic dysfunction. Overall survival compared favorably to that of patients with HCM listed for heart transplantation in a national database.

Early Operative Mortality

In this series, early mortality declined as surgical experience increased over the past 2 decades (Figure 2). In-hospital (30-day) death occurred in a total of 4\%, with no early mortality in our 35 most recent cases since 2013. The improving early outcomes may be due to a number of
factors, including better patient selection and refinement of surgical technique. Patients who are most likely to benefit from apical myectomy are those with diastolic heart failure, a small LV cavity, and reduced stroke volume. Those with normal LV end-diastolic dimensions are unlikely to experience symptomatic improvement and thus should not be considered for surgery. LV cavity size can be assessed by TTE or cardiac MRI. Cardiac MRI is especially useful in determining ventricular volumes and stroke volume. At operation, adequate resection of muscle is necessary to ensure enlargement of the LV cavity. It is important to preserve the papillary muscles, because injury to these structures can lead to adverse events, including mortality.

Midventricular Obstruction and Apical Aneurysms

Apical HCM with concomitant midventricular obstruction may be a more severe phenotype than isolated apical HCM. Apical aneurysms are reported to occur in 10% to 20% of patients with nonobstructive HCM. In the present series, apically distributed HCM with midventricular obstruction was observed in 23%, and concomitant aneurysms were present in 22%. Of the 4 in-hospital (30-day) deaths, 1 occurred in a patient with associated midventricular obstruction, and 2 occurred in patients with concomitant aneurysms. However, it should be noted that adverse event rates in unoperated patients with apical aneurysms are high. For patients with ventricular arrhythmias associated with apical aneurysms, surgery appears to decrease adverse event rates.15,24

Functional Improvement

In a previous study, we documented that apical myectomy enlarges LV end-diastolic volume, thereby increasing stroke volume and reducing left atrial pressure. These hemodynamic changes were associated with early and late functional improvement. In the present study, self-reported health status at last follow-up was improved in the majority of patients, and general health had improved.

FIGURE 4. Survival of patients with preoperative NYHA class III or IV dyspnea undergoing apical myectomy compared with transplant waitlist patients and recipients. A, Unweighted survival of patients receiving apical myectomy (blue) and patients with HCM on the SRTR list (red). B, Age- and sex-weighted survival of patients receiving apical myectomy (blue) and SRTR transplant list (red). C, Unweighted survival of patients receiving apical myectomy (blue) and transplant recipients (red). D, Age- and sex-weighted survival of patients receiving apical myectomy (blue) and transplant recipients (red).
in more than 75% (Figure 3). Postoperative imaging studies other than TTE were not performed routinely in our patients. Indeed, visualization of the apical region of the LV by echocardiography can be problematic early after operation.

Survival and Comparison With Waitlisted Patients

Data on long-term survival in patients with apical HCM are scarce, but a recent review by Jan and colleagues\(^\text{10}\) reported overall mortality rates of 9% to 10.5% over a mean/median follow-up of 2 to 6.5 years. Further, in follow-up of 193 patients with nonsurgical apical HCM from our Clinic, Klarich and colleagues\(^\text{2}\) described an overall mortality rate of 29% over a median follow-up of 6.5 years. In these patients, survival was reduced in older and female patients. In the present surgical cohort, survival estimates at 1, 5, and 10 years were 96%, 87%, and 74%, respectively, which is consistent with our earlier experience.\(^\text{7}\)

When compared with patients listed for heart transplant, survival appeared better in patients who underwent apical myectomy (Figure 4, A and B). Patients who were waitlisted for transplantation were younger than our surgical cohort and more likely to be male, characteristics associated with more favorable prognosis.\(^\text{1,7}\) Survival of patients with apical HCM who had apical myectomy was similar to patients with HCM who underwent cardiac transplantation (Figure 4, C and D). In view of the shortage of organ donors in the United States, apical myectomy should be considered as initial treatment in appropriately selected patients with apical HCM and advanced heart failure symptoms.\(^\text{25,26}\)

Risk of Worsening Heart Failure After Myectomy

In patients with apical hypertrophy, percutaneous treat-ment options such as alcohol septal ablation have been discouraged, because targeted ablation would not significan-tly alter chamber size and stroke volume.\(^\text{10}\) Thus, advanced treatment options in patients with apical HCM who are not amenable to medical therapy include heart transplantation and our unique surgical technique of apical myectomy.\(^\text{7}\) The present study shows that apical myectomy can avert or delay the need for cardiac transplant in the majority of patients. At late follow-up, cardiac transplantation had been performed in only 3 patients, and 1 needed an LV assist device implanted because of worsening heart failure.

Study Limitations

This is a retrospective study of a single institution and is limited by inherent selection bias. The relatively small size of our study is due to apical HCM being an uncommon disease in Western countries. Echocardiographic and other imaging follow-up were not available in the entire cohort. Patients with HCM who were waitlisted for heart transplant were identified using a national database, but the SRTR dataset does not include specific diagnosis of apical HCM or preoperative echocardiographic variables; this should be considered when interpreting our results. Causes of mortality were obtained through the NDI, but data were available only for the small subset of patients who died during the study period.

CONCLUSIONS

Apical myectomy is a unique treatment option for patients with nonobstructive apical HCM and small LV cavity size who have severe symptoms due to diastolic heart failure. Early postoperative outcomes are encouraging, and risk of the procedure is acceptably low. Survival in surgical patients appears to be superior to patients with HCM listed for cardiac transplantation. The majority of patients undergoing apical myectomy have sustained improvement in heart failure symptoms, and heart transplant, which is currently the only alternative surgical option, may be delayed or avoided entirely.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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