

Clinical Profile of Nonresponders to Surgical Myectomy with Obstructive Hypertrophic Cardiomyopathy

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ABSTRACT

BACKGROUND: Surgical myectomy reverses heart failure symptoms in the vast majority of obstructive hypertrophic cardiomyopathy patients. However, a small subgroup fails to experience sustained postoperative improvement despite relief of obstruction. Clinical profile of such patients has not been well defined.

METHODS: Consecutive obstructive hypertrophic cardiomyopathy patients undergoing myectomy at Tufts Medical Center for drug-refractory New York Heart Association III/IV heart failure symptoms, 2004 to 2017, were followed postoperatively for 2.5 ± 2.8 years and assessed for outcome.

RESULTS: Of the 503 patients, there were 4 postoperative deaths (0.8%); 480 patients (96%) had sustained improvement to New York Heart Association classes I or II (responders), but 19 (3.8%) developed advanced symptoms (classes III or IV) in the absence of obstruction (nonresponders). Compared with responders, nonresponders were younger (40 ± 13 vs 53 ± 14 years; $P < .001$) and had greater septal thickness (25 ± 9 vs 20 ± 4 mm; $P < .001$). Massive hypertrophy (≥ 30 mm) was 5-fold more common in nonresponders ($P < .01$). Seven nonresponders developed systolic dysfunction (ejection fraction 20%-47%), 2 days to 6.1 years postoperatively. Four nonresponders underwent heart transplant 3.4 to 9.2 years after myectomy, and 2 others have been listed.

CONCLUSIONS: Surgical myectomy is highly effective at reversing heart failure symptoms in the vast majority of patients with obstructive hypertrophic cardiomyopathy. However, a small minority experience persistent functional limitation despite surgical relief of outflow obstruction. Predictors of adverse postoperative course were substantial/massive septal thickness and youthful age. Patients who failed to respond symptomatically to myectomy were considered for advanced heart failure treatment, including heart transplantation.

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BACKGROUND

In patients with obstructive hypertrophic cardiomyopathy and drug-refractory heart failure, surgical septal myectomy is the

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preferred treatment option, relieving subaortic gradient with reversal of heart failure in the vast majority of patients.¹⁻⁸ Excellent surgical outcomes have been reported from experienced myectomy centers, associated with low operative mortality (<1%) and long-term survival similar to that in an age- and gender-matched US population.³⁻¹¹ However, a small but important subgroup of patients fails to experience symptomatic benefit after myectomy despite relief of outflow obstruction.³⁻¹² Therefore, it is timely to assess in detail the prevalence, clinical course, and profile of this underappreciated subset of hypertrophic cardiomyopathy patients.

METHODS

Patient Selection

A total of 503 consecutive obstructive hypertrophic cardiomyopathy patients underwent surgical myectomy at Tufts Medical Center, 2004 to 2017, to relieve left ventricular outflow tract gradient and heart failure symptoms. Diagnosis of hypertrophic cardiomyopathy was made in each on the basis of echocardiographic demonstration of the typical disease phenotype, with outflow obstruction predominantly due to systolic anterior motion of the mitral valve and septal contact. Each patient had outflow tract gradient ≥ 50 mm Hg at rest (61 ± 38 mm Hg) or after exercise (83 ± 33 mm Hg).

Patients were presented with all risks and benefits of the available treatment options, including myectomy surgery and alcohol septal ablation, in a context of shared decision making, considering personal preference and cardiac anatomy. Patients undergoing aortic valve replacement were excluded, although patients with coronary artery bypass grafting, mitral valve repair, and subaortic membrane resection are included.

Transesophageal echocardiograms were performed intraoperatively, with isoproterenol provocation immediately after myectomy to assess outflow gradient. Patients were followed postoperatively for 2.5 ± 2.8 years (range to 12), with the most recent clinical assessment obtained by hospital visit or telephone contact.

Statistical Analysis

Data are mean \pm standard deviation for continuous variables and proportions for categorical variables. Student's *t* test and Wilcoxon rank-sum tests assessed statistical significance of continuous variables, and χ^2 or Fisher's exact test for categorical variables. Variables with a *P* value of $<.05$ for univariate associations were entered into a stepwise multivariable Cox proportional hazards model to identify independent predictors. *P* $\leq .05$ was considered significant (Figure).

RESULTS

Operative Results

In 503 myectomy patients, age at operation was 52 ± 14 years; 56% were male. There were 4 postoperative deaths (0.8%); 480 of the remaining 499 (96%) achieved sustained improvement to New York Heart Association (NYHA) classes I

(*n* = 272) or II (*n* = 208) at last follow-up (*responders*). However, 19 patients (3.8%) developed advanced symptoms (classes III or IV) over 5.4 ± 3.1 years postoperatively (*nonresponders*). When measured immediately postoperatively and/or at the time of reoccurring NYHA class III symptoms, none of the 19 nonresponders had hemodynamically significant mitral valve systolic anterior motion or outflow gradients (0-15 mm Hg). Atrial fibrillation was judged not to significantly contribute to clinical course or progressive heart failure.

CLINICAL SIGNIFICANCE

- Although the vast majority of obstructive hypertrophic cardiomyopathy patients undergoing septal myectomy for advanced heart failure experience significant, sustained improvement postoperatively, a small minority ($<4\%$) incur residual or recurrent symptoms despite relief of obstruction.
- Predictors of adverse clinical response to myectomy include youthful age and substantial/massive left ventricular hypertrophy.
- Patients who fail to respond to surgical myectomy may be considered for advanced heart failure therapies, including heart transplant.

Nonresponders

Compared with myectomy responders, patients who failed to benefit were younger (age 40 ± 13 vs 53 ± 14 years at surgery; *P* $< .001$), with greater preoperative septal thickness (25 ± 9 vs 20 ± 4 mm; *P* $< .001$). Massive left ventricular hypertrophy (wall thickness ≥ 30 mm; range to 48 mm) was 5-fold more common in nonresponders than responders (4 of 19 [21%] vs 19 of 480 [4%]; *P* $< .01$); 2 other nonresponders had wall thicknesses of 27 mm and 28 mm.

On multivariate analysis, greater preoperative septal thickness and younger age were independent predictors of failure to respond symptomatically to myectomy (*P* = .03).

Otherwise, morphology was similar between responders and nonresponders (Table), without differences in preoperative ejection fraction, left ventricular end-diastolic dimension, left atrial size, atrial fibrillation, or overall surgical strategy. Of the 6 nonresponders with cardiac magnetic resonance imaging studies, mild late gadolinium enhancement was evident in 4. Diastolic function, assessed by echocardiography in 18 nonresponders was as follows: grade II (*n* = 14), grade I (*n* = 2), or indeterminate (*n* = 2); none had restrictive filling.¹³

Of 19 nonresponders, 6 had comorbid conditions that may have contributed to long-term postoperative course: 3 with morbid obesity (body mass index 42-52 kg/m²) and one each with recurrent pericarditis, cocaine usage, or pulmonary hypertension and right ventricular failure.

Clinical Course and Outcome

In the 19 nonresponders, clinical course was highly variable. Nine patients reported persistent heart failure symptoms soon after myectomy (95 ± 45 days), whereas 10 experienced initial symptom improvement postoperatively but returned to classes III/IV after 3.5 ± 2 years (range, 2-9 years).

Of the 19 clinical nonresponders, 7 developed adverse left ventricular remodeling by echocardiography, 2 days to 6.1 years postoperatively, with systolic dysfunction (ejection

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