Relationship between left ventricular mass, wall thickness, and survival after subaortic septal myectomy for hypertrophic obstructive cardiomyopathy

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Objective: In natural history studies, increased left ventricular mass and wall thickness are strongly associated with increased late mortality in patients with hypertrophic cardiomyopathy. Our objective was to determine the impact of left ventricular mass and wall thickness on survival after myectomy for hypertrophic obstructive cardiomyopathy.

Methods: We reviewed the case histories of 796 patients who underwent transaortic septal myectomy for hypertrophic obstructive cardiomyopathy from January 1993 to December 2006. We then selected for study patients who had transthoracic echocardiography within 30 days after myectomy, which included complete measurements of interventricular wall thickness, posterior wall thickness, and left ventricular end diastolic dimension. Late survival was determined for all patients using medical records and surveys.

Results: Our study group included 416 patients with a mean age of 50 ± 15 years, and 58% were male. Eight percent of patients had coronary artery disease, 17% had a history of arrhythmia, and 17% had a previous or concomitant insertion of an internal cardioverter defibrillator. All patients had successful myectomy, and 17% required an additional mitral valve procedure, most often mitral valve repair. On predismittal echocardiography, the average interventricular wall thickness was 16 ± 5 mm, the posterior wall thickness was 13 ± 3 mm, and the left ventricular end diastolic dimension was 45 ± 6 mm. The indexed left ventricular mass was 135 ± 46 g/m². Late survival at 1, 5, and 10 years was 99%, 97%, and 85%, which was similar to that of an age- and gender-matched population ($P = .453$). On multivariate analysis, preoperative and postoperative wall thickness and left ventricular mass were not associated with death; only a history of coronary artery disease (hazard ratio 4.9) was predictive of late mortality.

Conclusions: Left ventricular mass and wall thickness were not predictors of late survival after myectomy for hypertrophic obstructive cardiomyopathy, and this is in contrast to natural history studies of patients who were not treated surgically. Late survival was similar to that of an age- and gender-matched population. (J Thorac Cardiovasc Surg 2011;141:439-43)

Patients with hypertrophic cardiomyopathy (HCM) may have resting or provoked gradients owing to outflow tract obstruction caused by basal septal hypertrophy and systolic anterior motion of the mitral valve apparatus. In these patients, who are often symptomatic, transaortic septal myectomy can successfully relieve gradients. In multiple studies,¹⁻³ septal myectomy for hypertrophic obstructive cardiomyopathy (HOCM) has been shown to have a low operative mortality (<1%) and morbidity, and late

survival of patients after myectomy is similar to that of an age- and gender-matched population.

The mechanism whereby septal myectomy improves survival of patients with HOCM is poorly understood. In patients with obstructive or nonobstructive HCM who are not treated surgically, a correlation between left ventricular (LV) wall thickness and risk of sudden death, progression to heart failure, and overall death has been identified.⁴ Our objective was to determine the impact of LV wall thickness and LV mass on survival after septal myectomy for HOCM.

METHODS

After obtaining appropriate institutional review board approval waiving the need to obtain specific patient consent, we reviewed the case histories of 796 patients who underwent myectomy for HOCM from January 1993 to December 2006. Patients were selected for further study if complete early postoperative (<30 days) transthoracic echocardiography was available. Data were collected from both prospective clinical databases and a prospective echocardiographic database. Late survival was determined for all patients from medical records, Accurint (www.accurint.com), and surveys.

Echocardiography was considered complete if it included comprehensive measurements of interventricular septal wall thickness (IWT),

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Abbreviations and Acronyms

HCM	= hypertrophic cardiomyopathy
HOCM	= hypertrophic obstructive cardiomyopathy
ICD	= internal cardioverter defibrillator
IWT	= interventricular septal wall thickness
LV	= left ventricle (ventricular)
MWT	= maximal wall thickness
PWT	= posterior wall thickness

posterior wall thickness (PWT), and LV end-diastolic dimensions. Maximal wall thickness (MWT) was considered to be the thickest wall of the LV (posterior or septal). Echocardiographic measurements were performed according to the standards described by the American Association for Echocardiography.⁵ We analyzed both the premyectomy and postmyectomy value for the IWT to account for any possible error resulting from a measurement in the myectomy trough. All measurements were also indexed to body surface area.

Statistical analyses were performed using SAS software (version 9.1; SAS Institute, Inc, Cary, NC). Data are presented as means and standard deviations or numbers and percentages, as appropriate. Univariate and stepwise multivariate models were created using logistic regression for binary outcomes and Cox proportional hazards for time-related data. Kaplan-Meier curves were compared using a log-rank test.

RESULTS

Our study group included 416 patients with a mean age of 50 ± 15 years, and 58% were male. Eight percent of patients had coronary artery disease, 17% had a history of arrhythmia, and 17% had a previous or concomitant insertion of an internal cardioverter defibrillator (ICD) (Table 1).

Before the operation, the mean echocardiographic measurement of IWT was 19.4 ± 5.6 mm, PWT was 14.0 ± 3.3 mm, and MWT was 19.5 ± 5.6 mm. The average LV end-diastolic dimension was 44.9 ± 6.3 mm and LV mass index was 162.5 ± 55.8 g/m². The mean ejection fraction was $72\% \pm 6\%$.

All patients had successful myectomy, and 17% required an additional mitral valve procedure including chordal or papillary muscle division or resection ($n = 34$), mitral valve replacement ($n = 9$), leaflet only repair ($n = 15$), leaflet repair and annuloplasty ($n = 7$), or annuloplasty alone ($n = 6$). Forty-one patients required aortic valve procedures, with aortic valve replacement ($n = 21$) the most common for concomitant aortic stenosis. Coronary artery bypass was performed in 28 patients and a maze procedure in 11 patients.

On predismittal echocardiography, the average IWT was 15.9 ± 4.9 mm, the PWT was 13.1 ± 2.9 mm, and the LV end-diastolic dimension was 44.5 ± 6.4 mm. The average indexed LV mass was 134.7 ± 45.9 g/m² and the MWT was 16.3 ± 14.7 mm after subaortic septal myectomy. The ejection fraction was $66\% \pm 7\%$ at dismissal.

The mean follow-up time was 3.6 ± 3.2 years. Late survival at 1, 5, and 10 years was 99%, 97%, and 85%, which was similar to an age- and gender-matched Minnesotan population ($P = .453$) (Figure 1). Univariate analysis is shown in Table 2. Significant univariate associations with mortality included older age, presence of coronary artery disease, and lower preoperative ejection fraction. Survival was similar for patients with and without ICDs. Wall thickness was not a univariate predictor of survival when considered as a continuous or integer variable (Figure 2). On multivariate analysis, wall thickness (preoperative and pre-dismissal) and LV mass were not associated with death; only a history of coronary artery disease (hazard ratio 4.9; $P = .006$) was predictive of late mortality (Figure 3).

DISCUSSION

In this study of patients who underwent transaortic subaortic septal myectomy for HOCM, measures of LV hypertrophy (IWT, PWT, MWT, LV mass, and indexed values) were not associated with late death. Our findings differ from the natural history of patients with HCM who were not treated surgically. In a study of 480 patients who were followed up over a mean interval of 6.5 years, Spirito and associates⁴ found a strong correlation between degree of ventricular hypertrophy (defined as MWT) and sudden cardiac death. Indeed, in their investigation, the cumulative risk of sudden death 20 years after diagnosis was negligible for patients with a wall thickness of 19 mm or less but almost 40% for patients with wall thicknesses of 30 mm or more. Only 25% of the overall group had outflow tract obstruction, and only 5.4% had surgery for septal myectomy.⁴

The present study differs in several important ways. Our study patients appear to have less severe concentric ventricular hypertrophy than do those in the natural history study who had an average MWT of 21 ± 5 mm including 43 patients (9%) with an MWT of 30 mm or more.⁴ In our study, only 18 (4%) patients had a preoperative MWT of 30 mm or more. It may be that patients selected for surgery who have marked basal hypertrophy have less severe thickening of the remainder of the ventricle.

As well, our study patients were more severely symptomatic, inasmuch as 81% were in New York Heart Association class III or IV compared with only 7% in the investigation by Spirito and associates.⁴ In a study from Italy of HOCM patients with severe symptoms, deteriorating functional class became a predictor of cardiovascular death, independent of outflow tract gradient.⁶ Spirito's group⁴ reported that extreme hypertrophy was associated with younger age but not associated with advanced symptoms. We did not include children in our study, whereas their study included some patients less than 18 years of age.

Finally, our analysis includes both unindexed and indexed values for LV hypertrophy. Although we acknowledge Spirito and colleagues'⁴ arguments for using the more

TABLE 1. Patient demographics

Variable	Mean ± SD
Age (y)	50 ± 15
Body surface area (m ²)	2.0 ± 0.2
Ejection fraction (%)	72 ± 6
	N (%)
Male	242 (58)
Coronary artery disease (MI or CABG)	34 (8)
Angina	153 (37)
New York Heart Association class III or IV	337 (81)
History of congestive heart failure	40 (10)
History of arrhythmia	72 (17)
Preoperative or concomitant ICD	69 (17)

MI, Myocardial infarction; CABG, coronary artery bypass grafting; ICD, internal cardioverter defibrillator.

clinical relevant unindexed measures, we included indexed data to provide a more complete analysis. We did not find indexed values to be superior to the unindexed measures in our study.

In a study by Sorajja and colleagues,⁷ patients who had massive myocardial hypertrophy (myocardial thickness ≥30 mm) had a poorer survival than did an age- and gender-matched population. The most common cause of death was sudden cardiac death in young (<30 years) patients and heart failure in older (≥60 years) patients. These authors did not identify any excess mortality in middle-aged patients. Our study differs, in that this cohort includes patients with HOCM who had surgical relief of the LV outflow tract obstruction.

LV outflow tract obstruction appears to be a risk factor for poor outcome in patients with HCM.^{8,9} The presence of a resting LV outflow tract gradient of 30 mm Hg or more is reported to be an independent predictor (odds ratio 4.4) of progression to heart failure and death from heart failure or stroke in patients with HCM.⁸ However, in the study

FIGURE 1. Overall survival after transaortic interventricular septal myectomy for hypertrophic obstructive cardiomyopathy compared with an age- and gender-matched Minnesotan, white population.

TABLE 2. Univariate predictors of mortality

Preoperative clinical variables	P value
Coronary artery disease	.006*
Older age (1 y)	.020*
New York Heart Association class III or IV	.136
Male gender	.334
Congestive heart failure	.554
Preoperative/concomitant internal cardiac defibrillator	.845
Angina	.872
Preoperative arrhythmia	.905
Echocardiographic variables†	P value
Preoperative	
Decreasing ejection fraction (1%)	.044*
Interventricular wall thickness	.843
Indexed interventricular wall thickness	.392
Postoperative	
Interventricular wall thickness	.065
Indexed interventricular wall thickness	.885
Posterior wall thickness	.279
Indexed posterior wall thickness	.070
Left ventricular end-diastolic dimension	.057
Indexed left ventricular end-diastolic dimension	.557
Left ventricular mass	.402
Indexed left ventricular mass	.681
Maximal wall thickness	.733
Indexed maximal wall thickness	.776

*Significant univariate associations with mortality. †All echocardiographic variables were analyzed in a continuous fashion.

by Ommen and colleagues¹ from our clinic, patients with obstruction who subsequently had interventricular septal myectomy had improved survival (hazard ratio 0.43) compared with patients not treated surgically, and this association was independent of other clinical or hemodynamic characteristics. The difference in survival of HOCM patients with or without septal myectomy may be related to relief of the hemodynamic burden and/or improvement in diastolic function. Improvement of mitral inflow Doppler velocity curves and decreased mitral E velocity suggest enhancement of diastolic filling after surgical myectomy.¹⁰ The improvement in diastolic function may be due to a decrease in subendocardial ischemia resulting from lower intracavitary pressure after myectomy.

Subaortic septal myectomy also results in LV mass regression after successful relief of the LV outflow tract obstruction. In prior studies from our clinic, LV mass regression has been shown to occur early postoperatively and persist up to 2 years after operation.^{10,11} At less than 2 years after myectomy, a statistically significant reduction in the IWT and PWT was demonstrated.¹¹ We did not examine late echocardiography in our study patients and thus cannot assess the potential role of LV mass regression over time.

Improved survival after septal myectomy may be related to decreased risk of sudden cardiac death. McLeod and

FIGURE 2. Survival stratified by preoperative maximal wall thickness. A maximal wall thickness of 30 mm or more was considered massive hypertrophy.

colleagues¹² reviewed 125 patients with HCM who had ICDs and stratified patients into groups who did or did not undergo myectomy. The average annualized event rate (sudden death or appropriate ICD discharge) was 4.3% per year in the nonmyectomy group and 0.24% per year after myectomy ($P = .004$). The mechanism responsible for the lower risk of ventricular arrhythmias after myectomy is unknown, but the decrease in LV pressure may be a contributor. The late (>5 years) frequency of sudden death after myectomy, however, remains uncertain, and ongoing assessment for the risk of sudden death is important.

It is notable that survival after subaortic septal myectomy in this series was similar for patients with and without ICDs, but these data should be interpreted with caution. Recent guidelines¹³ advise placement of a prophylactic ICD in patients with HCM who have a major risk factor for sudden death (prior cardiac arrest, spontaneous sustained ventricular tachycardia, family history of sudden cardiac death, syncope, an abnormal blood pressure response to exercise, and massive LV hypertrophy ≥ 30 mm). However, our study contained only 18 premyectomy patients and 9 postmyectomy with an MWT of 30 mm or more. Thus, our results may not be applicable in patients with severe ventricular hypertrophy. Almost 17% of our patients had an ICD either preoperatively or at the time of the operation, but we did not find that an ICD was protective in our patients.

In this cohort of patients, the only associations with late mortality were older age, coronary artery disease, and lower preoperative ejection fraction. On multivariate analysis, only coronary artery disease was predictive of late mortality. These risk factors would be similar to the common predictors of mortality in a generalized population. Coronary artery disease has previously been shown to impend a poor prognosis in patients with HCM, both surgically treated and not surgically treated.¹⁴

We used the clinically reported measurements on echocardiography for all patients. We did not remeasure

FIGURE 3. Survival stratified by presence or absence of coronary artery disease.

echocardiograms because this is the clinical information that was provided to make decisions regarding therapy. It is possible that the preoperative IWT and postoperative IWT measurements were taken in either the bulge of the interventricular septum or in myectomy trough. In an effort to account for this, both preoperative and postoperative measurements of IWT were included in our analysis. We also used both nonindexed and indexed values and calculated the MWT, which is a measurement reported in previous studies.^{1,4}

CONCLUSIONS

The preoperative and postoperative LV mass and wall thickness, as well as the echo changes observed within 1 month of myectomy, were not predictors of late survival after myectomy for HOCM, and this is in contrast to natural history studies of patients who are not treated surgically. Late survival was similar to that of an age- and gender-matched population up to 10 years after myectomy. Longer-term follow-up is needed to determine both the mechanism of the improved survival and the duration of benefit.

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