

ORIGINAL ARTICLE

Effect of Left Ventricular Outflow Tract Obstruction on Clinical Outcome in Hypertrophic Cardiomyopathy

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ABSTRACT

BACKGROUND

The influence of left ventricular outflow tract obstruction on the clinical outcome of hypertrophic cardiomyopathy remains unresolved.

METHODS

We assessed the effect of outflow tract obstruction on morbidity and mortality in a large cohort of patients with hypertrophic cardiomyopathy who were followed for a mean (\pm SD) of 6.3 ± 6.2 years.

RESULTS

Of the 1101 consecutive patients, 273 (25 percent) had obstruction of left ventricular outflow under basal (resting) conditions with a peak instantaneous gradient of at least 30 mm Hg. A total of 127 patients (12 percent) died of hypertrophic cardiomyopathy, and 216 surviving patients (20 percent) had severe, disabling symptoms of progressive heart failure (New York Heart Association [NYHA] functional class III or IV). The overall probability of death related to hypertrophic cardiomyopathy was significantly greater among patients with outflow tract obstruction than among those without obstruction (relative risk, 2.0; $P=0.001$). The risk of progression to NYHA class III or IV or death specifically from heart failure or stroke was also greater among patients with obstruction (relative risk, 4.4; $P<0.001$), particularly among patients 40 years of age or older ($P<0.001$). Age-adjusted multivariate analysis confirmed that outflow tract obstruction was independently associated with an increased risk of both death related to hypertrophic cardiomyopathy (relative risk, 1.6; $P=0.02$) and progression to NYHA class III or IV or death from heart failure or stroke (relative risk, 2.7; $P<0.001$). The likelihood of severe symptoms and death related to outflow tract obstruction did not increase as the gradient increased above the threshold of 30 mm Hg.

CONCLUSIONS

In patients with hypertrophic cardiomyopathy, left ventricular outflow tract obstruction at rest is a strong, independent predictor of progression to severe symptoms of heart failure and of death.

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HYPERTROPHIC CARDIOMYOPATHY IS A genetic cardiac disease with heterogeneous phenotypic expression and a diverse clinical course characterized by both sudden death and disabling symptoms related to heart failure.¹⁻¹² Historically, even from the first clinical descriptions, the left ventricular outflow tract gradient has been a prominent and quantifiable feature of hypertrophic cardiomyopathy.^{1-5,13-22} Major therapeutic interventions (such as ventricular septal myectomy, percutaneous alcohol septal ablation, and dual-chamber pacing) have been introduced to relieve disabling symptoms associated with outflow tract obstruction.^{5,6,23-26} However, the long-term effect of the subaortic gradient on clinical outcome continues to be a source of uncertainty. Therefore, we analyzed a large cohort of patients with hypertrophic cardiomyopathy in order to define the relation between the outflow tract gradient and the clinical course.

METHODS

STUDY POPULATION

A total of 1101 consecutive patients with hypertrophic cardiomyopathy were enrolled: 364 at Azienda Ospedaliera Careggi in Florence, Italy; 200 at Federico II University of Naples in Naples, Italy; and 537 at the Minneapolis Heart Institute in Minneapolis. The initial clinical evaluation was defined as the time at which the left ventricular outflow tract gradient was first assessed by continuous-wave Doppler echocardiography at each institution from July 1983 to December 2001. The mean (\pm SD) duration of follow-up, from the initial measurement of the gradient to the most recent evaluation or death, was 6.3 ± 6.2 years. All patients enrolled in the study signed a statement, previously approved by Allina Health System in Minneapolis or conforming to the Authority for Privacy Act in Italy, agreeing to the use of their medical information for research purposes.

ECHOCARDIOGRAPHY

Echocardiographic studies were performed with the use of commercially available instruments. Obstruction of the left ventricular outflow tract, which was due to the anterior motion of the mitral valve during systole and septal contact,^{22,27} was considered to be present when the peak instantaneous outflow gradient was estimated to be at least 30 mm Hg with the use of continuous-wave Doppler echocardiography

under basal (resting) conditions.²² Care was taken to avoid contamination of the left ventricular outflow waveform by the mitral regurgitation jet.²²

DEFINITIONS

The diagnosis of hypertrophic cardiomyopathy was based on the demonstration by two-dimensional echocardiography of a hypertrophied, nondilated left ventricle (wall thickness of at least 15 mm in adults or the equivalent relative to body-surface area in children)²⁸ in the absence of another cardiac or systemic disease capable of producing a similar degree of hypertrophy.²⁹ Sudden death was defined as a sudden and unexpected collapse in patients who had previously had a relatively uneventful clinical course.³⁰ Death related to heart failure was regarded as that occurring in the context of cardiac decompensation and a progressive course with limiting symptoms, particularly when it was complicated by pulmonary edema or required hospitalization for treatment, or both.³⁰ In addition, potentially lethal events in which patients were successfully resuscitated from cardiac arrest or received appropriate shocks from an implanted defibrillator were regarded as equivalent to sudden death. Heart transplantation in patients with advanced, end-stage disease and systolic dysfunction^{5,6} was considered to be a surrogate for death related to heart failure.³⁰ Stroke-related deaths were judged to be a consequence of embolic events related to hypertrophic cardiomyopathy, usually in the setting of atrial fibrillation.³¹

STATISTICAL ANALYSIS

Data are expressed as means \pm SD. The unpaired Student's *t*-test or one-way analysis of variance was used to compare normally distributed data. Fisher's exact test was used to compare noncontinuous variables expressed as proportions. Relative risks and 95 percent confidence intervals were calculated with univariate and multivariate Cox proportional-hazards regression models. Multivariate analyses were performed with a stepwise forward regression model, in which each variable with a *P* value of 0.05 or less (based on the univariate analysis) was entered into the model. Survival curves were constructed according to the Kaplan–Meier method. *P* values are two-sided, and a *P* value of less than 0.05 was considered to indicate statistical significance. Calculations were performed with use of SPSS software (version 8.0).

The primary clinical end points used in this study

were death from any cause, death related to hypertrophic cardiomyopathy (i.e., sudden death or death as a consequence of heart failure or stroke), a combined end point of death from heart failure or stroke or progression to New York Heart Association (NYHA) functional class III or IV (i.e., severe symptoms), and sudden, unexpected death alone. Analyses of deaths from all causes and deaths related to hypertrophic cardiomyopathy included the total study group of 1101 patients. Evaluations of progression to NYHA class III or IV and death from heart failure or stroke or of sudden death alone were confined to the 994 patients who were in NYHA class I or II at entry into the study and thus excluded the 107 patients who were already in NYHA class III or IV. For the 66 severely symptomatic patients who underwent major therapeutic interventions known to relieve outflow tract gradient most effectively (septal myectomy, mitral-valve replacement, or alcohol septal ablation),^{1,3,5-7,23-26} follow-up was terminated at the time of the procedure.

RESULTS

BASE-LINE CHARACTERISTICS

The clinical and demographic characteristics of the overall study population of 1101 patients are shown in Table 1. The mean age at initial evaluation was 45 ± 20 years. A total of 273 patients (25 percent) had peak instantaneous left ventricular outflow tract gradients of at least 30 mm Hg under basal conditions (range, 30 to 176 mm Hg); the other 828 patients (75 percent) had a gradient of less than 30 mm Hg or no gradient and were considered to be without obstruction. As compared with patients without obstruction, those with left ventricular outflow tract obstruction were older (and less commonly male), more often had severe limiting symptoms (NYHA class III or IV), and had thicker left ventricular walls and larger left atrial dimensions (Table 1).

At the time of the last follow-up visit, 914 patients (83 percent) were still alive, 60 patients (5 percent) had died of causes unrelated to hypertrophic cardiomyopathy, and 127 patients (12 percent) had died of hypertrophic cardiomyopathy, either suddenly or as a consequence of heart failure or stroke. Among the 914 surviving patients, 216 had severe, disabling symptoms of exertional dyspnea (with or without chest pain) and were in NYHA class III or IV (Table 1).

MORTALITY AND HEART FAILURE-RELATED MORBIDITY

During the follow-up period, patients with obstruction had a significantly greater likelihood of death related to hypertrophic cardiomyopathy than patients without obstruction (relative risk, 2.0; 95 percent confidence interval, 1.3 to 3.0; $P=0.001$) (Fig. 1). Similarly, the probability of reaching the end point of progression to NYHA class III or IV or death from heart failure or stroke was significantly greater in patients with obstruction (relative risk, 4.4; 95 percent confidence interval, 3.3 to 5.9; $P<0.001$) (Fig. 2).

Among patients with obstruction, those with mild symptoms (NYHA class II) at entry were more likely to have progression to more severe symptoms or to die from heart failure or stroke than were asymptomatic patients ($P<0.001$) (Fig. 2). When the effect of age at the time of measurement of the gradient was analyzed, patients with obstruction who were at least 40 years old were more likely to die of causes related to hypertrophic cardiomyopathy or to have complications of this condition than were younger patients with obstruction ($P<0.001$) (Fig. 3). In addition, patients with obstruction had a significantly increased risk of death from any cause, as compared with patients without obstruction (relative risk, 2.0; 95 percent confidence interval, 1.4 to 2.7; $P<0.001$).

SUDDEN DEATH FROM HYPERTROPHIC CARDIOMYOPATHY

The probability of sudden death among patients with obstruction was significantly higher than that among patients without obstruction (relative risk, 2.1; 95 percent confidence interval, 1.1 to 3.7; $P=0.02$) (Fig. 4). However, the difference in the annual rate of sudden death between patients with obstruction and patients without obstruction was small (1.5 percent vs. 0.9 percent, or 0.6 percent per year). Outflow tract obstruction was also associated with a particularly low positive predictive value for sudden death (7 percent), although the negative predictive value was high (95 percent).

MAGNITUDE OF THE OUTFLOW GRADIENT

When clinical outcome was assessed with respect to the magnitude of the outflow gradient among the 994 patients in NYHA class I or II at study entry — 30 to 49 mm Hg (in 62 patients), 50 to 69 mm Hg (in 73), or 70 mm Hg or greater (in 89) — there

Table 1. Characteristics of 1101 Patients with Hypertrophic Cardiomyopathy According to the Presence or Absence of Left Ventricular Outflow Tract Obstruction at Base Line.*

Characteristic	All Patients (N=1101)	Patients without Obstruction (N=828)	Patients with Obstruction (N=273)	P Value
Base-line measurements				
Male sex — no. (%)	655 (59)	529 (64)	126 (46)	<0.001
Age — yr	45±20	44±19	50±21	<0.001
NYHA class				
Mean	1.6±0.7	1.5±0.6	1.8±0.8	<0.001
I — no. (%)	596 (54)	490 (59)	106 (39)	NA
II — no. (%)	398 (36)	280 (34)	118 (44)	NA
III or IV — no. (%)	107 (10)	58 (7)	49 (18)	NA
Atrial fibrillation — no. (%)	220 (20)	147 (18)	73 (27)	<0.01
Syncope — no. (%)	152 (14)	96 (12)	56 (21)	<0.001
Drugs — no. (%)				
Beta-blockers	429 (39)	278 (34)	151 (55)	0.20
Verapamil	381 (35)	260 (31)	121 (44)	0.30
Disopyramide	35 (3)	11 (1)	24 (9)	0.50
Amiodarone	153 (14)	113 (14)	40 (15)	0.70
Echocardiographic measurements				
Left ventricular outflow tract gradient — mm Hg	21±33	5±7	70±32	NA
Maximal left ventricular thickness — mm	22±33	22±6	24±6	<0.001
Left atrial dimension — mm	42±8	41±8	45±8	<0.001
Left ventricular end-diastolic dimension — mm	43±7	44±7	41±7	<0.001
Follow-up measurements				
Duration of follow-up — yr	6.3±6.2	6.7±6.4	5.1±5.3	<0.001
NYHA class†				
Mean	1.7±0.8	1.6±0.7	2.2±0.9	<0.001
I — no. (%)	506 (48)	435 (55)	71 (28)	NA
II — no. (%)	323 (31)	249 (31)	74 (29)	NA
III or IV — no. (%)	216 (21)	107 (14)	109 (43)	NA
Major interventions for obstruction or symptoms — no. (%)				
Septal myectomy	40 (4)	—	40 (15)	NA
Mitral-valve replacement	7 (1)	2 (0.2)	5 (2)	NA
Alcohol septal ablation	19 (2)	—	19 (7)	NA
Heart transplantation	8 (1)	8 (1)	—	NA
Dual-chamber pacemaker	8 (1)	—	8 (3)	NA
Age at death — yr	54±19	52±18	59±19	0.14
Death related to hypertrophic cardiomyopathy — no. (%)	127 (12)	88 (11)	39 (14)	NA
Sudden death	71 (6)	51 (6)	20 (7)	NA
Heart failure	41 (4)	29 (4)	12 (4)	NA
Stroke	15 (1)	8 (1)	7 (3)	NA

* Plus-minus values are means ±SD. NA denotes not applicable.

† The 56 patients who died of heart failure or stroke were excluded from the analysis.

were no significant differences in the overall risk of death related to hypertrophic cardiomyopathy, progression to NYHA class III or IV (Fig. 5), or sudden death. Furthermore, there was no significant difference in the average outflow tract gradient among patients with obstruction who died from various

causes related to hypertrophic cardiomyopathy (sudden death, 71±18 mm Hg; heart failure, 52±20 mm Hg; and stroke, 82±48 mm Hg) or among survivors, as compared with patients who died of causes unrelated to hypertrophic cardiomyopathy (69±29 mm Hg vs. 71±32 mm Hg). Also, among patients

with obstruction, the absolute gradient measured as a continuous variable was not associated with a significant increase in the risk of any of the study end points in the age-adjusted multivariate analysis.

PREDICTORS OF OUTCOME

Age-adjusted multivariate analysis showed that left ventricular outflow tract obstruction was a strong, independent determinant of outcome, including the overall risk of death related to hypertrophic cardiomyopathy (relative risk, 1.6; $P=0.02$), progression to severe heart failure or death from heart failure or stroke (relative risk, 2.7; $P<0.001$), and death from any cause (relative risk, 1.6; $P=0.02$) (Table 2). Other disease variables that were independently associated with an increased risk of death related to hypertrophic cardiomyopathy were atrial fibrillation, limiting symptoms (NYHA class II, III, or IV) at study entry, and maximal left ventricular wall thickness of at least 30 mm (Table 2). Only a minority of patients with obstruction had associated severe mitral regurgitation identified by color-flow imaging³² (27 of 273, or 10 percent), and this finding itself was not consistently associated with death related to hypertrophic cardiomyopathy or to progression to NYHA class III or IV ($P=0.50$ for both comparisons).

With regard to sudden death, left ventricular outflow tract obstruction was the only clinical variable independently associated with this outcome (relative risk, 1.9; $P=0.01$). None of the pharmacologic agents commonly used to control symptoms of hypertrophic cardiomyopathy (i.e., beta-blockers, calcium-channel blockers, and disopyramide) or amiodarone significantly affected any of the study end points when taken for more than 50 percent of the follow-up period.

ANALYSES AMONG CENTERS

The patients enrolled at the three participating centers did not differ significantly with regard to several demographic and disease-related variables, including age, sex, and the prevalence of outflow tract obstruction. The annual rates of death related to hypertrophic cardiomyopathy were also similar: 2.1 percent in Florence, 1.8 percent in Naples, and 1.7 percent in Minneapolis. Also, all three centers had higher annual rates of death among patients with obstruction than among those without obstruction: 1.8 percent vs. 1.4 percent in Florence, 3.3 percent vs. 1.3 percent in Naples, and 2.6 percent vs. 1.7 percent in Minneapolis.

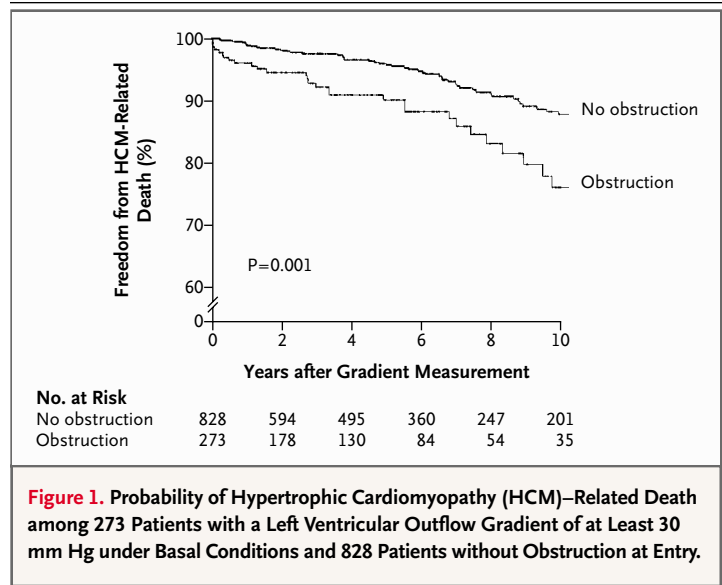


Figure 1. Probability of Hypertrophic Cardiomyopathy (HCM)-Related Death among 273 Patients with a Left Ventricular Outflow Gradient of at Least 30 mm Hg under Basal Conditions and 828 Patients without Obstruction at Entry.

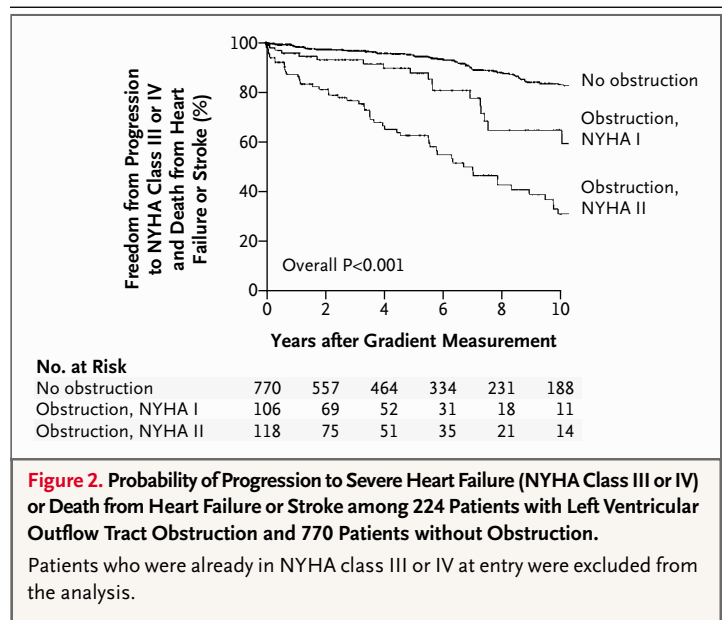


Figure 2. Probability of Progression to Severe Heart Failure (NYHA Class III or IV) or Death from Heart Failure or Stroke among 224 Patients with Left Ventricular Outflow Tract Obstruction and 770 Patients without Obstruction.

Patients who were already in NYHA class III or IV at entry were excluded from the analysis.

DISCUSSION

The left ventricular outflow tract gradient has been the most recognizable feature of hypertrophic cardiomyopathy from its initial clinical descriptions.^{1-27,33-36} A gradient of at least 50 mm Hg has historically been the threshold for performing major invasive interventions, such as septal myectomy,

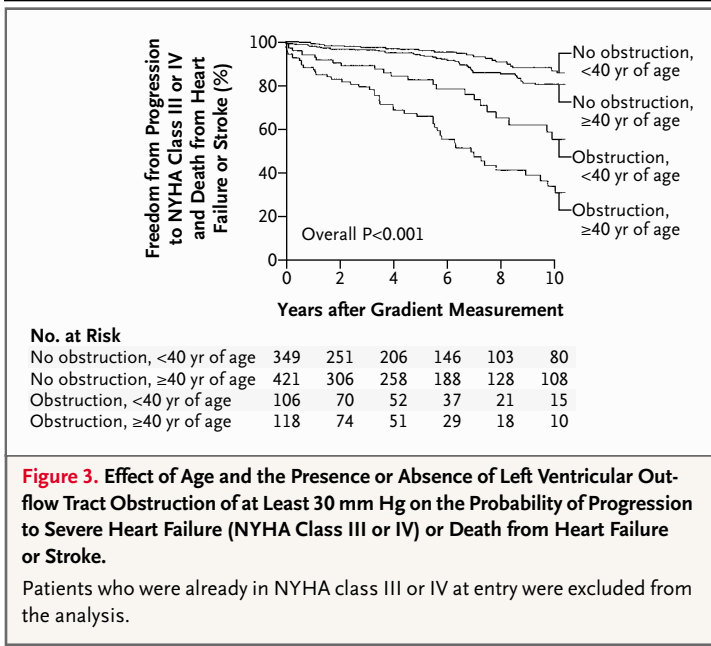


Figure 3. Effect of Age and the Presence or Absence of Left Ventricular Outflow Tract Obstruction of at Least 30 mm Hg on the Probability of Progression to Severe Heart Failure (NYHA Class III or IV) or Death from Heart Failure or Stroke.

Patients who were already in NYHA class III or IV at entry were excluded from the analysis.

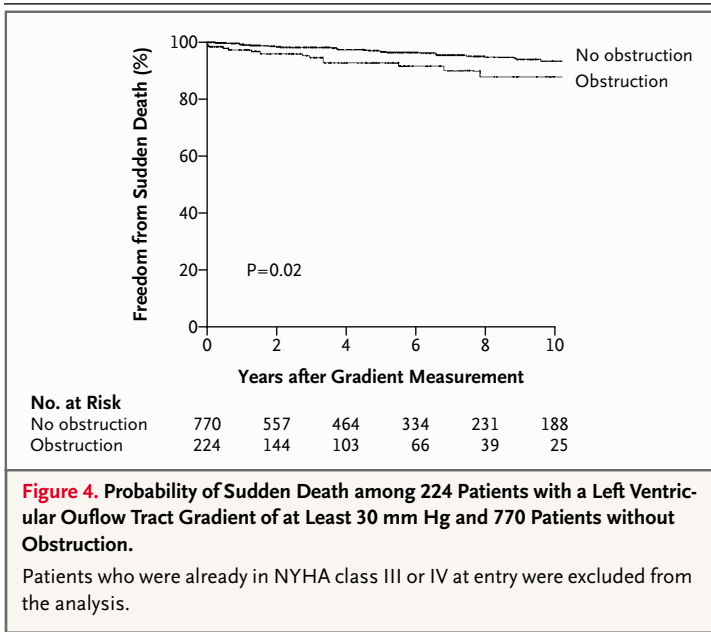


Figure 4. Probability of Sudden Death among 224 Patients with a Left Ventricular Outflow Tract Gradient of at Least 30 mm Hg and 770 Patients without Obstruction.

Patients who were already in NYHA class III or IV at entry were excluded from the analysis.

struction in patients with hypertrophic cardiomyopathy has periodically been the subject of intense controversy,^{1-4,13,18,19} and the long-term effect of the outflow gradient on outcome remains largely unresolved. Consequently, we took this opportunity to investigate the clinical significance of subaortic obstruction in a large cohort of patients with hypertrophic cardiomyopathy.

Our data show that obstruction of left ventricular outflow is of prognostic importance in patients with hypertrophic cardiomyopathy. Patients with outflow tract obstruction (defined here as a basal gradient of at least 30 mm Hg) had an increased risk of death from hypertrophic cardiomyopathy or progression to severe congestive symptoms, which was more than four times that among patients without obstruction. Outflow tract obstruction also proved to be a strong independent determinant of limiting symptoms and death after adjustment for other relevant disease-related and demographic variables. Patients with obstruction and mild symptoms (NYHA class II) were more likely than asymptomatic patients to have progression to severe symptoms or to die from heart failure. Furthermore, we have previously shown that the combination of outflow tract obstruction with atrial fibrillation is particularly deleterious in patients with hypertrophic cardiomyopathy.³¹

Our data have certain potentially important therapeutic implications for patients with the obstructive form of hypertrophic cardiomyopathy. Currently accepted clinical practice¹⁻⁶ encourages the use of aggressive medical therapy for patients with symptoms who have obstruction, including the use of drugs capable of reducing the outflow gradient under basal conditions or during exercise (predominantly beta-blockers and disopyramide)^{4-6,35}; our data support this strategy. However, when symptoms and the limitation in exercise capacity become refractory to maximal medical management, major interventions to reduce obstruction become necessary.^{1-7,23-26,36}

In this regard, our findings indicate that non-pharmacologic interventions (i.e., surgery or alcohol septal ablation) may be a reasonable treatment option earlier and at somewhat lower gradient thresholds than current clinical practice dictates.^{1,3,5,36} Such a strategy may be beneficial for some patients who have clear progression of symptoms despite medical treatment but who have not yet become substantially disabled, particularly those judged to have long-standing gradients.^{1,3,5,6,36}

alcohol septal ablation, and dual-chamber pacing, in patients with severe symptoms refractory to maximal medical management.^{3,5,6,23-26} Most previous studies addressing the clinical significance of obstruction have involved relatively small or highly selected populations, and reports have often been conflicting.^{4,8,9,13-19,33,34} Indeed, the issue of ob-

We could not directly assess the effects of treatment interventions on mortality. Furthermore, we do not believe that our data can be used to infer that a basic and sweeping alteration in the standard management of symptomatic obstructive hypertrophic cardiomyopathy is required. Indeed, the interventions that relieve obstruction most reliably (i.e., septal myectomy and alcohol septal ablation)^{5,6,23-26} should not be performed in patients without symptoms or with only mild symptoms, since such procedures are associated with some risk of complications and death.^{1,3-7,23-26,36} Therefore, our observations emphasize the importance of clinical judgment in planning a strategy to reduce left ventricular outflow tract obstruction in patients with hypertrophic cardiomyopathy.

We found that the likelihood of sudden death was also greater among patients with obstruction than among those without obstruction. However, because of the low annual rate of sudden death and the particularly low positive predictive value of obstruction, we believe that the contribution of obstruction to risk stratification remains limited. Indeed, although obstruction can probably be regarded as another potential risk factor for sudden death on the basis of present and prior analyses,^{8,9} the relation between the gradient and sudden death is not sufficiently strong for obstruction to be considered the sole or a substantial determinant of decisions to implant cardioverter-defibrillators prophylactically.³⁷

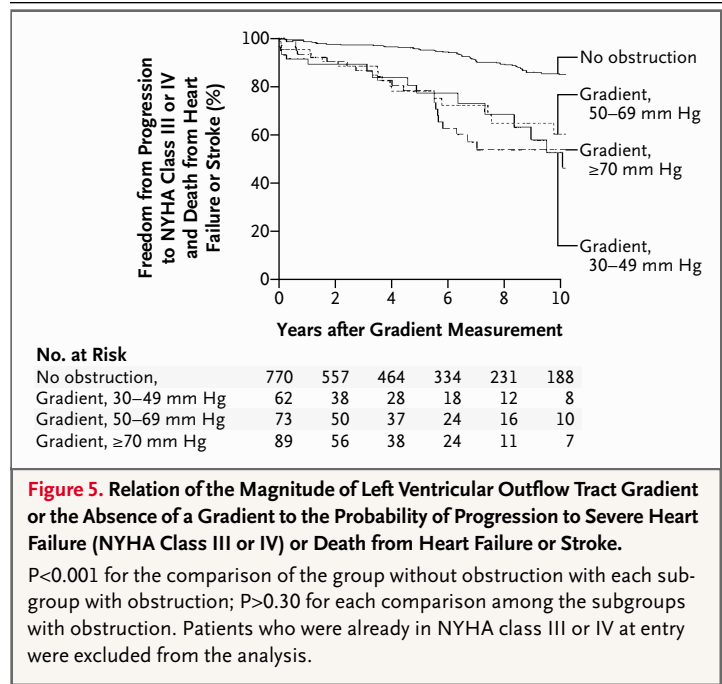


Figure 5. Relation of the Magnitude of Left Ventricular Outflow Tract Gradient or the Absence of a Gradient to the Probability of Progression to Severe Heart Failure (NYHA Class III or IV) or Death from Heart Failure or Stroke.

P<0.001 for the comparison of the group without obstruction with each subgroup with obstruction; P>0.30 for each comparison among the subgroups with obstruction. Patients who were already in NYHA class III or IV at entry were excluded from the analysis.

The threshold value for the outflow tract gradient that proved to be clinically relevant was relatively low—30 mm Hg. Furthermore, values above this threshold did not add to the likelihood of complications and death related to hypertrophic cardiomyopathy. This inability to stratify outcome with re-

Table 2. Results of Age-Adjusted Multivariate Cox Proportional-Hazards Analysis of the Relation between Base-Line Clinical Variables and Outcome.*

Variable	Death from Any Cause		HCM-Related Death		HCM-Related Progression to NYHA Class III or IV or Death from Heart Failure or Stroke†		Sudden Death from HCM†	
	Relative Risk (95% CI)	P Value	Relative Risk (95% CI)	P Value	Relative Risk (95% CI)	P Value	Relative Risk (95% CI)	P Value
Left ventricular outflow obstruction (≥30 mm Hg)	1.6 (1.1-2.2)	0.02	1.6 (1.1-2.4)	0.02	2.7 (2.0-3.5)	<0.001	1.9 (1.1-3.5)	0.014
NYHA class II, III, or IV at entry	1.5 (1.1-2.1)	0.02	1.9 (1.2-2.9)	0.002	3.4 (2.4-4.8)	<0.001	—	0.12
Paroxysmal or chronic atrial fibrillation	1.4 (1.0-1.9)	0.04	1.6 (1.1-2.4)	0.01	1.3 (1.1-1.6)	0.046	—	0.72
Maximal left ventricular thickness ≥30 mm	1.6 (1.1-2.4)	0.01	1.8 (1.1-2.8)	0.01	—	0.09	—	0.82
Female sex	—	0.22	—	0.29	1.4 (1.1-1.8)	0.02	—	0.75

* All models included age (<20, 20 to 39, 40 to 60, and >60 years) as a stratification factor. Dashes denote variables that were not included in the final model. HCM denotes hypertrophic cardiomyopathy, and CI confidence interval.

† Patients who were already in NYHA class III or IV at entry were excluded from the analysis.

spect to the magnitude of the gradient probably reflects the dynamic nature of outflow tract obstruction in hypertrophic cardiomyopathy.^{15,20,21} Consequently, we cannot exclude the possibility that particularly marked degrees of obstruction may adversely affect prognosis in certain patients.

We assessed the clinical significance of the subaortic gradient under basal conditions, the variable traditionally used to formulate clinical decisions in patients with symptomatic hypertrophic cardiomyopathy.^{1-9,23-26,36} The participating institutions did not routinely provoke outflow tract gradients under physiologic conditions in ambulatory patients with hypertrophic cardiomyopathy. Nevertheless, in symptomatic patients with relatively low gradients at rest (e.g., 30 to 50 mm Hg), much more substantial gradients are likely to develop with exertion under conditions in which symptoms of hypertrophic cardiomyopathy usually occur. It is therefore reasonable to assume that the relatively low basal gradient threshold of 30 mm Hg probably increases greatly with physical exertion and thus probably leads to disabling symptoms.

Because our study was designed to assess longitudinally the relation of the basal left ventricular outflow tract gradient to outcomes, we used the value obtained during the initial continuous-wave Doppler assessment to evaluate in a standardized fashion the clinical effect of obstruction over the longest possible follow-up period. Although we are aware of the potential limitations of the use of single measurements in individual patients, we believe this

consideration is largely compensated for by the substantial size of our cohort.

The mechanisms by which chronic subaortic obstruction causes symptoms of or death from heart failure in patients with hypertrophic cardiomyopathy are largely unknown. It is likely, however, that the greatly elevated left ventricular pressures created by obstruction lead to increased wall stress, myocardial ischemia, and eventually, cell death and replacement scarring.³⁸⁻⁴⁰ This cellular remodeling, in turn, probably increases the likelihood that the left ventricle will become stiff and noncompliant, leading to diastolic dysfunction,^{1,3,36} and may also increase susceptibility to electrical instability and sudden death.³⁷ Consistent with this hypothesis is our finding that older patients (those at least 40 years of age) with obstructive hypertrophic cardiomyopathy were more likely to have disease progression than younger patients. This observation suggests (if chronologic age is assumed to approximate the duration of obstruction) that longer periods of exposure to left ventricular outflow tract obstruction and systolic pressure overload are deleterious. In addition, most patients who undergo interventions to relieve outflow tract obstruction (i.e., septal myectomy or alcohol septal ablation) have substantial relief of disabling symptoms^{1-7,36}; this finding also supports the principle that the outflow gradient in patients with hypertrophic cardiomyopathy has important pathophysiological implications.

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