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**Primary Myocardial Disease**

# Maximum Left Ventricular Thickness and Risk of Sudden Death in Patients With Hypertrophic Cardiomyopathy

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**OBJECTIVES** We sought to assess the relationship between maximum left ventricular (LV) wall thickness and outcome in patients with hypertrophic cardiomyopathy (HCM).

**BACKGROUND** An association between maximum LV wall thickness and risk of sudden death was suggested in HCM. This finding requires further investigation, given the important implications for risk stratification and treatment.

**METHODS** We analyzed the mortality and risk profile of 237 patients (age 41 ± 17 years; 63% male) classified into five groups based on echocardiographic maximum LV thickness.

**RESULTS** During follow-up (12 ± 7 years), 36 patients died of cardiovascular causes, including 16 sudden deaths. Maximum LV thickness was not associated with a risk of sudden death ($p = 0.37$) nor with overall cardiovascular mortality ($p = 0.7$). With the exception of the small subset with thickness values ≤15 mm, with a consistently benign clinical course, the distribution of sudden death and overall cardiovascular mortality was not significantly different among the other four classes, ranging from 16 to 19 mm to ≥30 mm. Among 30 patients with extreme LV thickness (≥30 mm), only one sudden event occurred among six patients diagnosed at <18 years of age (17%) and none among 24 diagnosed at ≥18 years of age. The prevalence of nonsustained ventricular tachycardia, syncope, an abnormal blood pressure response to exercise, and atrial fibrillation was similar among the five thickness classes.

**CONCLUSIONS** During 12-year follow-up, we observed no association between maximum LV thickness and cardiovascular mortality in a community-based population with HCM. The degree of maximum LV wall thickness should be considered in the context of a multifactorial approach to risk stratification, rather than as an isolated risk factor. Only in those patients diagnosed at a very young age might the presence of extreme LV wall thickness represent, per se, a potential marker of risk of sudden death. (J Am Coll Cardiol 2003;41:315–21) © 2003 by the American College of Cardiology Foundation

Sudden death and heart failure (HF) are the most common causes of death in patients with hypertrophic cardiomyopathy (HCM) (1–5). To this day, the identification of patients at high risk remains a major challenge, as the predictive value of several potential markers of risk is disappointingly low. A direct relationship between maximum left ventricular (LV) wall thickness and risk of sudden or HF-related death has recently been reported (6). In particular, extreme wall thickness (i.e., ≥30 mm) has been advocated as a major risk factor for sudden death (7) and consequently suggested as a potential indication for an implantable cardioverter-defibrillator (6). However, evidence from other studies is controversial and does not seem to support aggressive treatment based solely on the degree of LV hypertrophy (2,3,8,9). Therefore, further investigation is required in different patient populations, given the important implications for risk stratification and treatment. In the present study, we analyzed the prognosis of a large community-based patient cohort over an extended period of follow-up, with respect to maximum LV wall thickness measured at diagnosis.

## METHODS

**Selection of patients.** The study group comprised 237 consecutively enrolled and prospectively followed patients with HCM, predominantly from the region of Tuscany and Umbria in central Italy. Their age at diagnosis was 41 ± 17 years, and 71% were male (Table 1). The period of follow-up from first hospital evaluation for the overall study group was 12 ± 7 years; during this period, patients were followed regularly, usually at one-year intervals (3). Management strategies employed for the study groups over the years have been previously described (3,10,11). Of note, asymptomatic patients were not thought to require drug treatment, except in the presence of additional clinical variables regarded as risk factors for either sudden death, such as repetitive, nonsustained runs of ventricular tachycardia (treated with amiodarone), or long-term clinical

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**Abbreviations and Acronyms**
HCM = hypertrophic cardiomyopathy
HF = heart failure
LV = left ventricular

deterioration and HF, such as severe rest outflow obstruction (6) (treated with beta-adrenergic blocking agents).

**Echocardiography.** Echocardiographic studies were performed with commercially available Hewlett-Packard and Toshiba instruments. Left ventricular hypertrophy was assessed with two-dimensional echocardiography, and the site and extent of maximum wall thickness were identified (7). The peak instantaneous LV outflow gradient was estimated with continuous wave Doppler under basal conditions (12).

**Classes of hypertrophy.** The outcome and individual risk profile of the 237 study patients were assessed based on their maximum LV thickness value, as measured on the first visit at our institution, usually at the time of the first diagnosis of HCM. Patients were divided into five classes according to maximum LV wall thickness: ≤15 mm, 16 to 19 mm, 20 to 24 mm, 25 to 29 mm, and ≥30 mm. To obtain comparable data, these values were deliberately taken from a recent study performed on a large HCM patient cohort similar to ours in terms of demographic features, management strategies, and cardiovascular mortality rates (6).

**Table 1.** Clinical and Demographic Features of 237 Patients With HCM

| | |
|---|---|
| Age at initial evaluation (yrs) | 41 ± 17 |
| Age at end of follow-up (yrs) | 56 ± 23 |
| Male gender | 170 (63%) |
| NYHA class III/IV at diagnosis | 24 (10%) |
| NYHA class III/IV at end of follow-up | 56 (23%) |
| Duration of follow-up (years) | 12 ± 7 |
| Outflow pressure gradient ≥ 30 mm Hg* | 46 (19%) |
| Atrial fibrillation | 60 (25%) |
| Family history of HCM and sudden death | 35 (15%) |
| Syncope | 34 (14%) |
| NSVT | 91 (38%) |
| ABPR to exercise | 51 (26%)† |
| Receiving beta-blocking agents | 104 (43%) |
| Receiving verapamil | 94 (39%) |
| Receiving amiodarone | 75 (32%) |
| Receiving other anti-arrhythmics‡ | 37 (15%) |
| Dual-chamber pacing (for gradient/symptoms) | 1 (0.4%) |
| Implantable defibrillator | 6 (2%) |
| Myotomy-myectomy (or MVR) | 8 (3%) |
| Maximum LV wall thickness (mm) | 23 ± 5 |
| LVED (mm) | 42 ± 9 |
| Left atrium (mm) | 40 ± 10 |
| No. of HCM-related deaths, total | 36 (15%) |
| Sudden (including resuscitated cardiac arrest and appropriate ICD interventions) | 16 (7%) |
| HF-related (including stroke and heart transplant) | 20 (8%) |

*Peak instantaneous outflow gradient estimated by continuous wave Doppler. †Calculated for 192 patients who underwent exercise testing. ‡Including disopyramide, sotalol, quinidine, and propafenone. Data are presented as the mean value ± SD or number (%) of patients.

ABPR = abnormal blood pressure response; HCM = hypertrophic cardiomyopathy; HF = heart failure; ICD = implantable cardioverter-defibrillator; LV = left ventricular; LVED = left ventricular end-diastolic cavity dimension; MVR = mitral valve replacement; NSVT = nonsustained ventricular tachycardia; NYHA = New York Heart Association.

**Definitions HYPERTROPHIC CARDIOMYOPATHY.** The diagnosis of HCM was based on the two-dimensional echocardiographic identification of a hypertrophied, nondilated LV (wall thickness >15 mm in adults, and the equivalent relative to body surface area in children), in the absence of another cardiac or systemic disease capable of producing the magnitude of wall thickening evident (2).

**MODE OF DEATH.** For survival analysis, two modes of HCM-related death were defined (2): 1) sudden and unexpected death: collapse occurring in the absence or within <1 h of the onset of symptoms in patients who previously experienced a relatively stable or uneventful course (including resuscitated cardiac arrest and appropriate implantable defibrillator interventions); and 2) HF-related death due to progressive cardiac decompensation or directly related to complications of HF, such as stroke (including patients with a heart transplant).

**Statistical methods.** Data are expressed as the mean value ± SD. The Student *t* test or one-way analysis of variance, as appropriate, was employed for comparison of normally distributed data. The chi-square test was utilized to compare noncontinuous variables expressed as proportions. Univariate and multivariate analyses were performed with the Cox proportional hazard regression model. Survival curves were constructed according to the Kaplan-Meier method. Linear trend in survival distributions across the different classes of LV wall thickness was tested using the log-rank test. All analyses were performed using the SPSS 8.0 statistical package (SPSS Inc., Chicago, Illinois).

## RESULTS

**Degree and distribution of maximum LV thickness values.** General clinical and demographic data for the overall study group are reported in Table 1. The mean value of maximum LV thickness for the overall study group was 23 ± 5 mm (range 13 to 42). Figure 1 shows the distribution of the five classes of LV thickness in different age groups at diagnosis. Overall, 30 patients (13%) had a maximum LV thickness ≥30 mm: the proportion of these patients with extreme thickness values showed a decline after age 30, although this was not statistically significantly (overall $p = 0.18$) (Fig. 1). Of these 30 patients with extreme LV thickness, 17 (57%) were 50 years old at the end of follow-up, and six (20%) were or ≥60 years old. At the other end of the spectrum, 10 patients had maximum LV thickness ≤15 mm at the time of HCM diagnosis. These patients were either in the pediatric age range (<18 years; n = 6) or affected relatives of patients with an unequivocal diagnosis of HCM (n = 4) (13).

**Differential features among thickness classes.** A comparison of the principal clinical and instrumental findings among the five thickness classes showed that patients with mild hypertrophy (≤15 and 16 to 19 mm) were, on average,

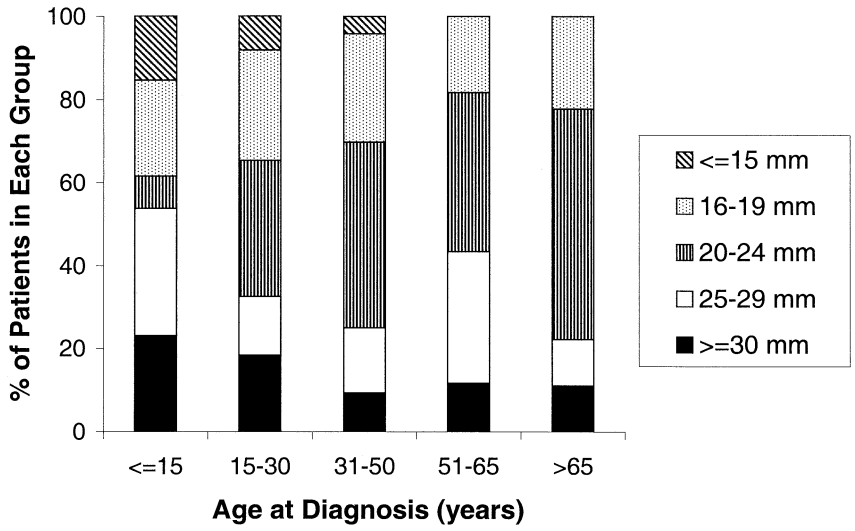


**Figure 1.** Distribution of maximum left ventricular (LV) thickness among 237 patients with hypertrophic cardiomyopathy (HCM), according to age. The **stacks in each bar** represent the percentage of patients in each age group and LV thickness class at the time of the first diagnosis of HCM.

younger at diagnosis, had a lower prevalence of atrial dilation, outflow obstruction, and severe symptoms, and less often required treatment with beta-blockers or amiodarone (Table 2). However, the remaining classes of patients with moderate or severe degrees of maximum LV wall thickness (20 to 24 mm to ≥30 mm) were comparable in terms of clinical features, associated risk factors, and pharmacologic treatment (Table 2).

**HCM-related mortality.** During follow-up, 36 patients died of cardiovascular causes: 16 due to sudden unexpected death (including resuscitated cardiac arrest) and 20 due to HF and its complications (including stroke) (Table 1). Seven additional patients died of noncardiovascular causes. On average, patients with HCM-related death were more symptomatic, had larger atria, and more often had atrial fibrillation, as compared with those who survived, but were otherwise similar with regard to the other baseline features, including maximum LV wall thickness (24 ± 4 vs. 23 ± 5 mm, p = NS). Overall cardiovascular mortality and sudden death rates were 1.3% and 0.6% per year, respectively. The mean age at the time of death was 56 ± 23 years; patients dying suddenly were significantly younger than those with HF-related or stroke death (34 ± 21 vs. 48 ± 17 years, $p < 0.05$). Of note, seven sudden deaths occurred among the 75 patients receiving amiodarone (9%).

**Impact of maximum LV wall thickness on outcome.** Cardiovascular mortality rates for the five classes of LV thickness are shown in Table 2. No deaths occurred among patients with LV thickness ≤15 mm. Among the other thickness classes, annual cardiovascular mortality ranged

**Table 2.** Clinical Features, Risk Profile, and Mortality Rates Among the Five LV Thickness Classes

| | ≤ 15 mm (n = 10) | 16–19 mm (n = 56) | 20–24 mm (n = 94) | 25–29 mm (n = 47) | ≥ 30 mm (n = 30) | Overall p Value |
|---|---|---|---|---|---|---|
| Age at diagnosis (years) | 25 ± 13 | 40 ± 16 | 44 ± 15 | 43 ± 17 | 38 ± 19 | 0.05* |
| Follow-up (years) | 9.3 ± 6.1 | 9.9 ± 6.2 | 12.1 ± 6.7 | 12.4 ± 7.2 | 12.4 ± 8.0 | 0.2 |
| Left atrium (mm) | 26 ± 15 | 39 ± 8 | 42 ± 8 | 43 ± 10 | 42 ± 9 | < 0.01* |
| LV end-diastolic dimension (mm) | 37 ± 13 | 43 ± 10 | 42 ± 7 | 43 ± 8 | 40 ± 5 | < 0.05* |
| LV outflow tract obstruction (peak gradient ≥30 mm Hg) | 0 | 3 (5%) | 18 (19%) | 11 (23%) | 14 (47%) | < 0.001*† |
| NYHA III/IV at diagnosis | 0 | 2 (4%) | 13 (14%) | 4 (8%) | 5 (17%) | < 0.01* |
| NYHA III/IV at end of follow-up | 0 | 5 (9%) | 26 (28%) | 19 (40%) | 6 (20%) | 0.005*‡ |
| Syncope | 2 (20%) | 7 (12%) | 13 (14%) | 5 (11%) | 7 (23%) | 0.6 |
| NSVT | 1 (10%) | 15 (27%) | 41 (44%) | 20 (42%) | 14 (47%) | 0.9 |
| ABPR | 3 (30%) | 11 (19%) | 21 (22%) | 8 (17%) | 8 (27%) | 0.6 |
| Atrial fibrillation | 0 | 10 (18%) | 26 (28%) | 17 (36%) | 7 (23%) | 0.2 |
| Receiving beta-blocking agents | 2 (20%) | 14 (25%) | 44 (47%) | 27 (57%) | 17 (57%) | < 0.05§ |
| Receiving amiodarone | 1 (10%) | 9 (16%) | 32 (34%) | 21 (45%) | 12 (40%) | < 0.02§ |
| Total cardiovascular deaths | 0 | 7 (13%) | 15 (16%) | 10 (21%) | 4 (13%) | 0.7 |
| Sudden deaths | 0 | 6 (11%) | 5 (5%) | 4 (8%) | 1 (3%) | 0.3 |
| HF/stroke-related | 0 | 1 (2%) | 10 (11%) | 6 (13%) | 3 (10%) | 0.7 |

*$p < 0.05$ for ≤ 15 mm versus other classes at post hoc analysis. †$p < 0.05$ for ≥ 30 mm versus other classes. ‡$p < 0.05$ for 25–29 mm versus other classes. §$p < 0.05$ for ≤ 15 and 16–19 mm versus other classes. Data are presented as the mean value ± SD or number (%) of patients.

Abbreviations as in Table 1.

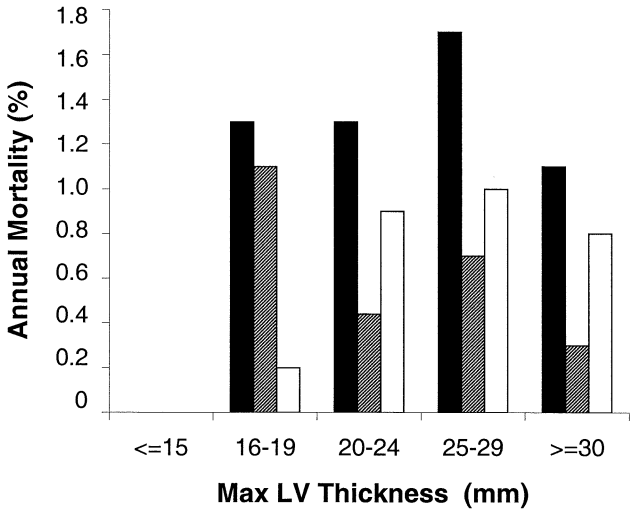


**Figure 2.** Annual rates of cardiovascular mortality according to maximum left ventricular (LV) thickness at diagnosis. **Solid bars** = total cardiovascular mortality; **shaded bars** = sudden death; **open bars** = congestive heart failure/stroke-related death.

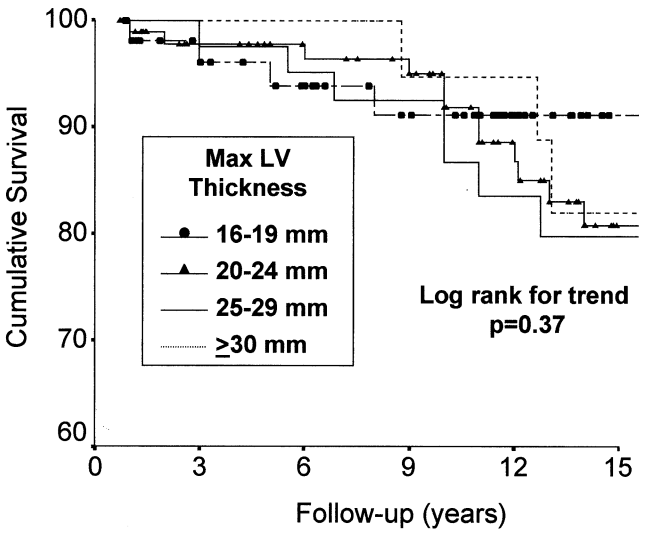


**Figure 3.** Kaplan-Meier curves showing cumulative survival according to maximum left ventricular (LV) thickness. Survival free of cardiovascular mortality is shown for four different thickness classes. Because no event occurred in patients with maximum LV thickness ≤15 mm, this particular subgroup was excluded from the analysis, for added clarity. A comparison of survival curves showed that there was no trend toward increasing mortality for increasing values of maximum LV wall thickness.

from 1.1% to 1.7%, with no significant excess in any class (Fig. 2, Table 2) . The rate of sudden and unexpected death ranged from 0.3% to 1.1% per year; the lowest value was recorded in the group of 30 patients with maximum LV thickness ≥30 mm (Table 2). In this group with extreme LV hypertrophy, only one sudden event occurred during 12-year follow-up (i.e., resuscitated cardiac arrest with documented ventricular fibrillation in 1 of the 6 patients diagnosed in the pediatric age range [<18 years]). Conversely, no sudden deaths or cardiac arrests (including appropriate implantable cardioverter-defibrillator discharges) occurred among the 24 patients with extreme LV hypertrophy diagnosed at age ≥18 years.

Univariate survival analysis showed no association between maximum LV wall thickness and overall cardiovascular mortality ($p = 0.37$) (Fig. 3) or sudden death ($p = 0.27$).

**Functional limitation, acute events, and arrhythmias.** The individual risk profile was analyzed in study patients by assessing the most important potentially adverse prognostic markers, including a family history of sudden death, syncope, multiple and repetitive nonsustained ventricular tachycardia on Holter electrocardiography, and atrial fibrillation. In the present study cohort, all of these factors were relatively uniformly distributed among the five thickness classes, and there was no trend suggesting a progressively more severe risk profile with greater maximum LV wall thicknesses (Table 2). In particular, none of these indicators of risk had a significantly higher prevalence among patients with extreme LV hypertrophy, as compared with other classes (Table 2).

## DISCUSSION

**Controversies over the prognostic role of maximum LV thickness.** The debate as to whether the magnitude of LV hypertrophy has an influence on prognosis in HCM patients spans almost 20 years and has produced conflicting results (2,3,5–9,14). Recently, two large studies have reported a direct relationship between maximum LV wall thickness and risk of HCM-related mortality, particularly due to an increase in sudden and unexpected death (6,8). In both studies, risk appeared to be particularly high in the small subsets of patients with maximum LV thickness ≥30 mm. However, even extreme degrees of maximum LV wall thickness showed a disappointingly low positive predictive accuracy (6,8). Thus, the prognostic implications of the magnitude of LV hypertrophy remain controversial. This issue is of relevance because extreme LV hypertrophy has been suggested as a potential indication, per se, for aggressive prophylactic treatment in HCM patients (6). For this reason, we chose to assess cardiovascular mortality and individual risk profile with respect to maximum LV hypertrophy in a large, consecutively enrolled and prospectively followed community-based patient population with HCM.

**Left ventricular wall thickness and HCM-related mortality.** In the present study, the severity of hypertrophy expressed as maximum LV wall thickness did not represent a significant prognostic indicator in HCM patients, as no trend was observed suggesting an increasing long-term risk of overall mortality, sudden death, or HF-related death for increasing degrees of maximum LV wall thickness. Indeed, with the exception of the small subset with thickness values ≤15 mm, with a consistently benign clinical course, the distribution of sudden death and overall cardiovascular mortality was not significantly different in the other four thickness classes ranging from 16 to 19 to ≥30 mm. A benign prognosis among patients with maximum LV thickness ≤15 mm is a constant finding (6,8). However, we agree with Elliott et al. (5,8) that even mild degrees of hypertro-

phy cannot be used to reassure patients, but must be seen in the context of a multifactorial approach to risk stratification.

Among patients with extreme LV hypertrophy (≥30 mm), total cardiovascular mortality and sudden death rates were lower or equal to those in the three classes ranging from 16 to 29 mm. The only sudden event in this group was cardiac arrest associated with ventricular fibrillation in a patient diagnosed at <18 years of age, whereas no sudden deaths nor resuscitated cardiac arrests occurred among adult patients. Our findings, however, are not in disagreement with the report by Spirito et al. (6), in which the increase in risk among patients with extreme LV hypertrophy was also confined to those individuals diagnosed at <18 years of age, whereas mortality rates among patients diagnosed during adulthood was relatively low (7%) and comparable to those of patients with only mild hypertrophy. Indeed, a combined analysis of the three existing studies consistently shows that, among patients with extreme LV thickness, an increased risk of sudden death is confined to those diagnosed at a very young age (Table 3). Conversely, in adult patients, even extreme maximum LV thickness does not seem to represent a meaningful predictor of risk and should not lead to aggressive management in the absence of other documented risk factors (5). This conclusion is supported by two additional observations originating from this study. First of all, we did observe a declining prevalence of patients with extreme hypertrophy who were >30 years old, as also reported by the other two studies (6,8), which may suggest reduced survival in this particular group. However, this trend was not statistically significant and should be interpreted with caution, as other explanations such as the occurrence of LV remodeling with a progressive decrease in LV thickness should also be considered (15). In our patient population, maximum LV wall thickness ≥30 mm was not incompatible with a normal life-expectancy, nor was it associated with an increase in disease-related complications over an average period of follow-up of 12 years. Moreover, the overall risk profile of patients with massive hypertrophy, assessed by the main established risk factors for HCM, did not show significant differences among thickness classes. Indeed, none of the most relevant markers of electrical or hemodynamic instability, including syncope, nonsustained ventricular tachycardia, abnormal blood pressure response to exercise, and atrial fibrillation (1,8,10,16), were significantly associated with the degree of maximum LV thickness. Therefore, although greater degrees of LV hypertrophy may theoretically predispose to a higher likelihood of arrhythmogenic foci due to disarray, subendocardial ischemia, and fibrosis (8), no direct relationship was found between maximum LV thickness and clinical evidence of arrhythmic risk.

**Comparison with previous studies.** In the present study, the sudden death rate observed among patients with extreme LV thickness (≥30 mm) was six to seven times lower than those reported by two other recent and extensive studies based on large HCM populations (6,8) (Table 3),

**Table 3.** Comparison of Outcomes Among HCM Patients With Extreme Hypertrophy (Maximum LV Thickness ≥ 30 mm) in Three Different Patient Populations

| Study (Ref.) | (% of Overall Study Group) | Mean Age at Dx (yrs) | < 18 Years Old at Dx | Mean Follow-Up (yrs) | Total Patient-Years | Sudden Deaths* | Annual Rate of Sudden Death | Prevalence of Sudden Death in Patients < 18 Years Old at Dx | Prevalence of Sudden Death in Patients ≥ 18 Years Old at Dx |
|---|---|---|---|---|---|---|---|---|---|
| Present study | 30/273 (13%) | 38 ± 19 | 6 (20%) | 12.4 | 372 | 1 (3%) | 0.3% | 1/6 (17%) | 0/24 |
| Spirito et al. (6) | 43/480 (9%) | 31† | 12 (28%) | n.p. | 279‡ | 7 (16%) | 1.8%‡ | 5/12 (42%) | 2/31 (6%) |
| Elliott et al. (8) | 78/630 (12%) | 32 ± 15 | 16 (20%) | 6.1 | 476 | 10 (13%) | 2.1% | 4/16¶ (25%) | 6/62¶ (10%) |
| Overall | 151/1,383 (11%) | 33 | 34 | — | 1127 | 18 (12%) | 1.6% | 10/34 (29%) | 8/117 (7%) |

*Including resuscitated cardiac arrests ad appropriate implantable cardioverter defibrillator discharges. †Standard deviation not provided in the paper. ‡Calculated over the mean follow-up period of the overall study group (6.5 years). ¶Data provided by P.M. Elliott in personal communication.

Dx = diagnosis; HCM = hypertrophic cardiomyopathy; LV = left ventricular; n.p. = not provided in the study.

despite similar clinical features in the three cohorts (including a similar proportion of patients with maximum LV thickness ≥30 mm) and comparable cardiovascular mortality ranging from 1.2% to 2% per year. Furthermore, although our study group was smaller, the average follow-up duration was almost double that of the other two studies, thus covering a comparable number of patient-years in the subgroup with extreme LV thickness (Table 3).

Potentially accounting for a more benign prognosis in our subset with LV thickness ≥30 mm, is the smaller proportion of patients diagnosed in the pediatric age range, as compared with the other two studies (Table 3). In this respect, our results are not incompatible with the two previous studies, but rather support the lack of predictive accuracy of extreme LV thickness among adult patients, as compared with children and adolescents. Moreover, the widespread use of amiodarone in our HCM population (32%) may partly account for the discrepancy observed with the study by Spirito et al. (6) (6% of patients on amiodarone treatment), although not with that by Elliott et al. (8) (28%). In the present study, the extensive use of antiarrhythmic drugs, particularly amiodarone, may have played a role in determining the favorable clinical outcome and preventing sudden cardiac death, by both suppressing ventricular tachyarrhythmias and preventing atrial fibrillation (11,16). Nevertheless, such an effect is not quantifiable. Of note, 9% of the study patients receiving amiodarone died suddenly during follow-up. In the two previously quoted studies, this value was 17% (6) and 3% (8). Although these discrepancies are not easy to interpret and may reflect differences in the selection of patients for treatment, all studies indicate that amiodarone does not convey absolute protection from sudden death.

To date, primary prevention of sudden death remains extremely challenging in HCM patients. The most appropriate approach based on current knowledge is necessarily multifactorial, because each of the presently known predictors of risk, including maximum LV wall thickness ≥30 mm (in younger patients), a family history of sudden death, an abnormal blood pressure response to exercise, nonsustained ventricular tachycardia, and unexplained syncope, has very low positive predictive accuracy on an individual basis (5). Moreover, important potential risk factors, such as LV outflow obstruction and demonstrable myocardial ischemia, still require adequate prognostic assessment in HCM.

**Qualitative evaluation of hypertrophy in HCM.** A limitation of the present study, which is shared by the other studies on the subject (6,8), is that a single measurement of maximum LV thickness, although reproducible and practical for clinical purposes, does not accurately reflect the total burden of hypertrophy in individual patients and thus represents only a crude estimate of the morphologic severity of HCM. Unfortunately, due to the highly asymmetric morphology of the LV in HCM patients, formulas devised to more accurately assess the total extent of ventricular mass cannot be satisfactorily applied in this disease (17). Moreover, a quantitative approach to hypertrophy is necessarily limited in that it overlooks individual differences in the LV wall structure. Indeed, several pathophysiologic substrates coexisting in the hypertrophic myocardium, including disarray, fibrosis, and ischemia, are possibly more relevant than the extent of hypertrophy itself in determining HCM-related risk and ideally require a comprehensive assessment in each patient (18–20). For example, a severe reduction and transmural maldistribution of myocardial blood flow, which have been clearly demonstrated in HCM patients with massive LV hypertrophy (20), are strongly predictive of an adverse long-term outcome, irrespective of individual maximum LV thickness values (21).

**Conclusions.** In the course of a 12-year average follow-up period, there was no significant association between the severity of LV hypertrophy and the risk of sudden death or overall cardiac mortality in our community-based population with HCM. Thus, our results support the view that the degree of maximum LV wall thickness should be considered in the context of a multifactorial approach to risk stratification in HCM patients, rather than as an isolated risk factor. However, a likely exception is represented by patients diagnosed at a very young age, in whom the presence of massive LV hypertrophy might be considered, per se, as a potential marker of increased risk for sudden death.

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