Implantable Cardioverter-Defibrillators and Prevention of Sudden Cardiac Death in Hypertrophic Cardiomyopathy

Barry J. Maron, MD
Paolo Spirito, MD
Win-Kuang Shen, MD
Tammy S. Haas, RN
Francesco Formisano, MD
Mark S. Link, MD
Andrew E. Epstein, MD
Adrian K. Almquist, MD
James P. Daubert, MD
Thorsten Lawrenz, MD
Giuseppe Boriani, MD, PhD
N. A. Mark Estes III, MD
Stefano Favale, MD
Marco Piccininno, MD
Stephen L. Winters, MD
Massimo Santini, MD
Sandro Betocchi, MD
Fernando Arribas, MD
Mark V. Sherrid, MD
Gianfranco Buja, MD
Christopher Semsarian, MB, BS, PhD
Paolo Bruzzi, MD, PhD

Context Recently, the implantable cardioverter-defibrillator (ICD) has been promoted for prevention of sudden death in hypertrophic cardiomyopathy (HCM). However, the effectiveness and appropriate selection of patients for this therapy is incompletely resolved.

Objective To study the relationship between clinical risk profile and incidence and efficacy of ICD intervention in HCM.

Design, Setting, and Patients Multicenter registry study of ICDs implanted between 1986 and 2003 in 506 unrelated patients with HCM. Patients were judged to be at high risk for sudden death; had received ICDs; underwent evaluation at 42 referral and nonreferral institutions in the United States, Europe, and Australia; and had a mean follow-up of 3.7 (SD, 2.8) years. Measured risk factors for sudden death included family history of sudden death, massive left ventricular hypertrophy, nonsustained ventricular tachycardia on Holter monitoring, and unexplained prior syncope.

Main Outcome Measure Appropriate ICD intervention terminating ventricular tachycardia or fibrillation.

Results The 506 patients were predominately young (mean age, 42 [SD, 17] years) at implantation, and most (439 [87%]) had no or only mildly limiting symptoms. ICD interventions appropriately terminated ventricular tachycardia/fibrillation in 103 patients (20%). Intervention rates were 10.6% per year for secondary prevention after cardiac arrest (5-year cumulative probability, 39% [SD, 5%]), and 3.6% per year for primary prevention (5-year probability, 17% [SD, 2%]). Time to first appropriate discharge was up to 10 years, with a 27% (SD, 7%) probability 5 years or more after implantation. For primary prevention, 18 of the 51 patients with appropriate ICD interventions (35%) had undergone implantation for only a single risk factor; likelihood of appropriate discharge was similar in patients with 1, 2, or 3 or more risk markers (3.83, 2.65, and 4.82 per 100 person-years, respectively; $P=.77$). The single sudden death due to an arrhythmia (in the absence of advanced heart failure) resulted from ICD malfunction. ICD complications included inappropriate shocks in 136 patients (27%).

Conclusions In a high-risk HCM cohort, ICD interventions for life-threatening ventricular tachyarrhythmias were frequent and highly effective in restoring normal rhythm. An important proportion of ICD discharges occurred in primary prevention patients who had undergone implantation for a single risk factor. Therefore, a single marker of high risk for sudden death may be sufficient to justify consideration for prophylactic defibrillator implantation in selected patients with HCM.

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THE RISK OF SUDDEN DEATH IN PAtients with hypertrophic cardiomyopathy (HCM) has been known for almost 50 years.[1-6] Indeed, this disease is the most common cause of sudden cardiac death in young people,[1-6] including trained athletes.[7] However, only in the last few years has the implantable cardioverter-defibrillator (ICD) been systematically used as a potentially life-saving

For editorial comment see p 452.

Author Affiliations are listed at the end of this article.
Corresponding Author: Barry J. Maron, MD, Minneapolis Heart Institute Foundation, 920 E 28th St, Ste 620, Minneapolis, MN 55407 (hcm.maron@mhif.org).

treatment in high-risk patients with HCM.[8-10] Since HCM represents a less common indication for ICDs than coronary artery disease[11-14] it is important to document its effectiveness in a large HCM population. In addition, although there is little residual controversy regarding the appropriateness of ICDs for secondary prevention, considerable uncertainty persists concerning patient selection for prophylactic ICD therapy in HCM. Therefore, to provide insights into these important clinical issues, we report here the findings in a large, international, multicenter cohort of patients with HCM who have received an ICD.

METHODS

Patient Selection

The study group comprised 506 unrelated patients with HCM who had received implanted cardioverter-defibrillators at 42 referral and nonreferral institutions in the United States, Europe, and Australia. At each participating center, all patients with HCM and an ICD implanted for high-risk status between 1986 and 2003 were included in the study group and data analysis and underwent follow-up until April 2005. Decisions regarding risk status and ICD implantation were made according to customary practice by the managing cardiovascular specialists (usually involving electrophysiologists) and using established risk stratification markers for primary or secondary prevention of sudden death.[2,4-6,8]

Each patient had an unequivocal diagnosis of HCM based on 2-dimensional echocardiographic evidence of a hypertrophied and nondilated left ventricle in the absence of another cardiac or systemic disease that could account for the magnitude of hypertrophy.[2,4] Of the 506 study patients, 150 were included in earlier investigations[8,9] and are reported here with extended follow-up. Institutional review board approval or the equivalent was obtained from all participating institutions. All participants provided written and oral informed consent.

Defibrillators

Single- or dual-chamber ICDs were implanted with transvenous (n=482) or epicardial (n=24) lead systems, with the capacity for antitachycardia and antibradycardia pacing.[15,16] Eventually, over the follow-up period, all patients had received device models with diagnostic memory and capacity for recording and storage of electrocardiographic data. Device implantations were performed according to customary practice, with defibrillation thresholds routinely tested to document successful termination of ventricular tachyarrhythmias.[15] Rate cutoff criteria for detection of ventricular tachyarrhythmias were programmed, and antitachycardia pacing was activated, at the discretion of the electrophysiologist.

Interpretation of Events

Stored intracardiac electrograms were analyzed to classify arrhythmias responsible for precipitating defibrillator discharges, according to accepted definitions.[8,17] Defibrillator discharges (shocks or pacing) were considered appropriate when triggered by ventricular fibrillation or rapid ventricular tachycardia (rate >200 per minute) documented by stored electrographic or cycle length data. For events with older defibrillator models, discharges were judged appropriate based on clinical findings consistent with ventricular arrhythmia.[8] Interventions were considered inappropriate when triggered by heart rate exceeding the programmed threshold, as a consequence of either supraventricular arrhythmias, sinus tachycardia, or device malfunction documented by ICD interrogation.

Risk Factor Analysis

Appropriate ICD interventions were analyzed with respect to previously identified HCM risk factors.[2,4-6,17,18] These clinical markers included previous cardiac arrest (with documented ventricular fibrillation) or sustained ventricular tachycardia, for secondary prevention. The 4 primary prevention risk factors were (1) history of premature HCM-related sudden death in 1 or more first-degree or other relatives younger than 50 years; (2) massive left ventricular hypertrophy (maximum wall thickness ≥30 mm), as judged by the managing cardiovascular specialist; (3) 1 or more runs of nonsustained ventricular tachycardia at heart rates of 120 per minute or greater on 24-hour ambulatory Holter electrocardiographic monitoring; and (4) prior unexplained syncope judged inconsistent with a neurocardiogenic origin. Hypotensive blood pressure response to exercise[2,4] was excluded from this analysis because exercise testing for risk stratification was customary practice in only a minority of patients. In 74 of 383 primary prevention patients, an ambulatory Holter electrocardiographic recording was not deemed necessary by the investigators before implantation; therefore, 309 patients had all 4 risk factors tested.

Statistical Analyses

Probability of appropriate intervention within 5 years from defibrillator implantation was estimated as cumulative incidence of ICD discharges, computed by Kaplan-Meier method and compared in patient subgroups by log-rank test.[19] Follow-up duration was computed from the date of device implantation to the time of first appropriate ICD discharge. In patients without an ICD intervention, follow-up was to date of death, most recent follow-up evaluation, or April 2005, whichever came first. ICD discharges known to occur after March 31, 2005, are reported only in the text.

Rates of first appropriate intervention were computed as the ratio between the number of events observed and sum of person-years accumulated during follow-up; 95% confidence intervals (CIs) were calculated assuming a Poisson distribution of rare events. Rates were compared among patient subgroups by χ^2 tests for heterogeneity and trend or by Fisher test, as appropriate. Incidence rates were computed as ratios between first appropriate intervention rates and 95% CIs, using

the Taylor series approximation method. To investigate the role of primary prevention risk factors and the differential effects of each marker on likelihood of ICD discharge, multivariate Cox models were fitted to the data, adjusting for other risk factors. Synergism between any 2 of the 4 risk factors was assessed by introducing into the model information on each risk factor, individually. Likelihood ratio tests evaluated statistical significance of each risk marker and interaction term. Statistical significance was computed based on binomial distribution. For continuous variables, means (SDs) are reported; *P* values are 2-sided and considered statistically significant at the <.05 level. All analyses were performed using SPSS version 14.0 (SPSS Inc, Chicago, Illinois).

Table 1. Clinical, Demographic, and Echocardiographic Data in 506 Patients With Hypertrophic Cardiomyopathy and Implantable Defibrillators[a]

Characteristics	All Patients	Primary Prevention		Secondary Prevention	
		Overall	≥1 Appropriate Intervention	Overall	≥1 Appropriate Intervention
No. of patients	506	383	51	123	52
Age, mean (SD), y	42 (17)	41 (16)	38 (17)	45 (19)	47 (22)
Male sex, No. (%)	323 (64)	241 (63)	34 (67)	82 (67)	34 (65)
Follow-up duration, mean (SD), y	3.7 (2.8)	3.6 (2.6)	2.3 (2.4)	4.0 (3.3)	2.3 (2.6)
NYHA class, No. (%)					
I	277 (55)	200 (52)	32 (63)	77 (63)	36 (69)
II	162 (32)	127 (33)	13 (25)	35 (28)	11 (21)
III or IV	67 (13)	56 (15)	6 (12)	11 (9)	5 (10)
Maximal left ventricular wall thickness, mean (SD), mm	22.8 (7)	23.3 (7)	23.0 (6)	21.0 (7)	19.8 (5)
Left ventricular end-diastolic cavity dimension, mean (SD), mm	45.0 (8)	44.6 (8)	44.2 (9)	46.3 (8)	47.3 (8)
Left atrial dimension, mean (SD), mm	44.4 (8)	44.4 (8)	44.7 (9)	44.3 (8)	44.1 (9)
Left ventricular outflow gradient (rest), %					
≥30 mm Hg	25	28	22	18	13
<30 mm Hg	75	72	78	82	87

Abbreviation: NYHA, New York Heart Association.
[a]Data documented at time of implantation.

RESULTS

Baseline Clinical Characteristics

The 506 patients were aged 42 (SD, 17) years at device implantation for secondary (n=123) or primary (n=383) prevention; 140 (28%) were aged 30 years or younger and 323 (64%) were male (TABLE 1). Follow-up period was 3.7 (SD, 2.8; range, to 16) years.

Appropriate ICD Interventions

Overall Study Group. Of the 506 study patients, 103 (20%) experienced 1 or more appropriate device interventions, in which the ICD terminated ventricular fibrillation (n=49) or ventricular tachycardia (n=54), immediately restoring sinus rhythm. Initial ICD activations were defibrillation shocks in 94 and overdrive pacing in 9.

Appropriate intervention rate for the study group was 5.5% per year (95% CI, 4.5%-6.6%); cumulative probability of discharge at 5 years was 23% (SD, 2%). Most patients with appropriate interventions (92/103 [90%]) had no or only mild symptoms of heart failure (Table 1). After the close of follow-up, initial appropriate ICD shocks were reported in 6 additional patients, each of whom had received ICDs prophylactically.

Secondary Prevention. Of the 506 study patients, 123 (24%) received ICDs after a resuscitated cardiac arrest or sustained ventricular tachycardia; mean age was 45 (SD, 19) years. Of these 123 patients, 52 (42%) experienced appropriate ICD discharges. Intervention rate was 10.6% per year (95% CI, 7.9%-13.9%); cumulative probability of discharge at 5 years was 39% (SD, 5%) (FIGURE 1).

Primary Prevention. Of the 506 study patients, 383 (76%) judged to be at high risk (without prior cardiac arrest) received prophylactic ICDs[2,4,17]; mean age was 41 (SD, 16) years. Of these 383 patients, 51 (13%) experienced an appropriate ICD discharge. Intervention rate was 3.6% per year (95% CI, 2.7%-4.8%); cumulative probability of discharge at 5 years was 17% (SD, 2%) (Figure 1). Rate of first appropriate ICD shock for secondary prevention exceeded by 3-fold that for primary prevention (rate ratio, 2.9; 95% CI, 1.9-4.4; log-rank $P<.001$) (Figure 1).

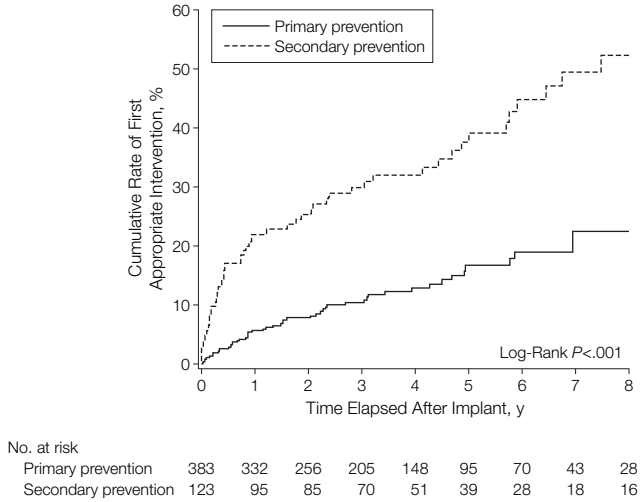
Demographics of Appropriate Interventions

Multiple Discharges. Of 103 patients with appropriate interventions, 38 had a single appropriate intervention, and 44 had 2 to 5 discharges. The remaining 21 patients had more than 5 interventions. Of the 65 patients with multiple discharges, 41 (63%) underwent ICD implantation for secondary prevention and 24 (37%) for primary prevention.

Timing. Time lapsed between device implantation and initial appropriate discharge varied considerably, and in 16 patients was 5 to 10 years. Cumulative probability of first appropriate intervention beyond 5 years was 27% (SD, 7%).

Age and Sex. At first appropriate ICD activation, mean age was 44 (SD, 19; range, 5-83) years, including 31 patients (30%) 30 years or younger. Of note, 23 of 83 patients (28%) who had received an implant at 20 years or younger had appropriate ICD intervention at age 18 (SD, 4) years (7.3% per year), including 13 of 37 children (35%) who had received an implant at 15 years or younger. In primary prevention patients, no overall association was present between age at implantation and subsequent risk of appropriate discharge ($P=.64$).

Figure 1. Cumulative Rates for First Appropriate Implantable Defibrillator Intervention in Patients Who Had Received Devices for Primary (n=383) or Secondary Prevention (n=123)



Appropriate interventions occurred in 68 of 323 men (21%) and 35 of 183 women (19%) ($P=.60$). Annual intervention rates were 5.4% (95% CI, 4.2%-6.8%) for men and 5.5% (95% CI, 3.7%-7.5%) for women.

Drugs. Appropriate ICD interventions were most common among patients taking amiodarone (22/82 [27%]), but also occurred with verapamil (19/131 [15%]), β-blockers (46/277 [17%]), or disopyramide (5/25 [20%]).

Alcohol Septal Ablation and Myectomy. Appropriate discharge rates were 4-fold more common in patients with prior alcohol septal ablation[20-22] (4/17 [24%], or 10.3% per year [95% CI, 2.0%-28.4%]), compared with patients who had previously undergone surgical septal myectomy[22] (6/50 [12%], or 2.6% per year [95% CI, 1.2%-7.2%]) ($P=.04$).

Risk Factor Analysis

Number of Risk Factors. Among all primary prevention patients, appropriate ICD discharges occurred in 24 of 173 patients (14%) with 1 risk factor, in 16 of 143 (11%) with 2 risk factors, and in 10 of 59 (17%) with 3 or more risk factors (TABLE 2). Intervention rates per 100 person-years were similar in patients with 1, 2, or 3 or more risk factors (3.83, 2.65, and 4.82, respectively; $P=.77$). Cumulative probability of ICD discharge was unrelated to the number of risk factors in all primary prevention patients ($P=.85$) (FIGURE 2) and also in the 309 patients with all 4 risk factors tested ($P=.22$).

Of the 51 primary prevention patients with an appropriate ICD intervention, 18 (35%) were known to have only 1 of the 4 risk factors. For patients with only 1 risk factor, rates of appropriate intervention per 100 person-years were: syncope (5.22); nonsustained ventricular tachycardia (3.99); family history of sudden death (2.70); and massive left ventricular hypertrophy (2.05) (TABLE 3).

Specific Risk Factors. The association between each of the individual risk factors and likelihood of an appropriate ICD discharge (Table 3) was tested in a series of multivariate Cox models adjusting for the other risk factors in all primary prevention patients, in those with all 4 risk factors tested, and in those with only 1 risk factor. No specific individual risk marker was associated with an increased risk of ICD intervention as compared with the others ($P=.35$). Similarly, no significant interaction between any 2 risk factors was observed ($P>.10$).

Survival and Causes of Death

Of the 506 study patients, 467 (92%) survived to the end of follow-up (including 10 with heart transplants), while 39 others died. Nineteen of these 39 patients died of non–HCM-related causes (eg, cancer, renal disease, coronary artery disease, or accidents). Twenty others died of causes related to HCM, including end-stage systolic dysfunction and advanced heart failure (n=12) or embolic stroke (n=7). The remaining patient was an asymptomatic 21-year-old man with nonobstructive HCM who died suddenly and unexpectedly due to ICD malfunction at the time of appropriate defibrillation shock.[23]

Complications

Of the 506 study patients, 136 (27%) experienced 1 or more inappropriate shocks due to sinus tachycardia, atrial fibrillation, or lead malfunction. Inappropriate shocks occurred in 102 patients without and in 34 with appropriate ICD interventions ($P=.15$). Major complications included infection in 19 (3.8%), hemorrhage/thrombosis in 8 (1.6%), and lead fractures, dislodgement, and oversensing in 34 (6.7%). Inappropriate shocks occurred with similar frequency in primary prevention patients (97/383 [25%]) and secondary prevention patients (39/123 [32%]) ($P=.38$) and also were no more common in patients 30 years or younger (35/110 [32%]) than in those older than 30 years (63/273 [23%]) ($P=.22$).

COMMENT

The results of this international, multicenter study show the effectiveness and reliability of the ICD in prevention of sudden cardiac death in high-risk patients with HCM. Over an average follow-up of approximately 3½ years, appropriate device discharges for life-threatening ventricular tachyarrhythmias occurred in 20% of our large study group of more than 500 high-risk patients, including a sizeable number of children, and predominantly in patients with no or only mildly limiting symptoms. About 50%

of ICD interventions occurred for ventricular fibrillation, while the other appropriate discharges were triggered by rapid, prolonged ventricular tachycardia. Our 4% per year appropriate discharge rate for primary prevention is consistent with previously reported sudden-death rates in similar high-risk HCM populations from tertiary referral centers[2,4,5] and is 4-fold the rate reported in unselected community-based HCM cohorts.[2,24,25]

Cumulative probability of an appropriate ICD intervention 5 years after implantation was almost 25%, consistent with a substantial ongoing risk for sudden death in the absence of an ICD. These intervention rates, similar to those reported in a much smaller patient cohort 8 years previously,[8] underscore the preventive power of ICDs in HCM. It should be noted, however, that our data were assembled in a selected HCM cohort judged to be at high risk in clinical practice. As a consequence, the reported event rates are not necessarily representative of what could be expected in a truly general HCM population (ie, one with a more benign clinical profile).[2-5,24,25]

Prevention of sudden death with ICDs is likely to prolong life substantially in patients with HCM at high risk.[2] We had anticipated that, after our initial report in 2000,[8] greater numbers of ICDs would be implanted in patients with HCM, and enthusiasm created by those data could trigger an excessive number of device implants, including those in patients unlikely to experience ICD therapy. However, this concern now seems largely unfounded, given that in the present cohort only 4 defibrillators were implanted for each 1 that had interrupted life-threatening tachyarrhythmias over a relatively brief mean follow-up period of 3.7 years. ICD therapy in HCM also has been shown to be cost-effective (and even cost-saving) due to additional years of productive life afforded young high-risk patients, made possible by device intervention.[26] Finally, more than 25% of our patients taking amiodarone experienced appropriate ICD interventions, reemphasizing the relative ineffectiveness of pharmacological therapy alone in preventing sudden death in patients with HCM.[6,8]

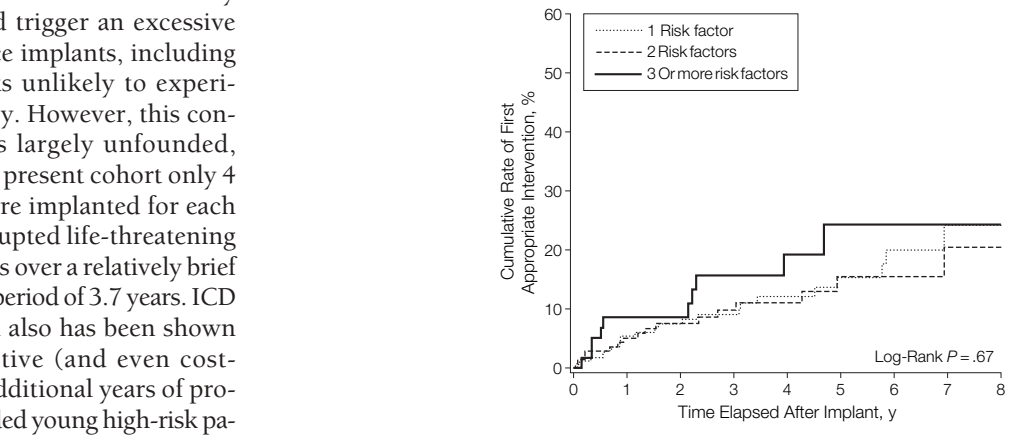
There is little residual controversy concerning defibrillators for secondary prevention of sudden death in patients who have fortuitously survived cardiac arrest due to ventricular fibrillation.[2,4,17,27-30] On the other hand, considerable uncertainty persists regarding the precise selection of patients with HCM for primary prevention ICD strategies. Certainly, recognition of multiple noninvasive risk factors creates an environment in which ICD decision making becomes easier and more comfortable. Of note, however, one-third of

Table 2. Relation Between Number of Primary Prevention Risk Factors and Appropriate Implantable Defibrillator Interventions

	No. of Risk Factors			
	1	2	≥3	0
All Patients (n = 383)				
Patients with risk factor, No. (%)	173 (45)	143 (37)	59 (15)	8 (2)
Appropriate interventions, No. (%)	24 (14)	16 (11)	10 (17)	1 (13)
Person-years	649.68	499.14	219.27	27.15
Appropriate interventions per 100 person-years (95% CI)	3.69 (2.37-5.50)	3.21 (1.84-5.21)	4.56 (2.18-8.38)	3.68 (0.07-20.51)
Patients With All 4 Risk Factors Assessed (n = 309)				
Patients with risk factor, No. (%)	126 (41)	122 (39)	58 (19)	3 (1)
Appropriate interventions, No. (%)	18 (14)	11 (9)	10 (17)	1 (33)
Person-years	469.86	414.37	207.39	5.82
Appropriate interventions per 100 person-years (95% CI)	3.83 (2.27-6.05)	2.65 (1.32-4.75)	4.82 (2.31-8.86)	17.17 (0.34-95.65)

Abbreviation: CI, confidence interval.

Figure 2. Cumulative Rates for First Appropriate Implantable Defibrillator Intervention in Patients With 1, 2, or 3 or More Risk Factors Who Had Received Devices for Primary Prevention



No. at risk									
1 Risk factor	173	150	119	98	70	48	31	18	16
2 Risk factors	143	123	95	71	53	34	28	16	6
3 Or more risk factors	59	52	38	32	23	11	9	8	6

our primary prevention patients who received device interventions for potentially lethal ventricular tachyarrhythmias had only 1 risk factor. In addition, we were not able to detect any significant difference in the probability of appropriate ICD discharges between patients with 1, 2, or 3 or more noninvasive risk markers.

Consequently, the present findings appear to contradict the view that 2 or more risk factors are mandatory to trigger recommendations for primary prevention ICDs.[30] Nevertheless, we wish to emphasize that it is not our intention to promote a strategy for universal ICD implantation in all patients with HCM who have only 1 risk factor. Inevitably in a heterogeneous genetic disease such as HCM, there are numerous complex clinical scenarios for which ambiguities and gray areas arise with respect to the presence, strength, or number of risk factors and ultimately to those decisions regarding prophylactic ICDs. One specific example would be elderly patients with unexplained syncope as a single risk factor. Such patients may not be candidates for primary prevention, given that HCM-related sudden death is uncommon in this age group,[31] survival to advanced age itself declares lower risk status in this disease, and syncope is not uncommon in elderly individuals.[2,4] In addition, each HCM risk factor comprises a large spectrum of clinical presentations that, for example, may vary from a family history of several sudden deaths in first-degree relatives to a single death in a distant family member, or from an isolated brief run of nonsustained ventricular tachycardia on ambulatory Holter electrocardiography to multiple and prolonged runs. Our multicenter ICD registry did not permit quantitative assignment of the severity for each risk factor in individual patients, nor could we demonstrate that any particular risk marker conveyed greater likelihood of an ICD intervention.

Therefore, at present, assessment of the magnitude of sudden death risk potentially associated with a single marker often may rely in part on the experience and clinical judgment of the individual physician evaluating the patient's overall risk profile. Indeed, of note in the present multicenter study, the prognostic weighting of risk factors clinically by managing physicians proved to be sufficiently accurate to closely approximate (in terms of ICD interventions) the sudden death rates previously reported in high-risk HCM populations.[2,4] Also, patient autonomy considerations[23] and the strong desires of the fully informed patient with HCM can contribute measurably to the resolution of uncertainties that may arise due to insufficient evidence-based data.

The observational design of this registry-based study was unavoidable, since it is virtually impossible to contemplate a prospective randomized ICD trial in HCM given the infrequency of the disease in cardiologic practice, its heterogeneous clinical expression, and the low postimplantation event rate dispersed over many decades, as well as ethical considerations. However, despite the limitations of the primary prevention risk markers now used in HCM, and the fact that by design our registry did not include patients judged to be at low risk without ICDs at the participating centers or allow precise definition of each patient requiring an implanted device within the broad disease spectrum, 20% of the study patients nevertheless received appropriate ICD interventions for life-threatening arrhythmias during a mean follow-up of less than 4 years. The latter findings suggest that the current risk factor strategy is a useful guide for identifying patients with HCM who are susceptible to sudden death.

The fact that more than 40% of our patients who experienced appropriate ICD activations were younger than 40 years emphasizes the unique clinical cir-

Table 3. Individual Primary Prevention Risk Factors and Appropriate Implantable Defibrillator Interventions

	Risk Factor			
	Family History of Sudden Death	Syncope	Massive LVH	NSVT (Holter)
All Patients (n=383)				
No. of patients	197	181	91	175
Patients with appropriate interventions, No. (%)	25 (13)	26 (14)	11 (12)	25 (14)
Person-years	754.51	684.50	304.47	597.97
Appropriate interventions per 100 person-years (95% CI)	3.31 (2.14-4.89)	3.80 (2.48-5.57)	3.61 (1.80-6.46)	4.18 (2.71-6.17)
Patients With All 4 Risk Factors Assessed (n=309)				
No. of patients	157	140	80	175
Patients with appropriate interventions, No. (%)	17 (11)	19 (14)	10 (13)	25 (14)
Person-years	579.14	525.64	252.00	597.97
Appropriate interventions per 100 person-years (95% CI)	2.94 (1.71-4.69)	3.61 (2.18-5.64)	3.97 (1.90-7.29)	4.18 (2.71-6.17)
Patients With Only 1 Risk Factor (n=173)				
No. of patients	67	52	17	37
Patients with appropriate interventions, No. (%)	7 (10)	10 (19)	1 (6)	6 (16)
Person-years	258.83	191.70	48.68	150.47
Appropriate interventions per 100 person-years (95% CI)	2.70 (1.09-5.05)	5.22 (2.50-9.59)	2.05 (0.04-11.44)	3.99 (1.47-8.69)

Abbreviations: CI, confidence interval; LVH, left ventricular hypertrophy; NSVT, nonsustained ventricular tachycardia.

cumstance common to genetic heart diseases[32] such as HCM. Indeed, high-risk patients with HCM are usually much younger than those with more traditional device indications related to coronary artery disease.[11-14] Furthermore, the interval from implantation to first appropriate device activation can be considerable—up to 10 years in the present cohort—and may prove even longer should the follow-up be extended. However, the not infrequent occurrence of inappropriate shocks and other device-related complications, as well as lost employment opportunities or limitations in quality of life, underscore the importance of balancing the sudden death risk and potential ICD benefit (ie, protection from sudden death) against the possibility of adverse defibrillator-related events over long periods, particularly in patients who have undergone implantation early in life. It is possible that some patients judged to be at high risk will experience only ICD-related complications rather than life-saving interventions. Alternatively, reassurance conveyed by the ICD represents an important psychological benefit to many patients.

ICDs restored sinus rhythm, even in the presence of extreme functional and morphologic disease features such as marked left ventricular outflow tract obstruction and massive left ventricular hypertrophy.[2,4] Furthermore, ICDs were effective in preventing sudden arrhythmic death in virtually every patient with a typical clinical expression of HCM (ie, absence of progressive heart failure associated with systolic dysfunction; embolic stroke).[33,34] The single notable exception was a college student with a history of syncope and extreme left ventricular hypertrophy, associated with preserved systolic function, who died suddenly when his mechanically defective (known only to the manufacturer) ICD failed due to massive electrical overstress while delivering a defibrillation shock.[23,35] Therefore, although only speculative at present, it is possible that protection from sudden death offered by the ICD will afford near-normal or normal longevity to many high-risk patients with HCM, assuming they are not encumbered by other major disease complications.

Percutaneous alcohol septal ablation[20,21] is a relatively new therapeutic strategy that reduces the left ventricular outflow gradient and heart failure symptoms in patients with HCM by creating a transmural scar in the hypertrophied proximal ventricular septum.[22] Our findings suggest that this procedure may increase risk of sudden death in some patients with HCM, given that ICD therapy was 4-fold more common after alcohol ablation than following the more established surgical myectomy.[2]

In conclusion, the ICD effectively and reliably aborted life-threatening ventricular tachyarrhythmias in a large group of patients with HCM who were judged to be at high risk for sudden death by their managing cardiologists based on the risk factor algorithm currently used in this disease. An important proportion of these device interventions occurred in patients who had undergone prophylactic ICD implantation for a single risk factor. Therefore, a single marker of high-risk status may justify consideration for a primary prevention defibrillator in selected patients with HCM.

Author Affiliations: Hypertrophic Cardiomyopathy Center of the Minneapolis Heart Institute Foundation, Minneapolis, Minnesota (Drs Maron and Almquist and Ms Haas); Ente Ospedaliero Ospedali Galliera, Genoa, Italy (Drs Spirito, Formisano, and Piccininno); Mayo Clinic, Rochester, Minnesota (Dr Shen); New England Medical Center and Tufts University School of Medicine, Boston, Massachusetts (Drs Link and Estes); University of Alabama at Birmingham (Dr Epstein); University of Rochester Medical Center, Rochester, New York (Dr Daubert); Academic Teaching Hospital of University of Muenster, Bielefeld, Germany (Dr Lawrenz); Universitá di Bologna, Bologna, Italy (Dr Boriani); Universitá degli Studi di Bari, Bari, Italy (Dr Favale); Morristown Memorial Hospital, Morristown, New Jersey (Dr Winters); Ospedale S. Filippo Neri, Rome, Italy (Dr Santini); Università Federico II, Naples, Italy (Dr Betocchi); Hospital 12 de Octubre, Madrid, Spain (Dr Arribas); St Lukes-Roosevelt Hospital Center, New York, New York (Dr Sherrid); University of Padua, Padua, Italy (Dr Buja); Department of Cardiology, Royal Prince Alfred Hospital and Centenary Institute, Sydney, Australia (Dr Semsarian); and Istituto Nazionale per la Ricerca sul Cancro, Genoa, Italy (Dr Bruzzi).

Author Contributions: Ms Haas had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Maron, Spirito, Link, Daubert, Estes, Favale.

Acquisition of data: Maron, Spirito, Shen, Haas, Formisano, Link, Epstein, Almquist, Daubert, Lawrenz, Boriani, Estes, Favale, Piccininno, Winters, Santini, Betocchi, Arribas, Sherrid, Buja, Semsarian.

Analysis and interpretation of data: Maron, Spirito, Shen, Haas, Daubert, Estes, Piccininno, Semsarian, Bruzzi.

Drafting of the manuscript: Maron, Spirito, Haas, Link, Estes, Winters, Sherrid, Bruzzi.

Critical revision of the manuscript for important intellectual content: Maron, Spirito, Shen, Formisano, Link, Epstein, Almquist, Daubert, Lawrenz, Boriani, Estes, Favale, Piccininno, Winters, Santini, Betocchi, Arribas, Buja, Bruzzi.

Statistical analysis: Haas, Buja, Semsarian, Bruzzi.

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Study supervision: Maron, Spirito, Shen, Link, Epstein, Lawrenz, Boriani, Estes, Betocchi, Sherrid.

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Participating Centers and Investigators: Minneapolis Heart Institute Foundation, Minneapolis, Minnesota (B.J. Maron, A.K. Almquist, R.G. Hauser); Ente Ospedaliero Ospedale Galliera, Genoa, Italy (P. Spirito, F. Formisano, D. Molini, M. Piccininno); Mayo Clinic, Rochester, Minnesota (W-K Shen, R.F. Rea); New England Medical Center, Boston, Massachusetts (M.S. Link, N.A.M. Estes III); University of Alabama at Birmingham Hospital (A.E. Epstein); University of Rochester Medical Center, Rochester, New York (J.P. Daubert); Universitá di Bologna, Bologna, Italy (G. Boriani, C. Rapezzi); Royal Prince Alfred Hospital and Centenary Institute, Sydney, Australia (C. Semsarian, J. Ingles); Universitá Federico II, Naples, Italy (S. Betocchi); St Luke's-Roosevelt Hospital Center, New York, New York (M.V. Sherrid, F. Ehlert); University of Padua, Padua, Italy (G. Buja, D. Corrado); Universitá degli Studi di Bari, Bari, Italy (S. Favale, F. Nacci); Children's Hospital of New York–University Hospitals of Columbia and Cornell, New York, New York (R.H. Pass); Genesis Medical Center, Davenport, Iowa (M.C. Giudici); Morristown Memorial Hospital, Morristown, New Jersey (S.L. Winters); UCLA Medical Center, Los Angeles, California (K. Shannon); New York Presbyterian Hospital–Cornell University, New York, New York (B. Lerman); University of Pittsburg Medical Center, Pittsburgh, Pennsylvania (L. Ganz); Hospital 12 Octubre, Madrid, Spain (F. Arribas, M. López Gil); Cedars-Sinai Medical Center, Los Angeles, California (R.J. Siegel); Ospedale S. Filippo Neri, Rome, Italy (M. Santini, R. Ricci, C. Pignalberi); Hospital La Paz, Madrid, Spain (J.L. Merino, R. Peinado); Ospedale S. Camillo, Rome, Italy (F. Laurenzi); Ospedale Niguarda-Cá Granda, Milan, Italy (M. Lunati, M. Paolucci); Hospital Virgen de la Arrixaca, Murica, Spain (A.G. Alberola); Hospital Gregorio Marañón, Madrid, Spain (A. Arenal Maiz); Sheba

Medical Center, Tel Hashomer, Israel (M. Glikson, D.M. Luria); Ospedale degli Infermi, Torino, Italy (S. Bongioanni, M.R. Conte); Ospedale Civile, Asti, Italy (R. Massa, M. Bocchiardo); Ospedale Lancisi, Ancona, Italy (F. Capestro, A. Capestro); Ospedale Maggiore della Caritá, Novara, Italy (E. Occhetta); Ospedale S. Raffaele, Milan, Italy (P. Mazzone); Academic Teaching Hospital of University of Muenster, Bielefeld, Germany (T. Lawrenz, H. Kuhn); Ospedale San Gerardo, Monza, Italy (A. Vincenti); Ospedale S. Orsola, Brescia, Italy (A. Marchetti, C. Rusconi); Ospedale Civile di Lavagna, Lavagna, Italy (D. Oddone, M. Brignole); Ospedale di Lucca, Lucca, Italy (M. Masini); Centro Cardiologico Monzino, Milan, Italy (P. Della Bella, C. Carbucicchio); Baylor College of Medicine, Houston, Texas (H-T Shih); Azienda Ospedaliero S. Maria della Misericordia, Udine, Italy (A. Proclemer); Istituto Nazionale per la Ricerca sul Cancro, Genoa, Italy (P. Bruzzi, L. Boni).

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