Pharmacology and Chemical Biology

Original Article

Evaluation, Prognosis and Risk factors in Hypertrophic Cardiomyopathy

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Keywords
Hypertrophic cardiomyopathy, Management, Risk stratification, Sudden cardiac death (SCD).

Abbreviations
HCM: Hypertrophic cardiomyopathy; SCD: Sudden cardiovascular death; NSVT: None sustained ventricular tachycardia; LVH: Left ventricular hypertrophy; LVOT: Left ventricular outflow tract; ECG: Electrocardiogram; Echo: Echocardiogram; MRI: imaging Magnetic resonance; ICD: Implantable cardiac discharge; CAD: Coronary artery disease; Abnormal BPRs: Abnormal blood pressure response; AF: Atrial fibrillation; VF: Ventricular fibrillation; CVS: Cardiovascular system

Abstract

Introduction: *Hypertrophic cardiomyopathy is a common genetic disease characterized by the presence of abnormal wall thickness. Hyper-trophic cardiomyopathy can appear at any age, with the majority of the patients remaining clinically stable. When patients complain of symptoms, these include: dyspnea, syncope and angina. Hypertrophic cardiomyopathy is the most frequent cause of sudden cardiac death in young adults and sports. Sudden cardiac death risk has been associated with different clinical risk factors. However risk stratifications and prevention of sudden cardiac death are still challenges for the clinicians.*

Objectives: *Our objectives are to evaluate the relation between traditional and novel risk factors and SCD risk in our cohort of patients with HCM in order to improve the management of the disease.*

Methods: *In The institute of health sciences in the La coruña University we follow up more than 635 patients with HCM. The study will record the following risk factors for SCD A: Major risk factors: 1) Prior cardiac arrest or symptomatic sustained ventricular tachycardia. 2) Family history of a premature sudden cardiac death. 3) Unexplained syncope. 4) Non-sustained ventricular tachycardia. 5) Abnormal blood pressure response during exercise. 6) Extreme left ventricular hypertrophy with maximum wall thickness of 30 mm or more. B: Minor or possible risk factors: Atrial fibrillation ever, Intense (competitive) physical exertion, Late gadolinium enhancement in magnetic resonance imaging.*

The relation between the presence of these risks factors and development of SCD or appropriate implantable cardioverter defibrillator discharge (AICD) will be evaluated by univariate and multivariate survival analysis.

Introduction

Cardiomyopathy is a myocardial disorder in which the heart muscle is structurally and functionally abnormal, in the absence of coronary artery disease, hypertension, valvular disease and congenital heart disease suf-ficient to cause the observed myocardial abnormality, so hypertrophic car-diomyopathy (HCM) is a type of cardiomyopathy. It could be simply de-fined by the presence of increased ventricular wall thickness or mass in the absence of loading conditions (hypertension, valve disease) sufficient to cause the observed abnormality [1-3], figs I-IV. Left ventricular hyper-trophy (LVH) in the absence of hypertension and valve disease occurs in approximately 1:500 of the general population. And left ventricular cavity size is usually diminished accompanied with abnormal diastolic relaxation and fractional shortening typically higher than normal. Progression to left ventricular dilatation and systolic failure occurs in a minority of patients (up to 10% in some series). HCM is an important cause of sudden cardiac death (SCD); in most (but not all) series it is the most important cause of SCD in young adults and in athletes [2]. The incidence of HCM before puberty is rare and may not develop until later of life [5]. Today, more than 200 different genetic mutations have been identified to cause the disease. The development of signs and symptoms in HCM is slow, therefore, mak-ing early diagnosis often difficult [6-7].

Many of these deaths occur in patients with minimal or no symptoms (in-deed the diagnosis of HCM is sadly often made first at the postmortem examination, following the sudden cardiac death of a previously healthy individual). With the development of (AICDs), effective preventive therapy is now available. The challenge is to distinguish high risk from low risk patients with HCM in order to target prophylactic therapies (AICD ± ami-odarone) to those at risk. HCM patients who are implanted are much younger, and have a much lower annual event or AICD discharge rate. It is likely that their lifetime risk of serious AICD related complications will be high [8]. So the

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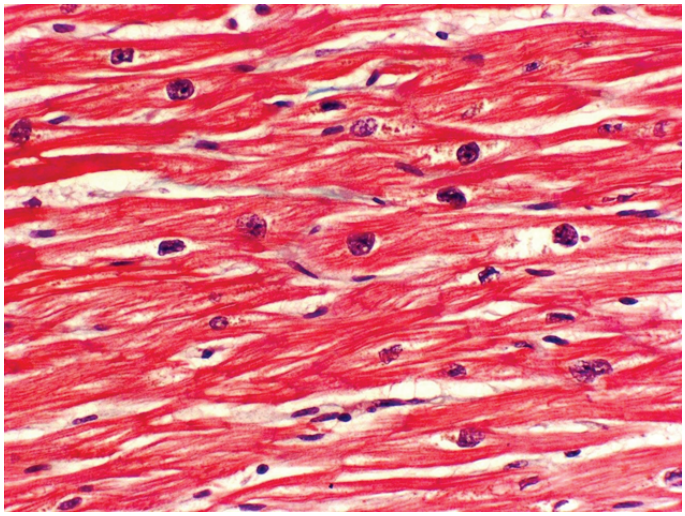


Figure 1. *This image showing normal structure of cardiac muscle (Faintly striated, branch-ing, mononucleotide cells, connected by intercalated disc to form a functional network)*

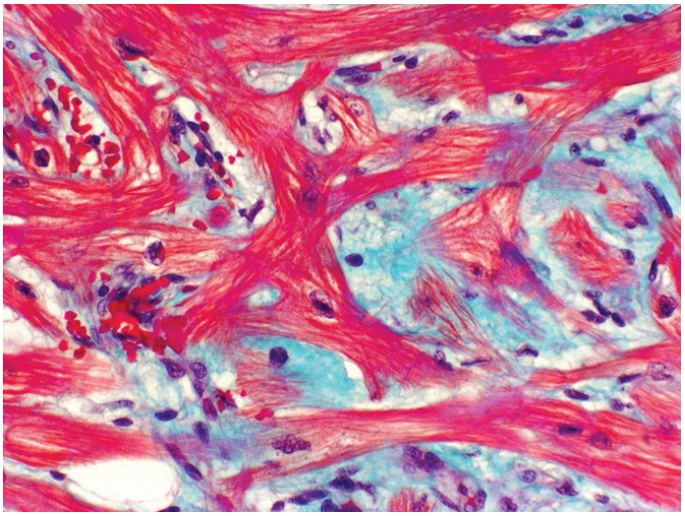
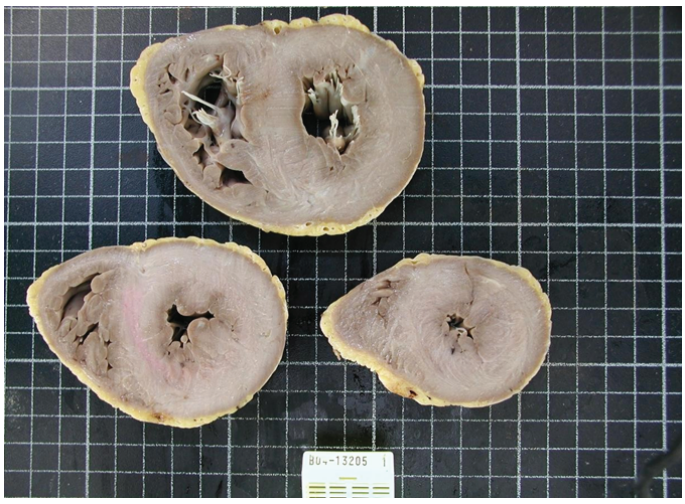


Figure 2. *A section of myocardium showing muscle fibre hypertrophy, muscle fibre disarray, and interstitial fibrosis.*



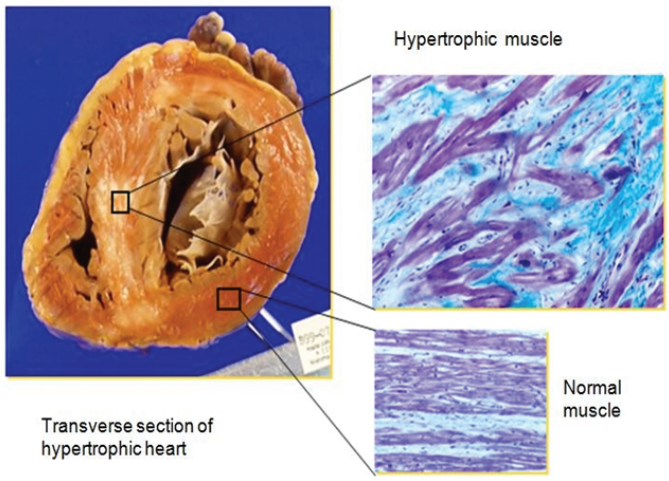


Figure 3. *Transverse section in hypertrophic heart*

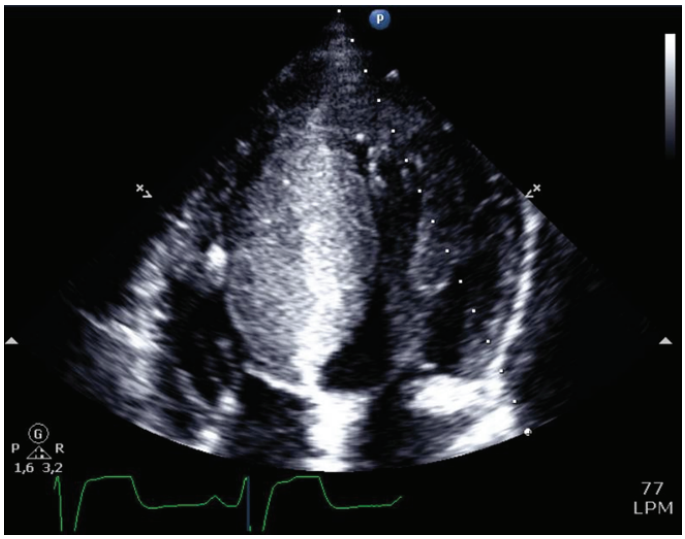


Figure 4. *Echocardiogram of hypertrophic heart.*

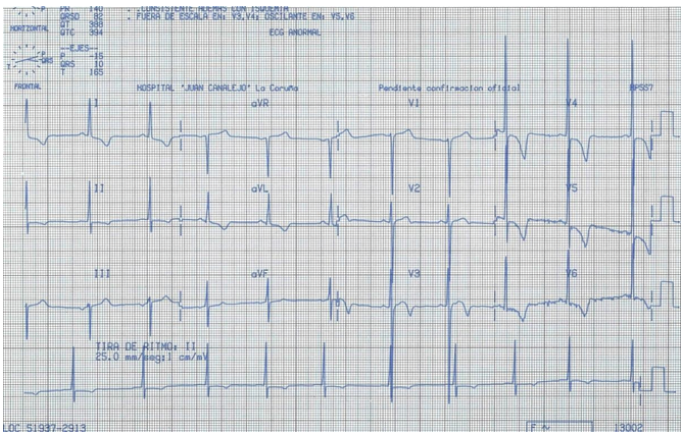


Figure 5. *Typical ECG of HCM showing high voltage and negative T. Waves.*

early detection of the disease to begin treatment is the ultimate goal in symptomatic HCM.

Hypothesis

The fundamental hypothesis of this cohort study is that the combination of traditional risk factors with new ones can improve the assessment of risk of SCD in patients with HCM. Second hypothesis posed in this thesis is that the relationship between risk factors and development of events in our population is not different from that existing in other previously studied populations.

Objectives

We aimed to 1) Evaluate in a large cohort of patients with HCM the prognostic value of traditional risk factors and new markers of risk SCD. 2) Al-so how to develop an improved model of risk stratification of SCD in patients with HCM. 3) Finally how to compare the relationship between traditional risk factors and prognosis in our population which has been described in other populations.

Materials and methods

Study population and study design.

In this retrospective study, we followed up the patients who were examined in HCM Clinic at the University Hospital of A Corunna in addition we used our institutional database in Health in Code. We studied the clinical outcome of 635 patients (391 males and 241 females), the mean of their age was 51, 12 ± 17, 37 years, They were been selected from patients with a diagnosis of HCM seen in the unit of familiar HCM between January 1976 and December 2010, during this period patients were fol-lowed regularly usually at one year intervals or incidence of important events of the disease, all of them were Spanish patients. Data were abstracted on demographic characteristics, coronary risk factors, family his-tory of HCM, symptoms and findings at physical examination at the time of presentation and diagnosis of HCM, as well as at the most recent follow-up. In addition, the results of Electrocardiogram (ECG), Echocardiography (ECHO), ambulatory ECG, monitoring and cardiac catheterization were reviewed. The study was approved by the Clinical Research Ethics Committee (CEIC) as well as we token an informed written consent from all participants, and in cases of children who had age <18 years, we token informed written consent of their parents or a legal guardian and informed consent of the child at the same time, also in cases of patients with cognitive impairment we asked for legal guardians consent.

Measurements

For the purposes of this study, patients were selected from the cohort of 635 patients using the following criteria: 1) patients with confirmed HCM. The diagnosis of HCM was based on the presence of unexplained left ventricular hypertrophy (>2 standard deviations from the normal ranges corrected for age and body size) or on the presence of unexplained ECG and Echo abnormalities in the relatives of patients with an unequivocal diagnosis of HCM, in accordance with recently proposed diagnostic criteria

Obtaining informed consent collected in a computerized database of diagnostic clinical data and follow-up data of the patients, the study protocol includes any age of diagnosis of the disease, the development of a family tree, the collection of personal and family history, symptoms and ECG data, ECHO, Holter, exercise ECHO, cardiac magnetic resonance imaging (MRI), treatments and events.

In addition to these data, collected the following clinical parameters: Start and last follow up (date), demographic variables: sex of the patient (male/female) , age of diagnosis of HCM (years), date of birth(date),age of last follow up (date), precipitating factors of the disease: Hypertension (Yes/No), Sport (Yes/No), physical examination height (CM) and weight (KG); Risk factors & symptoms of HCM and SCD: dyspnea at diagnosis: NYHA I, II, III, IV, dyspnea at last follow up, NYHA >=III ever(Yes/No), chest pain typical (Yes/No), chest pain was classified as exertional or atypical if it lasted 30 minute at rest in the absence of myocardial infarc-tion, syncope (ever), None sustained ventricular tachycardia (Yes/No), ventricular fibrillation (Yes/No), family history of SCD, abnormal blood pressure response (Yes/No), medication on the exercise test (Yes/No) with or without (BB or calcium antagonists)

Variables

ECG variables

All patients underwent 48 hour ambulatory ECG monitoring while perform-ing unrestricted daily activities to detect the following variables; Rhythm: sinus/Atrial fibrillation or flutter, NSVT, Atrial fibrillation ever (Yes/No), changes in depolarization and voltage of ECG as 1) R-wave and S-wave voltage measurements, 2) with inverted or biphasic T waves, 3) complete right or left bundle-branch blocks, Wolff-Parkinson White syndrome, or evidence of prior myocardial infarction.

Echo variables

Two-dimensional and M-mode echocardiography were performed to detect absence or presence of the following variables: maximal wall thickness (mm), wall thickness>=30 mm (Yes/No), systolic function (ejection fraction), left Atrial diameter, left ventricle outflow obstruction (LVOT) (Yes/No), LVOT gradient (mmHg), Moderate or Severe Mitral regurgitation (Yes/No), Mitral regurgitation (Mild/moderate/severe).

MRI

It is pain-free, non-invasive medical gold standard test used to pro-duce two dimensional images of the structures of the body. The process uses intense magnetic fields to make images of the inside of the body. MRI detect late enhancement (Yes/No), number of segments with late enhancement.

Events

Death (Yes/No) —cause and age of death‖, Cardiovascular death (Yes/No), SCD (Yes/No), Appropriate ICD discharge (Yes/No), cerebrovascular accident, or cardiac transplantation.

Treatment

Surgical treatment (Yes/No) —Age, Type‖, Pace maker implantation (Yes/No) —age &cause of implantation‖, Implantable cardiac defibrillator (Yes/No) —age and cause of implantation‖, Medical treatment (drug, dose, duration). But we should take in our account that The Characters of Exclusion included patients without a confirmed diagnosis of HCM, and patients without a confirmed written con-sent.

For each patient will be collected the following risk factors: Major factors includes prior cardiac arrest or symptomatic family history of SCD (was defined as SCD in two or more first-degree relatives ≤40 years old), un-explained syncope. A history of syncope was defined as one or more episodes of unexplained loss of consciousness, none sustained ventricular tachycardia (NSVT) was defined as a run of three or more consecutive ventricular beats at a rate of ≥120 beats/min, lasting <30 s,

abnormal blood pressure response (Abnormal BPRS) in effort (An abnormal BPRS was defined as a failure of blood pressure to rise, or a fall in blood pressure during exercise. According to previously published data, BPRs were only classified as a risk factor in patients aged ≤40 years, severe hyper-trophy (≥30mm). But the minor factors include severe sub aortic obstruction, atrial fibrillation, late enhancement magnetic resonance imaging (MRI), and Intense (competitive) physical exertion.

Statistical Analysis

They are expressed as mean value ± SD. Cumulative survival estimates and 95% confidence intervals (CIs) were calculated according to the Kaplan-Meier method. Among patient subgroups the log-rank test was used to compare the results for in survival between subgroups, with values of $P<0.05$ being considered significant. The yearly cumulative mortality rate was calculated on the basis of all available follow-up time. To assess risk factors for cardiac death. The chi-squared test was used to compare clinical characteristics from referral and non referral centers. All analyses were performed using the SPSS 18 statistical package.

Results

A total of 635 patients were diagnosed with HCM —apical, septal, atypical or concentric‖ between January 1976, and 2010 in the University Hospital of A Coruna or each patient had at least one time follow up in this hospital. All of the patients met inclusion criteria for HCM. Clinical characteristics of the patient population are listed in Table II. Patients presented with symptoms or signs including major risk factors were as following; 71(11.2%) patients had syncope but 548(86.3%) patients did not have this symptom. 127(20%) patients had Abnormal BPRs test but 208(32.8%) did not have. 41(6,5%) patients had maximal wall thickness of the heart ≥30 mm but 593(93,4%) their measurement of wall thickness were ≤30mm. Patients who had family history of SCD in their 1st or 2nd degree were 101(15.9%) patients, but who did not have were 527(83%) ones. Patients who had NSVT were 136(21.4%) but who did not had 235(37%) patients. There were missed data about a group of patients in each variable showed in the table. Patients with minor risk factors of HCM, Patients who were or still practicing sport —competitive or non competitive‖ were 91(14.3%) and who did not do any type of sport were 333(52.4%) patients. By MRI test showed that 81(12.8%) patient with late enhancement but 154 (24.3%) without it. Number of patient who had AF ever in his life was 190(29.9%) and others who did not have were 430 (67.7%) patients. There is 304(47.8%) patients did not have any one of the major risk factors. But there is (331, 117, 26, 2, 0) with percentage (52%, 18.4%, 4%, 0.3%, 0.0%) respectively have (1, 2, 3, 4, 5) major risk factors respectively. During the follow up of the patient's mean of age of diagnosis was 51.12 year ± SD 17.37 also for age of last follow up was 60.58 ± SD 16.53 years but for duration of follow up was 9.4 ± SD 7.5 years (Table I).

Table 1. *Characters of the patients*

Variables	Mean	SD
Age of diagnosis	51.12	17.37
Age of last follow up	60.58	16.53
Duration of follow up	9.4	7.5

The frequency of risk factors in HCM patients for —death, CVS death, SCD, and death due to non cardiovascular cause‖ are summarized in tables III, IV, V, and VI respectively.

Table II.

Data of the Patients	**Number**				**%**	
VARIABLES	Yes	%	No	%	Missed	%
Major risk factors						
Syncope	71	11.2	548	86.3	16	2.5
Abnormal BPRS in exc. Test.	127	20	208	32.8	300	47.2
Max. wall thickness ≥ 30mm.	41	6.5	593	93.4	1	0.1
FH SD.	101	15.9	527	83	7	1.1
NSVT	136	21.4	235	37	264	41.5
Minor risk factors						
Patient practicing Sport	91	14.3	333	52.4	211	33.3
Patient with MRI late enhancement	81	12.8	154	24.3	400	62.9
AF ever	190	29.9	430	67.7	15	2.3
Events						
Death	97	15.3	538	84.7		
SCD	13	2	622	98		
Death by any CVS cause	80	12.6	555	87.4		
Death by non CVS cause	17	2.7	618	97.3		
Number of risk factors						
Patients without risk factors	304	47.8	331	52.2		
Patients with ≥1 risk factors	331	52	304	48		
Patients with ≥2 risk factors	117	18.4	518	81.6		
Patients with ≥3 risk factors	26	4	609	96		
Patients with ≥4 risk factors	2	0.3	633	99.7		
Patients with ≥5 risk factors	0	0.0	635	100		

This table explains the number and percentage of patients in relation with each risk factor (major/minor), events and number of risk factors.

Clinical outcomes

During follow up period nineteen-seven deaths were reported. Eighteen patients (mean age71 ± 12) could be attributed due to CVS causes: 13 (mean age61 ± 13) died as SCD but 77 patients died from other CVS causes. 17 (mean age71 ± 12) died from non cardiovas-cular causes.

Univariate analysis risk factors

Clinical history is summarized in tables III, IV, V, and VI respectively.

Syncope clinical history showed that seventy-one (11%) had syncope at least one time in their history. Their death events include (16 death, 14 CVS death, 2 SCD, 2 none CVS death)

Table III.

variables	Death				
	No	%	Yes	%	Total
Sex					
Female	204	84.6	37	15.4	241
Male	334	85.4	57	14.6	391
Total	538	85.1	94	14.9	632
Syncope					
No	468	85.4	80	14.6	548
Yes	55	77.5	16	22.5	71
Total	523	84.5	96	15.5	619
Abnormal BPRS in exc. Test.					
No	193	92.8	15	7.2	208
Yes	113	89	14	11	127
Total	306	91.3	29	8.7	335
Max. wall thickness ≥ 30mm.					
No	501	84.5	92	15.5	593
Yes	36	87.8	5	12.2	41
Total	537	84.7	97	15.3	634
FH SCD					
No	440	83.5	87	16.5	527
Yes	91	90.1	10	9.9	101
Total	531	84.6	97	15.4	628
NSVT					
No	223	94.9	12	5.1	235
Yes	112	82.4	24	17.6	136
Total	335	90.3	36	7.3	371
Minor risk factors					
Sport					
No	271	81.4	62	18.6	333
Yes	84	92.3	7	7.7	91
Total	355	83.7	69	16.3	424
Patient with MRI late enhancement					
No	148	96.1	6	3.9	154
Yes	79	97.5	2	2.5	81
Total	227	96.6	8	3.4	235
AF ever					
No	386	89.8	44	10.2	430
Yes	142	74.7	48	25.3	190
Total	528	85.2	92	14.8	620

This table explains the number and percentage of patients with variable in relation to death.

Table IV.

variables	Death				
	No	%	Yes	%	Total
Sex					
Female	209	86.7	32	13.3	241
Male	346	88.5	45	11.5	391
Total	555	87.8	77	12.2	632
Syncope					
No	483	88.1	65	11.9	548
Yes	57	80.3	14	19.7	71
Total	540	87.2	79	12.8	619
Abnormal BPRS in exc. Test.					
No	198	95.2	10	4.8	208
Yes	117	92.1	10	7.9	127
Total	315	94	20	6	335
Max. wall thickness ≥ 30mm.					
No	517	87.2	76	12.6	593
Yes	37	90.2	4	9.8	41
Total	554	87.4	80	12.6	634
FH SCD					
No	454	86.1	73	13.9	527
Yes	94	93.1	7	6.9	101
Total	548	87.3	80	12.7	628
NSVT					
No	226	96.2	9	3.8	235
Yes	117	86	19	14	136
Total	343	92.5	28	7.5	371
Minor risk factors					
Sport					
No	280	84.1	53	15.9	333
Yes	85	93.4	6	6.6	91
Total	365	86.1	59	13.9	424
Patient with MRI late enhancement					
No	151	98.1	3	1.9	154
Yes	79	97.5	2	2.5	81
Total	230	97.9	5	2.1	235
AF ever					
No	393	91.4	37	8.6	430
Yes	150	78.9	40	21.1	190
Total	543	87.6	77	12.4	620

This table explains the number and percentage of patients with variable in relation to CVS death.

and P-values are (0.010, 0.007, 0.463, 0.748) respectively. The calculated hazard ratio for cardiac death if there was Syncope was 1.7 (95% confidence interval: 0.92 to 3.1). in our population we can consider that syncope is risk factor for death or CVS death but not for SCD.

ABN BPRS Exercise Testing

Three hundred thirty five patients had at least 1 exercise Treadmill test. 127 (40%) had an abnormal blood pressure response to exercise. Of those undergoing exercise testing, 68 (20%) were on beta-blockers and 4 (0.01%) were on calcium-channel blocker therapy, their death events were as follow (14death, 10 CVS death, 1 SCD, 4 None CVS death) and P-values are (0.058, 0.076, 0.816, 0.445), depending these results abnormal BPRS not is a risk factor for any of the events in our population. The calculated hazard ratio for cardiac death if there was an abnormal blood pressure response to exercise was 1.7 (95% confidence interval: .68 to 4.1) (table VIII).

Table V.

variables	Death				
	No	%	Yes	%	Total
Sex					
Female	237	99.2	2	0.8	239
Male	380	97.4	10	2.6	390
Total	617	98.1	12	1.9	629
Syncope					
No	534	98	11	2	545
Yes	69	97.2	2	2.8	71
Total	603	97.9	13	2.1	616
Abnormal BPRS in exc. Test.					
No	205	99	2	1	207
Yes	126	99.2	1	0.8	127
Total	331	99.1	3	0.9	334
Max. wall thickness ≥ 30mm.					
No	578	98	12	2	590
Yes	40	97.6	1	2.4	41
Total	618	97.9	13	2.1	631
FH SCD					
No	512	97.7	12	2.3	524
Yes	100	99	1	1	101
Total	612	97.9	13	2.1	625
NSVT					
No	234	99.6	1	0.4	235
Yes	130	96.3	5	3.7	135
Total	364	98.4	6	1.6	370
Minor risk factors					
Sport					
No	326	98.5	5	1.5	331
Yes	88	96.7	3	3.3	91
Total	414	98.1	8	1.9	422
Patient with MRI late enhancement					
No	154	100			154
Yes	81	100			81
Total	235	100			235
AF ever					
No	425	98.8	5	1.2	430
Yes	181	96.3	7	3.7	188
Total	606	98.1	12	1.9	618

This table explains the number and percentage of patients with variable in relation to SCD.

Table VI.

variables	None CVS death				
	No	%	Yes	%	Total
Sex					
Female	236	97.9	5	2.1	241
Male	379	96.9	12	3.1	391
Total	615	97.3	17	2.7	632
Syncope					
No	533	97.3	15	2.7	548
Yes	69	97.2	2	2.8	71
Total	602	97.3	17	2.7	619
Abnormal BPRS in exc. Test.					
No	203	97.6	5	2.4	208
Yes	123	96.9	4	3.1	127
Total	326	97.3	9	2.7	335
Max. wall thickness ≥ 30mm.					
No	577	97.3	16	2.7	593
Yes	40	97.6	1	2.4	41
Total	617	97.3	17	2.7	634
FH SCD					
No	513	97.3	14	2.7	527
Yes	98	97	3	3	101
Total	611	97.3	17	2.7	628
NSVT					
No	232	98.7	3	1.3	235
Yes	131	96.3	5	3.7	136
Total	363	97.8	8	2.2	371
Minor risk factors					
Sport					
No	324	97.3	9	2.7	333
Yes	90	98.9	1	1.1	91
Total	414	97.6	10	2.4	424
Patient with MRI late enhancement					
No	151	98.1	3	1.9	154
Yes	81	100	0	0	81
Total	232	98.7	3	1.3	235
AF ever					
No	423	98.4	7	1.6	430
Yes	182	95.8	8	4.2	190
Total	605	97.6	15	2.4	620

This table explains the number and percentage of patients with variable in relation to None CVS death.

Max

wall thickness ≥ 30mm. Forty one (6.5%) patient had max. wall thickness ≥ 30mm.Their death events were (5death, 4 CVS, 1 SD, 1 non CVS death) and P-values are (0.265, 0.294, 0.955, 0.698) respectively. The calculated hazard ratio for cardiac death if there is max. wall thick-ness ≥ 30mm was 0.735 (95% confidence interval: 0.255 to 2.121) (table VIII). Max. wall thickness ≥ 30mm not a risk factor for any of the events.

NSVT

Hundred thirty six patients had NSVT and death events were (24daeth, 19 CVS death, 5 SD, 5 non CVS death), and P-values are (0.004, 0.007, 0.082, 0.328) respectively. The calculated hazard ratio for cardiac death if there was an NSVT was 4.006 (95% confidence interval: 1.757to 9.132) (table VIII). NSVT is predictive risk factor for death or CVS death in cardiac patients.

Table VII. *Survival analysis by Kaplan-Meier Log Rank (Mantel-Cox)*

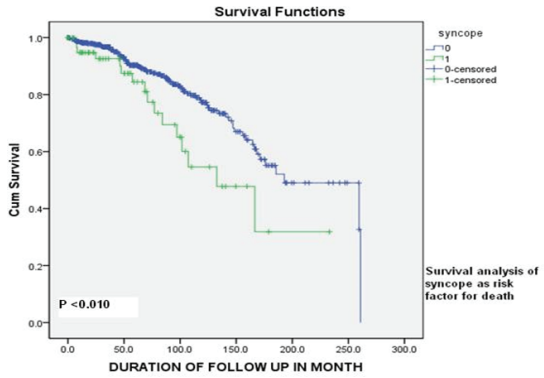
	Significance P value			
	Death	**CVS death**	**SCD**	**None CVS death**
Sex	0.527	0.332	0.197	0.573
Major risk factors				
Syncope	0.010*	0.007*	0.463	0.748
Abnormal BPRS in exc. Test.	0.058	0.076	0.816	0.445
Wall thickness ≥ 30mm.	0.265	0.294	0.955	0.698
FH SD.	0.868	0.787	0.783	0.349
NSVT	0.004*	0.007*	0.082	0.328
Minor risk factors				
Patient practice Sport	0.028*	0.041*	0.259	0.422
Patient with MRI late enhancement	0.877	0.601		0.327
AF ever	0.001*	0.004*	0.088	0.163
Number of major risk factors				
1 major risk factor	0.893	0.969	0.287	0.815
2 majors risks factors	0.8	0.953	0.831	0.648
3 majors risks factors	0.975	0.88	0.447	0.851
4 majors risks factors	0.413	0.448	0.805	0.762

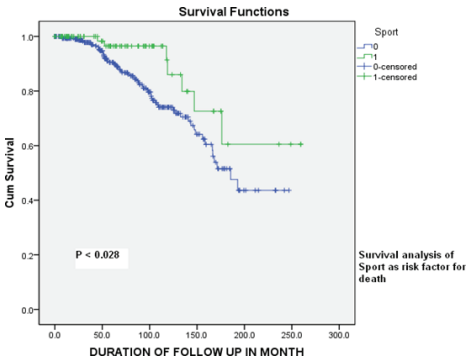
This table shows the P value of Survival analysis by Kaplan-Meier Log Rank (Mantel-Cox) for the different events in relation to different variables (*) significant P value

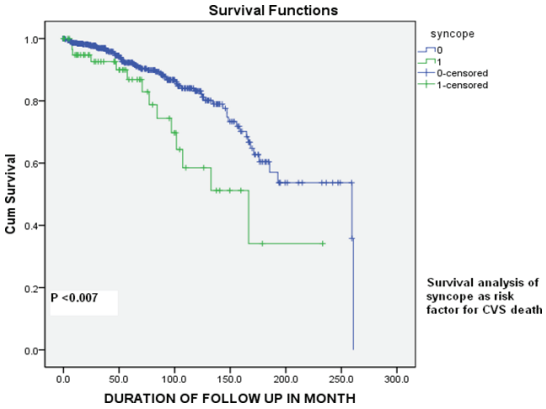
Table VIII. *Descriptive analysis for risk factors to detect odd ratio.*

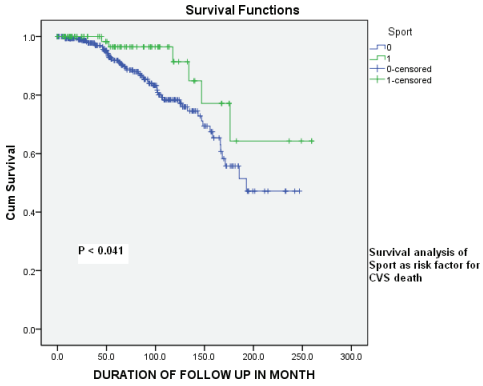
	Event	**P value**	**95% confidence interval**		**Risk for the event**
			lower	**upper**	**Yes/no**
Major risk factors					
Syncope	Death	1.702	0.929	3.117	Yes
	SD	1.407	0.305	6.481	Yes
	Death any CVS cause	1.825	0.963	3.459	Yes
	Death non CVS cause	1.03	0.231	4.6	Yes
Abnormal BPRS in exc. Test.	Death	1.594	0.742	3.424	Yes
	SD	0.813	0.073	9.064	Yes
	Death any CVS cause	1.692	0.684	4.187	Yes
	Death non CVS cause	1.32	0.348	5.011	Yes
Wall thickness ≥ 30mm.	Death	0.756	0.289	1.978	Yes
	SD	1.204	0.153	9.495	Yes
	Death any CVS cause	0.735	0.255	2.121	Yes
	Death non CVS cause	0.902	0.117	6.972	Yes
FH SD.	Death	0.556	0.278	1.111	Yes
	SD	0.427	0.055	3.318	Yes
	Death any CVS cause	0.463	0.207	1.038	Yes
	Death non CVS cause	1.122	0.316	3.976	Yes
NSVT	Death	3.911	1.886	8.11	Yes
	SD	8.846	1.022	76.536	Yes
	Death any CVS cause	4.006	1.757	9.132	Yes
	Death non CVS cause	2.901	0.682	12.334	Yes

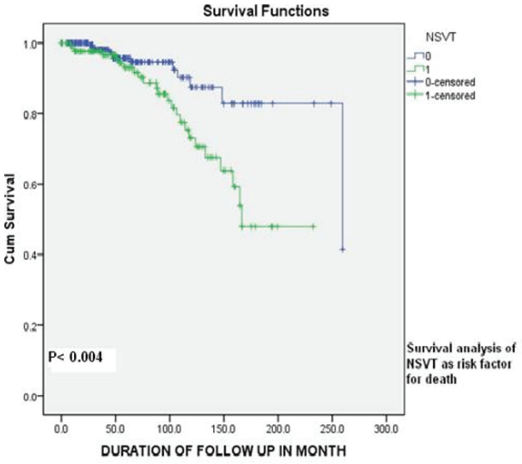
	Event	P value	95% confidence interval		Risk for the event
			lower	upper	Yes/no
Minor risk factors					
Patient practice Sport	Death	0.364	0.161	0.826	Yes
	SD	2.223	0.521	9.481	Yes
	Death any CVS cause	0.373	0.155	0.898	Yes
	Death non CVS cause	0.4	0.05	3.199	Yes
Patient with MRI late enhancement	Death	0.624	0.123	3.166	Yes
	SD				
	Death any CVS cause	1.274	0.209	7.785	Yes
	Death non CVS cause	0.981	0.959	1.003	Yes
AF ever	Death	2.965	1.887	4.66	Yes
	SD	3.287	1.03	10.494	Yes
	Death any CVS cause	2.832	1.744	4.6	Yes
	Death non CVS cause	2.656	0.949	7.434	Yes

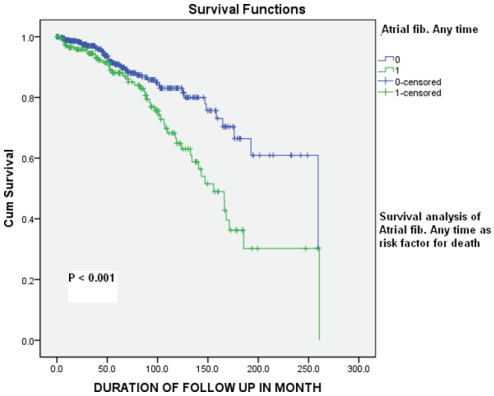


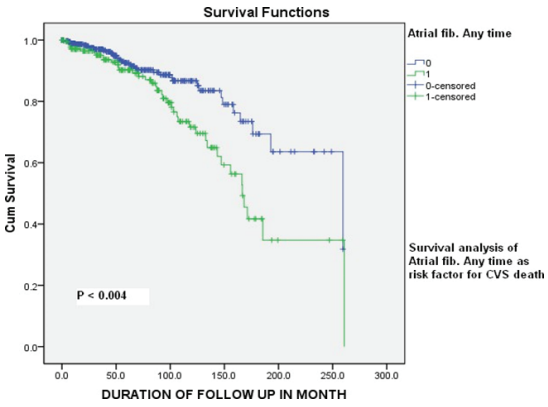












FH SCD

Hundred-one (16%) had FH of SCD at their 1st or 2nd degree relative. Their death events include (10 death, 7 CVS death, 1 SCD, 3 non CVS death) and P-values are (0.868, 0.787, 0.783, 0.349) respective-ly. The calculated hazard ratio for SCD if there was family history of this event was 0.55 (95% confidence interval: 0.278 to 1.111), so depending this results FH SCD not is a risk factor for any of the events of our population.

Sport

Nineteen one (14%) were doing sport in their life and their death events include (7 death, 6 CVS death including 3 SD, 1 non CVS death) and P-values are (0.028, 0.041, 0.259, 0.422) respectively. We can con-clude that sport is risk factor for death or CVS death in HCM patients.

MRI late enhancement

Two hundred thirty five patients undergone MRI of those patients 81(34%) showed late enhancement of imaging. Only two of them died due to cardiovascular causes. By the same statistical test used before the result showed that late MRI enhancement not predictive risk factor in this population.

AF ever

One hundred ninety had AF ever (48 death, 8 CVS death, 7 SD, 40 non CVS death) and P-values are (0.001, 0.004, 0.088, 0.163) respectively. The calculated hazard ratio for cardiac death if there was an AF ever was 2.832 (95% confidence interval: 1.744 to 4.600) (table VIII). From these results we can conclude that AF ever is predictive risk factor for death in cardiac patients.

Relation between number of risk factors and SCD

When we consider syncope and NSVT as one risk factor there is 22 (3.4%) patients had this factor 5 patients died by CVS causes. Survival analysis for it in relation to death, CVS death, SCD, and none CVS death showed the fol-lowing P-values (0.031, 0.003, 0.471, and 0.414). So this factor is predictive for CVS death. But when we consider any two, three, or four major risk factors as one risk factor for death the P-values were (0.893, 0.800, 0.975, and 0.413), for CVS death were (0.953, 0.880, 0.448), for SCD were (0.831, 0.447, 0.805), and for none CVS death (0.648, 0.851, 0.762), So none of these factors was not considered as a predictive risk factor for any of the events (Table VII).

ICDS

Sixteen-one patients (9.6%) received ICDs. Most of the patients who had an ICD placed for a history of ventricular tachycardia, syncope, and appropriate discharges for ventricular tachycardia. Five patients underwent cardiac transplantation after ICD placement due to persistent heart failure symptoms.

Outcomes

Over the period of follow up, there were 80 cardiac deaths which consisted of (14 SCD, and 66 other CVS causes of death) also there were 17 non cardiac death. So the number of dead patients is 97. There was 10 cardiac transplantations 3 (30%) of them died.

Discussion

The clinical course of HCM is variable may be asymptomatic or mildly symptomatic patients may die unexpectedly [30-33]. Although it has been postulated that the best determinant of outcome may be the specific molecular genetic defect [31], current patient management relies on clinical predictors of outcome not genetic one. This present study is a retrospective investigation based analysis, comprised largely of population with HCM for identifying patients at high and low risk of SCD or CVS death. Although many clinical features associated with an increased risk of SCD have been reported in the published data but it remain an impor-tant challenge of investigation particularly with the availability of an effec-tive but not hazard-free treatment option but it is problematic due to the relatively low annual mortality rates in most patient groups [19 –27], and the necessity for regression analysis of multiple risk factors in large popu-lation in long survival time. This study shows that a simpler model based on a smaller number of generally accepted risk factors can be used to identify a cohort of patients who are at a substantially increased risk of SCD and CVS death.

In previous studies, increased risk of mortality patients with HCM has been associated with a history of syncope on presentation [3], NSVT [11] and AF ever [36] In contrast, we found that the following factors (Syncope, NSVT, Sport, AF ever) were predictive of CVS death. The explanations for our contrasting findings may be related to methodology, statistical power, differences in practice or patient population.

Significance of individual risk factors, in the univariate analysis only syncope, NSVT, Sport, and AF ever achieved a statistically significant association with CVS death not SCD. The low risk associated with abnormal BPRS in exercise test, Maxwall thickness ≥ 30 mm, FH SCD, or MRI late enhancement alone seems counterintuitive. However, the small size of population of study, as well as the uncertain cause of SCD in some individuals, can make it difficult to define these factors as risk ones for SCD or

CVS death

Although several cross sectional studies have showed that (syncope, abnormal BPRS, max. wall thickness ≥ 30mm, FH SCD, NSVT, Basal gradient ≥ 30Mm Hg, Sport, MRI late enhancement, and AF ever) is associated with an increased incidence of SCD, in this study some of these variables as a single risk factor was not significantly associated with SCD nor CVS death. A recent study in a selected —low risk‖ cohort has suggested that these factors are prognostically significant only when re-petitive or associated with symptoms. However, even in the present study, all of them were associated with a relative SCD risk by using P values with 95% confidence level (Table7). Although this ratio did not attain conventional levels of statistical significance, they had wide confidence interval means that an association between SCD and these factors cannot be excluded.

Study Limitations

HCM can be caused by a mutation in one of the genes that encode proteins of the cardiac sarcomere, at present there are few obstacles to the translation of HCM genetic research into practical clinical applications and routine clinical strategy, exercise induced hypotension is common in young patients with HCM and this finding has been associated with an increased risk of sudden death. No single test can reliably predict risk in HCM, and the complexity of the disease continues to be an important obstacle to risk stratification.

Conclusion

Although overall SCD and CVS death rates are relatively low in patients with HCM, this study shows that relatively simple, non-invasive tests can be used to identify a cohort of patients who have a substantial risk of CVS or SD death. The results in our study show that prognosis of HCM in a community-based population is benign and confirm the current opinion on the natural history in HCM. The most striking finding was a substantial difference in the clinical stability of patients with and without (NSVT, Basal gradient≥30mmhg, Sport, AF ever).

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Definitions

- **Initial investigations:** are defined as the first ECHO, 48-h ambula-tory ECG and upright exercise test performed at our institution.
- **Start of follow-up:** Follow-up started with the date of the initial consult recorded at data base of the hospital which completed inclu-sion characters as defined before.
- **End point classification:**
- SCD was defined as witnessed SD with or without documented ven-tricular fibrillation or death within 1 hour of new symptoms. Nocturnal deaths with no antecedent history of worsening symptoms were in-cluded in this category.
- **Progressive heart failure:** It is death preceded by signs and/or symptoms of heart failure including cardiogenic shock.
- **Heart transplantation:** Orthotropic heart transplantation per-formed for end-stage disease with systolic impairment and refractory congestive symptoms.
- **Other cardiovascular death:** They include —Stroke, pulmonary or systemic embolism and myocardial infarction‖.
- **None cardiovascular death:** It is death secondary to non cardi-ovascular events and of unknown cause.
- **Survival analysis:** Survival data were collected in routine clinic visits and where necessary by direct communication with patients and their attending physicians. Additional information was obtained using a writ-ten questionnaire sent to all patients' general practitioners.

References

1. Elliott P, Andersson B, Arbustini E, Bilinska Z, Cecchi F, Charron P, et al. Classification of the cardiomyopathies: a position statement from the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. Eur Heart J. 2008;29(2):270-276.
2. Maron BJ, Shirani J, Poliac LC, Mathenge R, Roberts WC, Mueller FO. Sudden death in young competitive athletes: clinical, demographic, and pathological profiles. JAMA. 1996;276(3):199-204.
3. Kofflard MJM, Ten Cate FJ, van der Lee C, van Domburg RT. Hypertrophic cardiomyopathy in a large community-based population: clinical outcome and identification of risk factors for sudden cardiac death and clinical deterioration. J Am Coll Cardiol. 2003;41(6):987-993.
4. Goodwin JF. The frontiers of cardiomyopathy. Br Heart J. 1982;48:1-18.
5. Abelmann WH. Classification and natural history of primary myocardial disease. Prog Cardiovasc Dis. 1984;27:73-94.
6. Teske AJ, De Boeck BWL, Melman PG, Sieswerda GT, Doevendans PA, Cramer MJ. Echocardiographic quantification of myocardial function using tissue deformation imaging: a guide to image acquisition and analysis using tissue Doppler and speckle tracking. Cardiovasc Ultrasound. 2007;5:27.
7. Kato T, Noda A, Izawa H, Nishizawa T, Somura F, Yamada A, et al. Myocardial velocity gradient as a noninvasively determined index of left ventricular diastolic dysfunction in patients with hypertrophic cardiomyopathy. J Am Coll Cardiol. 2003;42:278-285.
8. Maron BJ, Shen WK, Link MS, et al. Efficacy of implantable cardioverter-defibrillators for the prevention of sudden death in patients with hypertrophic cardiomyopathy. N Engl J Med. 2000;342:365-373.
9. Maron BJ, McKenna WJ, Danielson GK, Kappenberger LJ, Kuhn HJ, Seidman CE, et al. American College of Cardiology/European Society of Cardiology Clinical Expert Consensus Document on hypertrophic cardiomyopathy. Eur Heart J. 2003;24:1965-1991.
10. Elliott PM, McKenna WJ. Hypertrophic cardiomyopathy. Lancet. 2004;363:1881-1891.
11. Monserrat L, Elliott PM, Gimeno JR, Sharma S, Penas-Lado M, McKenna WJ, et al. Non-sustained ventricular tachycardia in hypertrophic cardiomyopathy: an independent marker of sudden death risk in young patients. J Am Coll Cardiol. 2003;42:873-879.
12. Elliott PM, Poloniecki J, Dickie S, Sharma S, Monserrat L, Varnava A, et al. Sudden death in hypertrophic cardiomyopathy: identification of high-risk patients. J Am Coll Cardiol. 2000;36(7):2212-2218.
13. Dumont CA, Monserrat L, Soler R, Rodríguez E, Fernandez X, Peteiro J, et al. Interpretation of electrocardiographic abnormalities in hypertrophic cardiomyopathy with cardiac magnetic resonance. Eur Heart J. 2006;27(14):1725-1731.
14. Peteiro J, Bouzas A, Bouzas B, Castro-Beiras A. (This entry contains only author affiliations and manuscript history, not a reference. It should be removed or replaced with the complete publication details.)
15. Maron BJ, Wolfson JK, Ciro E, Spirito P. Relation of electrocardiographic abnormalities and patterns of left ventricular hypertrophy identified by two-dimensional echocardiography in patients with hypertrophic cardiomyopathy. Am J Cardiol. 1983;51:189-194.
16. Lemery R, Kleinebenne A, Nihoyannopoulos P, Aber V, Alfonso F, McKenna WJ. Q waves in hypertrophic cardiomyopathy in relation to the distribution and severity of right and left ventricular hypertrophy. J Am Coll Cardiol. 1990;16:368-374.
17. Kono T, Shimizu M, Ino H, Yamaguchi M, Terai H, Uchiyama K, et al. Diagnostic value of abnormal Q waves for identification of preclinical carriers of hypertrophic cardiomyopathy based on a molecular genetic diagnosis. Eur Heart J. 2004;25:246-251.
18. Charron P, Dubourg O, Desnos M, Isnard R, Hagege A, et al.

Diagnostic value of electrocardiography and echocardiography for familial hypertrophic cardiomyopathy in a genotyped adult population. Circulation. 1997;96:214-219.

19. Charron P, Dubourg O, Desnos M, Bouhour JB, Isnard R, Hagege A, et al. Diagnostic value of electrocardiography and echocardiography for familial hypertrophic cardiomyopathy in genotyped children. Eur Heart J. 1998;19:1377-1382.
20. Levy D, Salomon M, D'Agostino RB, Belanger AJ, Kannel WB. Prognostic implications of baseline electrocardiographic features and their serial changes in subjects with left ventricular hypertrophy. Circulation. 1994;90:1786-1793.
21. Shah PM, Adelman AG, Wigle ED, et al. The natural and unnatural history of hypertrophic obstructive cardiomyopathy. Circ Res. 1974;35(suppl II):II-179-II-195.
22. Loogen F, Kuhn H, Gietzen F, Losse B, Schulte HD, Bircks W. Clinical course and prognosis of patients with typical and atypical hypertrophic obstructive and hypertrophic nonobstructive cardiomyopathy. Eur Heart J. 1983;4(suppl F):145-153.
23. Koga Y, Itaya K, Toshima H. Prognosis in hypertrophic cardiomyopathy. Am Heart J. 1984;108:351-359.
24. Romeo F, Pelliccia F, Cristofani R, Martuscelli E, Reale A. Hypertrophic cardiomyopathy: is a left ventricular outflow tract gradient a major prognostic determinant? Eur Heart J. 1990;11:233-240.
25. McKenna WJ, Deanfield JE. Hypertrophic cardiomyopathy: an important cause of sudden death. Arch Dis Child. 1984;59:971-975.
26. Spirito P, Chiarella F, Carratino L, Zoni-Berisso M, Bellotti P, Vecchio C. Clinical course and prognosis of hypertrophic cardiomyopathy in an outpatient population. N Engl J Med. 1989;320:749-755.
27. Cecchi F, Olivotto I, Montereggi A, Santoro G, Dolara A, Maron BJ. Hypertrophic cardiomyopathy in Tuscany: clinical course and outcome in an unselected regional population. J Am Coll Cardiol. 1995;26:1529-1536.
28. Cannan CR, Reeder GS, Bailey KR, Melton LJ III, Gersh BJ. Natural history of hypertrophic cardiomyopathy: a population-based study, 1976 through 1990. Circulation. 1995;92:2488-2495.
29. Shapiro LM, Zezulka A. Hypertrophic cardiomyopathy: a common disease with a good prognosis—five-year experience of a district general hospital. Br Heart J. 1983;50:530-533.
30. Kofflard MJ, Waldstein DJ, Vos J, Ten Cate FJ. Prognosis in hypertrophic cardiomyopathy observed in a large clinic population. Am J Cardiol. 1993;72:939-943.
31. Maron BJ, Casey SA, Poliac LC, Gohman TE, Almquist AK, Aeppli DM. Clinical course of hypertrophic cardiomyopathy in a regional United States cohort. JAMA. 1999;281:650-655.
32. Spirito P, Seidman CE, McKenna WJ, Maron BJ. The management of hypertrophic cardiomyopathy. N Engl J Med. 1997;336(11):775-785.
33. Wigle ED, Rakowski H, Kimball BP, Williams WG. Hypertrophic cardiomyopathy: clinical spectrum and treatment. Circulation. 1995;92(7):1680-1692.
34. Wigle ED, Sasson Z, Henderson MA, et al. Hypertrophic cardiomyopathy: the importance of the site and extent of hypertrophy. Prog Cardiovasc Dis. 1985;28(1):1-83.
35. DeRose JJ, Banas JS, Winters SL. Current perspectives on sudden cardiac death in hypertrophic cardiomyopathy. Prog Cardiovasc Dis. 1994;36(6):475-484.
36. Stafford WJ, Trohman RG, Bilsker M, Zaman L, Castellanos A, Myerburg RJ. Cardiac arrest in an adolescent with atrial fibrillation and hypertrophic cardiomyopathy. J Am Coll Cardiol. 1986;7:701-704.