Prevalence of Risk Factors for Sudden Cardiac Death among Patients with Hypertrophic Cardiomyopathy in a Tertiary Care Centre in South India

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ABSTRACT

BACKGROUND

Hypertrophic Cardio-Myopathy (HCM) is the commonest genetic cardiovascular disease. Patients with HCM are at higher risk for sudden cardiac death (SCD) than the general population. There are some risk factors which identify patients with higher risk for SCD among HCM patients. There are very few studies from India regarding the prevalence of SCD risk factors among HCM patients. Studies have identified risk factors for sudden cardiac death (SCD) in patients with hypertrophic cardiomyopathy (HCM). We aimed to study the prevalence of established risk factors for SCD among Indian patients with HCM.

METHODS

A prospective registry for patients between 12 years and 85 years of age with HCM was started in Calicut Government Medical College, South India, from Jan 2016. Individual patients were assessed in detail with history, clinical examination, ECG, echocardiography, 24 hour Holter and treadmill test.

RESULTS

117 unrelated patients with HCM were studied. Mean age of the patients was 58 ± 11.5 years. 45.3% had no SCD risk factors as per AHA / ACC 2011 criteria for HCM. Rest of the patients had SCD risk factors as follows - family history of SCD in 6 %, NSVT in Holter in 18.8 %, unexplained syncope in previous six months in 18.8 %, abnormal BP response to treadmill exercise (9.8 %), maximum LV thickness ≥30 mm in 9.4 % and LVOT gradient ≥ 30 in 28 (24 %). Prevalence of apical HCM was 26.5 %.

CONCLUSIONS

There is high prevalence of apical HCM in India. Prevalence of conventional risk factors is low in Apical HCM. Prevalence of familial HCM and family history of SCD is low. Prevalence of other risk factors is comparable to studies from elsewhere.

KEYWORDS

Apical Hypertrophy, Hypertrophic Cardiomyopathy, Sudden Cardiac Death

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BACKGROUND

Hypertrophic Cardio-Myopathy (HCM) is the most common genetic cardiovascular disease. It affects 0.5 % of the general population.[1] In the natural history of patients with HCM, there is an increased risk of mortality due to sudden cardiac death (SCD), heart failure and stroke. The risk of SCD is not uniform in all patients. There are some established factors, presence of which has shown to increase the risk of ventricular arrhythmias and SCD.[2] The type of risk factor and strength of association of each factor with SCD is varying across studies.[3-11] For the primary prevention of SCD in patients with HCM, there are five established risk factors according to AHA / ACC guidelines. They are family history of SCD, non - sustained ventricular tachycardia (NSVT) in Holter, unexplained syncope in previous six months, abnormal BP response to treadmill exercise and maximum LV thickness of 30 or more mm.[12] ESC guidelines differ slightly from AHA / ACC guidelines in that it uses a risk calculation equation using above mentioned risk factors except abnormal BP response to treadmill exercise and additional risk factors namely age, Left atrial) size and left ventricular outflow tract (LVOT) gradient.[13]

Prevalence studies of these SCD risk factors are important to assess the burden of the problem and planning and policy making. As a tertiary care centre catering a large population of Kerala, a state of South India, a prospective registry of patients with hypertrophic cardiomyopathy was created. The present study looked in to the prevalence of SCD risk factors. As per our knowledge, no major studies looking in to prevalence of SCD risk markers have been published from India.

METHODS

The study was conducted in Government Medical College, Kozhikode, a tertiary care teaching hospital in south India. The study period was from Jan 2016 to Jan 2017. Study has got approval from the institutional ethics committee. Patients between 12 and 85 year age attending the department of cardiology and diagnosed to have HCM according AHA 2011 diagnostic criteria are included in this study. Patients with aortic valve disease with peak aortic velocity more than 3 m/s, those with blood pressure more than 150/100 or those with chronic kidney disease with creatinine clearance less than 30 ml per minute were excluded.

After informed consent, patients were assessed with detailed history, physical examination, 12 lead electrocardiography, echocardiography, 24 hour Holter and treadmill test. While considering the syncope history, those episodes with a definite cause other than a tachyarrhythmia like complete heart block, with a history suggestive a neurocardiogenic aetiology or if the syncope happened more than six months prior to inclusion in to the study were not taken as a risk marker. Family history of sudden cardiac death was positive if it happened in first or second degree relative with age less than fifty years. Sudden death was defined as natural death due to cardiac causes, within 1 h of the onset of acute symptoms or if un - witnessed, subjects should have been observed alive within 24 hours before the death.

Echocardiography was performed using vivid E9 (GE Healthcare, United Kingdom) by two cardiologists independently. Maximum LV hypertrophy was measured in parasternal short axis view and apical four chamber view depending on the type of hypertrophy. Type of LV Hypertrophy was divided into five – 1. Anterior septal hypertrophy, 2. Anterior and posterior septal hypertrophy, 3. Concentric hypertrophy, 4. All Other types other than apical and 5. Apical hypertrophy. Apical hypertrophy was defined as LV wall thickening confined to the most distal region at the LV with normal thickness in the basal region.

LVOTO gradient was measured in apical five chamber view. If the gradient in supine position was less than 30 mm of Hg, gradient was again assessed during strain phase of Valsalva manoeuvre and in standing position.

Exercise treadmill testing was performed on CASE, (GE Healthcare, UK) using Bruce protocol. Attaining a minimum workload of four METS was considered as a completed treadmill test. Systolic blood pressure was measured at the beginning and at two minutes intervals till five minutes post exercise. Any drop in systolic blood pressure from baseline value or peak exercise value for more than 20 mm of Hg or failure of blood pressure to rise more than 20 mm of Hg from baseline during exercise is considered positive response for SCD risk.

Statistical analysis was performed using SPSS software version 20 (IBM, New York, U.S.). Data are expressed as mean ± standard deviations and proportions. Comparison of nominal variables was performed using the chi-square test. p value of value <0.05 was considered statistically significant.

RESULTS

117 consecutive patients with HCM, between the age group 12 and 85 years were included in the study. Patient characteristics are summarized in table 1.

Description	N (%)
Male patients	86 (73.5 %)
Mean Age	58 ± 11.5 years
No symptoms	11 (9.5 %)
Dyspnoea	61 (52.1 %)
Chest pain	51(43.5 %)
Palpitations	12 (10.3 %)
Hypertension	43 (36.8 %)
Diabetes	25 (21.4 %)
Dyslipidaemia	9 (7.7 %)
Family history of HCM	21 (17.9 %)
Atrial Fibrillation	4 (3.4 %)

Table 1. Summary of Patient Characteristics Other than SCD Risk Factors (n=117)

Mean age of the patients were 58 ± 11.5 years. 73.5 % of them were males. 90.6 % of the patients had some symptoms at diagnosis. Those without symptoms were either detected during pre-operative evaluation for non - cardiac surgery, or presented for detailed evaluation when they had a relative with heart disease. Dyspnoea was the

most common presenting symptom. Other major symptoms were angina (43.5 %), Syncope (23 %) and palpitation (10.3 %). Only 28 (23.9 %) patients had significant LVOT obstruction at rest, in standing position or during Valsalva manoeuvre. ECG showed evidence of left ventricular hypertrophy and T wave changes in 87 % of patients. In 52 patients (44 %) in whom coronary angiogram was performed, 18 (15 %) patients had significant coronary artery disease and 34 (29 %) patients had normal coronaries or mild obstruction. Pattern of LV hypertrophy is summarised in table 2.

Types	Number of Patients
Atrial septal hypertrophy	36 (30.8 %)
Atrial and posterior septal hypertrophy	30 (25.6 %)
Concentric hypertrophy	14 (11.9 %)
Other	6 (5.1 %)
Apical hypertrophy	31 (26.5 %)

Table 2. Patterns of LV Hypertrophy

Prevalence of SCD risk factors are summarised in table 3. Successful treadmill testing was done only in 102 patients.

Risk Factor	Present Study	Vriesendorp et al	O'Mahony C, et al	Fananapazir L et al	Dimitrow PP et al
No. of patients n	117	706	1606	230	1306
Age	58 ± 11.5	49 ± 16	44.4 ± 15	39 ± 16	47
0 Risk factors	53 (45.3 %)	345 (49 %)	660 (41 %)	NA	NA
1 Risk factor	33 (28.3 %)	245 (35 %)	636 (40 %)	NA	NA
2 Risk factors	23 (19.7 %)	116 (16 %)	249 (15 %)	NA	NA
3 Risk factors	7 (6.0 %)	NA	51 (3 %)	NA	NA
4 Risk factors	1 (0.9 %)	NA	9 (0.6 %)	NA	NA
Resuscitated cardiac arrest	1 (0.9 %)	NA	NA	32 (14 %)	NA
Family history of SCD	7 (6 %)	141 (20 %)	481 (30 %)	68 (30 %)	274 (21 %)
NSVT in Holter	22 (18.8 %)	157 (22 %)	297 (18 %)	115 (50 %)	353 (27 %)
Unexplained syncope in previous six months	22 (18.8 %)	72 (10 %)	276 (17 %)	80 (35 %)	366 (28 %).
Abnormal BP response to treadmill exercise	10 (9.8 %)	89 (13 %)	158 (24 %)	NA	418 (32 %).
Maximum LV thickness ≥30 mm	11 (9.4 %)	46 (7 %)	116 (7 %)	NA	235 (18 %).

Table 3. Comparison of Six SCD Risk Factors in the Present Study with Those of Previous Studies

DISCUSSION

As far as we know, till date no sufficient epidemiological data is available with regard to the prevalence of SCD risk factors among patients with HCM from India. Age group of patients in present study is slightly older than the similar studies from western population.[14, 15, 16] This may be due to selection bias as most of the patients were symptomatic as well.

Number of female patients is less compared to male. This is a universal occurrence with unknown explanation. Although selection bias due to the high incidence of coronary heart disease among male patients and subsequent higher rate of cardiology evaluation among them was suggested, this was disproved in a Chinese and US population screening studies.[17,18,19]

The prevalence of definite familial HCM is low (17.9 %) in our study which is in contrast to the previous studies.[14,15,16] This is most likely due to inadequate family screening. Only 17 % of the eligible first - degree relatives did turn up for family screening. Due to the same reason, the detection rate of new cases by the family screening of index case was also low (4.8 % v/s 18 % in the previous reports.). But the fact that mean age of the patient cohort was high may in fact be reflecting a true higher prevalence of the sporadic form of the disease. Efforts are ongoing to complete the family screening and to know the true prevalence of familial disease in the registry population.

The most common type of hypertrophy on echocardiography is asymmetrical septal hypertrophy (56 %) which includes type one and type two (Table 2). Next common type is apical HCM (26.5 %). In this study there is high prevalence of apical HCM compared to western data (3 %).[20] Higher prevalence of apical hypertrophy ranging from 15 % to 25 % is present in studies from Japanese population.[20,21] Genotypic variability may be accounting for this difference in phenotype.

SCD Risk Factors

Table 3 shows comparison of prevalence of SCD risk factors in the present study to similar studies from large multinational registries from Europe and North America. The percentage of patients with at least one of the five risk factors in the present study (55 %) was similar to the reported values in two large scale studies published earlier by Vreiesendor et al[22] and O' Mahony et al[16] (51 % and 59 % respectively.)

The prevalence of individual risk factors vary considerably among the four studies shown in the table. In the case of the present study, the prevalence of family history of SCD is significantly low compared to the major studies.[14,15,16,22] This is explained obviously by the low prevalence of the familial form of the disease in the cohort.

The prevalence of NSVT in Holter (18.8 %) was similar to that in the study by O' Mahony et al, but much lower than those in the other studies.[14,15,16,22] This as well as the history of unexplained syncope is the commonest risk factor in the present study. The prevalence of unexplained syncope also more or less similar to that in the study by O'Mahony et al [14]. Except in the one study by Vriesendorp[22] et al, in other studies also, this risk factor was present in a considerable number of patients.

Proportion of patients with a hypotensive response during treadmill test was comparatively lower in our study (9.8 %). We have taken a low threshold of 4 or more METS as definition of successful treadmill test. This might not have been enough to bring about the hypotensive response. A quarter or more of patients had this response in the studies by O'Mahony et al[14] and Dimitrow PP.[16] These two studies were large studies with more than 1300 patients.

The proportion of patients with a maximum LVOT thickness more than or equal to 30 mm was low (9.4 %) similar to less than 10 % prevalence in other studies also, except the study by Dimitrow PP et al[16] which showed a prevalence of 18% probably attributable to its large sample size. SCD risk factors in apical versus non apical HCM

Apical HCM is considered as a relatively benign variant of HCM compared to other varieties. This was also looked in to in the present study. All of SCD risk factors except the history of unexplained syncope was low in patients with apical hypertrophy compared to rest of the HCM patients. (Table 4). This difference is statistically significant in case of abnormal BP response to treadmill exercise and maximum LV thickness ≥30 mm. Prevalence of history of unexplained syncope was high among patients with apical HCM but this difference was not statistically significant. Long term follow up studies with outcome measures are needed to establish the benign nature of this variant among our patients.

Risk Factor	Prevalence in Apical HCM	Prevalence in Non Apical HCM	P Value
Family history of SCD	0 (0 %)	7 (8.1 %)	0.10
NSVT in Holter	4 (12.9 %)	18 (20.9 %)	0.32
Unexplained syncope in previous six months	10 (32.2 %)	23 (26.7 %)	0.12
Abnormal BP response to treadmill exercise	0 (0 %)	10 (11.6 %)	0.04
Maximum LV thickness ≥30 mm	0 (0 %)	11 (12.8 %)	0.03

Table 4. Comparison of Six SCD Risk Factors of Apical Hypertrophy with Those of Non-Apical HCM

One patient had resuscitated cardiac arrest for him ICD was implanted subsequently. As per 2011 AHA / ACC guidelines 38 patients (32.5 %) had indications for ICD. 18 patients (15.4 %) require ICD as per ESC 2014 criteria. ESC guideline may underestimate the SCD risk in some population.[13] Although requirement for ICD is high as per the guidelines, only three patients agreed for the same.

Limitations

Although no larger studies are reported from India, compared to other international multicentre registries, the number of patients is low. Long term follow up is required for assessing strength of association of these risk factors with SCD in Indian population which is not done in the present study.

CONCLUSIONS

The present study looked in to the prevalence of SCD risk markers in Indian patients with hypertrophic cardiomyopathy. Prevalence of familial HCM and family history of SCD is low. Prevalence of other risk factors is comparable to studies from elsewhere. The prevalence of apical HCM is high in this cohort. The prevalence of SCD markers is low in patients with apical HCM than in non-apical HCM.

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