Available online at www.sciencedirect.com
SCIENCE DIRECT
ELSEVIER
125
JNMU
Journal of Nanjing Medical University, 2008, 22(2):125–129
www.elsevier.com/locate/jnmu
Research Paper

Clinical analysis of 121 patients with hypertrophic cardiomyopathy☆

Shilu Zhao, Hengfang Wu, Jizhen Ma, Xiangjian Chen, Junhong Wang, Di Yang, Jinan Zhang*
Institute of Cardiovascular Disease, the First Affiliated Hospital of Nanjing Medical University, Nanjing 210029, Jiangsu Province, China
Received 17 January 2008

Abstract

Objective: Several studies have analyzed the clinical profiles of patients diagnosed with hypertrophic cardiomyopathy(HCM). We sought to identify its characteristics in a regional cohort of Nanjing and its adjacent region. **Methods:**Clinical profiles of 121 referred patients were collected and analyzed retrospectively. Data including family history, clinical symptoms, electrocardiography and recent echocardiography were collected. **Results:** The mean age of this population was 42±17 years(range from 6 to 76) at diagnosis of HCM. Most patients were male(60%). 48 patients(39.7%) has a family history, 19 had a sudden death in a first degree relative and 96(79.3%) were recognized with cardiac symptoms. Left ventricular outflow obstruction (gradient≥30 mmHg at rest) was presented in 26(21.5%) patients. ECG abnormalities comprised of arrhythmia in 54(51.4%) and abnormal T wave in 72(68.6%) patients. FS were higher in female than male(P= 0.001). Among younger patients(age ≤ 50 years), LVDd and LVWP were smaller in females than males(P= 0.042 & 0.023 respectively). In older patients(age > 50 years), LVDs was higher in male(P= 0.016) and EF was higher in female (P= 0.048). **Conclusion:**HCM patients in the region are almost diagnosed with the presentation of cardiac symptoms; those without any symptoms could be recognized by ECG and family screening. Most cardiac hypertrophy affects the interventricular septum. LVDd, LVWP, LVDs, FS and EF showed significant differences related to age and gender.

Key words: Hypertrophic cardiomyopathy; Arrhythmia; Electrocardiography; Echocardiography

INTRODUCTION

Hypertrophic cardiomyopathy(HCM) is a primary and heterogeneous cardiac disease that affects sarcomeric proteins, resulting in hypertrophy, myofibrillar disorganization and enhanced interstitial fibrosis. The main hemodynamic feature is diastolic dysfunction with increased filling pressure, delayed relaxation, and increased muscle stiffness. It is an important cause of sudden death in the young and heart failure patients of all ages[1-5]. Previous echocardiographic screening studies in China have estimated that the prevalence of HCM is about 0.16%(160 per 100,000)[6], suggesting that at least 1 million cases exist in China. However, it is generally acknowledged that in most cardiology practices relatively few patients with HCM are diagnosed, and many patients miss clinical recognition, including some at high risk for sudden death, many of whom, could probably achieve prophylactic protection with implantable defibrillators. Therefore, the aim of the present investigation was to identify the clinical profile, in which HCM was diagnosed in the region of Nanjing and its adjacent region. These insights will constitute an important step in providing clues for cardiologists, permitting both clinical diagnosis and management of this patient population.

MATERIALS AND METHODS

Study sample

The present study cohort comprised of 121 consecutively enrolled patients with HCM, evaluated at the First Affiliated Hospital of Nanjing Medical University, Jiangsu province, China, from July of 2000 to April of 2007. Data was collected on family history of HCM, clinical symptoms, electrocardiogram and recent echocardiography(or nearest to clinical visit) and the

☆ This work was supported by a grant from National Natural Science Foundation of China (30570745)
*Corresponding author
*E-mail address:*Jinanzh506@yahoo.com

clinical triggers leading to the diagnosis of HCM were retrieved from the medical records, they were summarized in 7 categories(***Tab 1***).

Diagnosis of HCM

The diagnosis of HCM was based on the echocardiographic demonstration of a hypertrophied(wall thickn=13 mm during diastole) nondilated left ventricle in the absence of another cardiac or systemic disease that could account for cardiac hypertrophy[1,7-10].

Echocardiography

Echocardiography was performed with commercially available instruments. The greatest thickness measured at any site in the left ventricle wall was considered to be the maximal thickness[7,8]. The peak instantaneous left ventricle outflow gradient at rest was estimated with continuous wave Doppler[8,11].

Electrocardiogram

The scalar 12-lead electrocardiograms(standard calibration 10 mm/1mv) obtained at or nearest to the time of the initial diagnostic echocardiographic study were analyzed. Electrocardiogram was performed in a routine fashion in the supine position during quiet respiration and recorded at 25mm/s. Each record was measured manually by a single observer.

Ambulatory Holter ECGs

Ambulatory Holter ECG recording was obtained in a standard fashion with a portable tape recorder. In each case the arrhythmias were verified by experienced cardiologists who were blinded to the clinical and electrocardiography.

Statistical analysis

Statistical analyses were performed using SPSS 10.0. Data are expressed as means ± SD. The chi-square test was used when that variable was categorical and Student's *t* test when it was continuous. All *P* values are for 2-tailed test, with $P < 0.05$ regarded as statistically significant.

RESULTS

Triggers for clinical diagnosis

Of the 121 HCM cohort members, 96(79.3%) were recognized with cardiac symptoms, while the remaining patients(20.7%, $n = 25$) were recognized without any cardiac symptoms, including 10(8.3%) as a result of abnormal ECG after routine physical examination, and 15(12.4%) by family screening(***Tab 1***).

Tab 1 **Trigger for clinical diagnosis**

Trigger	*n* (%)
Chest distress and/or palpitation	56(46.3%)
Exertional chest pain and/or dyspnea	9(7.4%)
Dizziness or near syncope	2(1.7%)
Syncope	10(8.3%)
Other cardiovascular disease	19(15.7%)
Abnormal ECG results of routine medical examination	10(8.3%)
Family screening	15(12.4%)

General state of study population

The clinical characteristics of the 121 patients with HCM are listed in ***Tab 2***. The majority of the patients were male(60%). The age of onset was mainly concentrated between 30 and 60 years old. Among 105 patients' available ECG records and 56 Holter ECG results, we recognized arrhythmia in 54(51.4%) patients. 26 of those patients presented left ventricular outflow tract gradient(LVOTG)≥ 30 mmHg. Among the 26 patients, 14 were female. Echocardiographic features (***Tab 3***) suggesting Shortening fraction(FS) was higher in female than in males(40.1 ± 5.83% & 6.7 ± 4.8% $P = 0.001$). A subset of 53 highrisk[12-14] patients (43.8%) were identified(***Tab 2***) based on following factors:①Family history of HCM with sudden cardiac death ②History of syncope or presyncope ③Massive LV hypertrophy(septal wall thickness ≥ 30 mm) ④Nonsustained ventricular tachyarrhythmias(NSVT) ⑤presence of atrial fibrillation ⑥survived sudden cardiac death.

Comparative analysis

Gender

Generally speaking, women were more commonly diagnosed with HCM than men(88% vs 77%). After the onset of symptoms, men were more likely to be identified because of ECG examination among those without symptoms(21% vs 8%), while women were more likely to be identified by family screening(10% vs17%) as will as it being found as a trigger for other CV diseases(7% vs 10%)(shown in ***Fig 1***).

Age

Younger patients with HCM(age ≤ 50years) were more frequently diagnosed after the onset of symptoms, than older patients(88% vs77%). Among those without cardiac symptoms, older samples were most often diagnosed by ECG examination and family screening (15% vs 10%) especially by ECG examination(23% vs7%, $P = 0.02$) and less commonly diagnosed because of other CV disease(6% vs 13%)(shown in ***Fig 2***).

Phenotypic features

Patients with HCM with LV outflow obstruction (gradient ≥ 30 mmHg at rest) were more frequently diagnosed because of onset of symptoms(93% vs 77%) and less commonly by ECG examination, family screen-

Tab 2 **Demographic and clinical characteristics at presentation** ($\bar{x} \pm s$)

characteristic	All patients	Male(n = 73)	Female(n = 48)	P value
Age at diagnosis(yrs)	42 ± 17	43 ± 16	42 ± 19	0.90
< 30	28(23.1%)	15(20.5%)	13(27.1%)	
30–60	75(62.0%)	49(67.1%)	26(54.2%)	
⩾ 60	18(14.9%)	9(12.3%)	9(18.8%)	
Family history of HC	48(39.7%)	26(35.6%)	22(45.8%)	
Family history of HC with sudden cardiac death	19(15.7%)	11(15.1%)	8(16.7%)	
LVOTG ⩾ 30 mmHg	26(21.5%)	12(16.4%)	14(29.2%)	
Case of high risk	53(43.8%)	32(43.8%)	21(43.8%)	
Types of hypertrophy cardiomyopathy				
Apical	18(14.9%)	12(16.4%)	6(12.5%)	
Asymmetrical septal	99(81.8%)	58(79.5%)	41(85.4%)	
Others	4(3.3%)	2(2.7%)	2(4.2%)	
Electrocardiographic features	105	67	38	
sinus bradycardia	20(19.0%)	12(17.9%)	8(21.1%)	
atrial fibrillation	7(6.7%)	4(6.0%)	3(7.9%)	
preexcitation syndrome	2(1.9%)	1(1.5%)	1(2.6%)	
NSVT*(based on Holter ECG)	12(21.4%)	9(27.3%)	3(13.0%)	
right bundle branch block	5(4.8%)	0	5(13.2%)	
immaturity right bundle branch block	1(1%)	1(1.5%)	0	
left bundle branch block	3(2.9%)	3(4.5%)	0	
Atrial-ventricular block				
First degree	1(1%)	1(1.5%)	0	
Second degree	1(1%)	1(1.5%)	0	
Third degree	2(1.9%)	1(1.5%)	1(2.6%)	
Abnormal Q wave	35(33.3%)	19(28.4%)	16(42.1%)	
(depth=1/4R or width =0.04s)				
T-wave inversion	72(68.6%)	54(80.6%)	18(47.4%)	
Giant negative T wave(=10mm)	18(17.1%)	17(25.4%)	1(2.6%)	
Echocardiographic features				
LAD(mm)	40.4 ± 6.4	40.0 ± 6.3	41.2 ± 6.6	0.30
LVDd(mm)	44.8 ± 6.4	45.6 ± 6.1	43.7 ± 5.7	0.10
LVDs(mm)	27.9 ± 5.0	29.0 ± 4.6	26.3 ± 5.2	0.01
IVS(mm)	18.7 ± 5.1	18.6 ± 5.1	18.8 ± 5.2	0.80
13–15	11(11.1%)	5(8.6%)	6(14.6%)	
16–19	38(38.4%)	21(36.2%)	17(41.5%)	
20–24	36(36.4%)	23(39.7%)	13(31.7%)	
25–29	15(15.2%)	10(17.2%)	5(12.2%)	
=30	1(1%)	0	1(2.4%)	
LVPW(mm)	11.5 ± 2.7	11.8 ± 2.8	11.1 ± 2.6	0.15
FS(%)	38.1 ± 5.5	36.7 ± 4.8	40.1 ± 5.8	0.001
EF(%)	67.9 ± 7.3	67.0 ± 6.6	69.2 ± 8.3	0.13

LAD =Left atrial diameter, LVDd =Left ventricular end-diastolic internal dimension, LVDs= Left ventricular end–systolic internal dimension, IVS=Interventricular septum thickness, LVPW= Left ventricular posterior wall thickness, FS =shortening fraction, EF = Left ventricular ejection fraction, LVOTG= Left ventricular outflow tract gradient occurrence. NSVT= nonsustained ventricular tachyarrhythmias.

ing and other CV disease(8% vs 18%;8% vs 14%;7.7% vs 8.5% respectively)(shown in ***Fig 3***).

High risk

The detection rate of patients with HCM who were judged to be at high risk for sudden death by the trigger of onset of symptoms and family screening(82% vs 80%, 13% vs 11.7% respectively) were higher than those by ECG examination and other CV disease(12% vs18%, 7% vs 9% respectively)(shown in ***Fig 4***).

DISCUSSION

At present, the diagnosis of HCM is based on the examination of echocardiography, and this relies on the skill and judgment of the operator. In fact a patient (especially one whose hypertrophy is not very severe) owing of different operator, may go undetected.

The condition is characterized by its heterogeneity, its broad phenotypic expression and complexity has consistently generated uncertainty. It can present during any phase of life, from infancy and has been found in patients older than 90 years old[15]. Its pathological findings can vary widely from mild or focal hypertrophy, to marked septal hypertrophy and LV outflow tract obstruction. Similarly, clinical symptoms in HCM range from asymptomatic status to heart failure, atrial fibrillation, angina, syncope and sudden death. Often HCM is misdiagnosed and treated as coronary artery disease if patient does not take detailed examination. In our cohort, there were 19 patients who had other cardiovascular disease and were recognized by coronary

Tab 3 **Gender-based comparison of echocardiographic parameters**

	males	females	*P* value
Younger patients(≤ 50yrs)			
LAD	39.2–6.8	39.9–6.6	
LVDd	45.7–6.6	42.2–5.8	0.04
LVDs	28.6–5.2	25.8–6.3	
IVS	18.9–5.6	19.9–5.6	
LVWP	11.6–2.9	10.0–1.8	0.02
FS	37.1–5.7	40.3–5.8	
EF	67.6–7.9	68.9–9.8	
Older patients(> 50yrs)			
LAD	40.9–5.7	42.4–6.4	
LVDd	45.5–5.4	45.2–5.4	
LVDs	29.7–3.7	26.7–4.2	0.02
IVS	18.3–4.3	17.9–4.6	
LVWP	12.1–2.7	12.0–2.8	
FS	36.1–3.6	39.9–5.9	
EF	66.3–4.6	69.5–6.8	0.05

LAD =Left atrial diameter, LVDd =Left ventricular end-diastolic internal dimension, LVDs= Left ventricular end-systolic internal dimension, IVS=Interventricular septum thickness, LVPW= Left ventricular posterior wall thickness, FS =shortening fraction, EF = Left ventricular ejection fraction, LVOTG= Left ventricular outflow tract gradient occurrence. NSVT= nonsustained ventricular tachyarrhythmias.

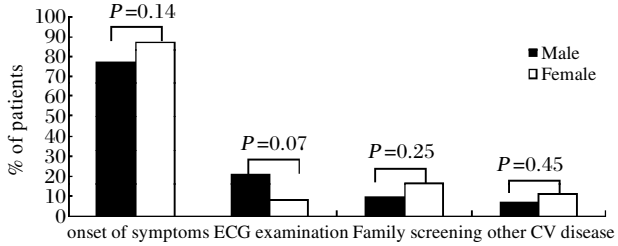

Fig 1 Clinical triggers for the initial diagnose with respect to gender in 121 patients with HCM

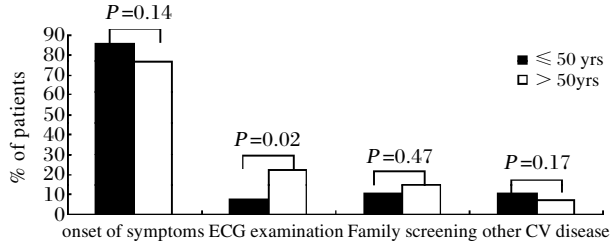

Fig 2 Clinical triggers for the initial diagnose with respect to age in 121 patients with HCM

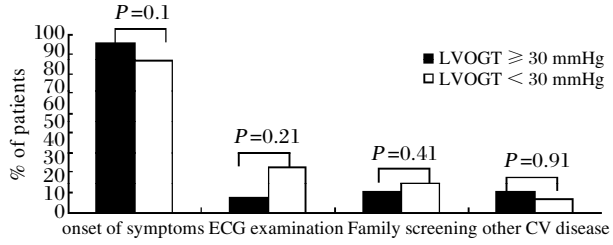

Fig 3 Clinical triggers for the initial diagnose with respect to LV outflow tract gradient(LVOTG) in 121 patients with HCM

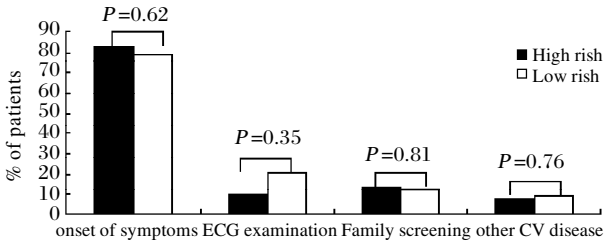

Fig 4 Clinical triggers for the initial diagnose with respect to high risk in 121 patients with HCM

arteriongraphy, however most of them showed apical hypertrophy.

In our sizable HCM cohort(which is largely regionally limited), the average age of presentation among patients(about 42 years) was similar to those reported among Caucasian patients(about 45 years)[1,16-17], but it was younger than research conducted in Hong Kong (about 54 years)[18]. The prevalence of the asymmetrical septal variant of HCM in our cohort was higher(82%) than that reported in Hong Kong(34%) also[18]. Whether the sample choice or regional differences lead to discrepancy, further analysis will need to be undertaken.

The high percentage of patients who were recognized with cardiac symptoms(79%) was far higher than that reported in Caucasian populations(54%)[19]. Chinese people have less opportunity to take routine medical examinations, which might make the difference. Consequently, those patients without any cardiac symptoms don't take any medical examination, and they were evaded from clinical recognition, including some at high risk for sudden death, for whom prophylactic protection may have been achieved with implantable defibrillators[20,21],therefore they were seldom identified compared to Caucasian populations.

Another question is the Holter ECG. It is fairly standard to evaluate the status of HCM patients, but it is not always a routine examination for them. Because some patients refused to take the examination, or clinician ignored the risk stratification, there only 56 patients', Holter ECG were achieved(46.3%)finally. The Holter ECG profile from our data demonstrated more than 21% (among 56 available patients) had non-sustained ventricular tachyarrhythmias which is one of the factors lead to sudden death. It is slightly higher than a previous report by Monserrat *et al*[22](19.6%), although their monitoring time was longer[mean(41 ± 11)h] compared to 24 hours.

In the present study, all the ECG data(except right bundle branch block) were more frequently identified especially among males, followed by T-wave inversion and abnormal Q wave. Although non-specific, it could provide some clue for clinical cardiologists to assess the possible diagnosis of HCM. In patients without any

symptoms, we can diagnose by routine examination of ECG, ECG can be expressed more valuably among those males, older, low risk, with LVOGT＜30 mmHg. Female patients, older, being of high risk, LVOGT＜30 mmHg had a higher chance to be recognized by family screening. Missed diagnosis often occurred in this group. This was supported by other cardiographic studies which revealed that females with HCM presented with a smaller left ventricular end-systolic internal dimension and higher shortening fraction (which were differ from the Hong Kong study[18]). So by a gender-based comparison of echocardiographic parameters, the younger male patients presented a significantly larger left ventricular end-diastolic internal dimension, and left ventricular posterior wall thickness than females. Among older patients, the left ventricular end-systolic internal dimension was also significantly larger than females(but not for the left ventricular posterior wall) while their left ventricular ejection fraction was significantly lower than females.

Risk stratification in our study were considered in 6 categories, all those are known or suspected to be risk factors for sudden cardiac death including those with an abnormal blood pressure response to exercise. Patients who had one or more risk factors were considered as high risk. In our study the latter factor was unavailable, but even if we don't consider the latter factor,we found our data of patients at high risk was more higher than prior reported by Barry J. Maron et al[14] (43.8% vs23%), so there may be two reasons that could explain it: ①The enrolled patients of the cohort, which was more fewer in our cohort than theirs(so our cardinal number was smaller) ②The different prevalence of hypertrophic cardiomyopathy from different racial groups ③The very different habits exercise and eating habbits.

References

[1] Maron BJ. Hypertrophic cardiomyopathy: a systematic review. *JAMA* 2002; 287:1308-20.

[2] Paulo Harada, Fernando Morita, Edmundo Arteaga, Afonso Akio Shiozaki, Jussara Bianchi Castelli. Case 01/2008-A Young Female Patient with the Familial Form of Hypertrophic Cardiomyopathy, who Evolved with Syncope, Complex Ventricular Arrhythmia and Cardiogenic Shock. *Arq Bras Cardiol* 2008; 90: 63-72

[3] Maron BJ, Maron MS, Lesser JR, Hauser RG, Haas TS, Harrigan CJ, *et al.* Sudden Cardiac Arrest in Hypertrophic Cardiomyopathy in the Absence of Conventional Criteria for High Risk Status. *Am J Cardiol* 2008;101:544-7.

[4] Alcalai R, Seidman JG, Seidman C. Genetic Basis of Hypertrophic Cardiomyopathy: From Bench to the Clinics. *J Cardiovasc Electrophysiol* 2008;19:104-10.

[5] Yao EF. Hypertrophic cardiomyopathy. *Aviat Space Environ Med* 2008; 79:147-9.

[6] Zou Y, Song L, Wang Z, Ma A, Liu T,Gu H, *et al.* Prevalence of idiopathic hypertrophic cardiomyopathy in China: a population-based echocardiographic analysis of 8080 adults. *Am J Med* 2004 ; 116:14-8.

[7] Pearlman AS. Hypertrophic cardiomyopathy:role of echocardiography in diagnosis and management. *Am Heart Hosp J* 2007;5:184-8

[8] Klues HG, Schiffers A, Maron BJ. Phenotypic spectrum and patterns of left ventricular hypertrophy in hypertrophic cardiomyopathy: morphologic observations and significance as assessed by two-dimensional echocardiography in 600 patients. *J Am Coll Cardiol* 1995; 26: 1699-708.

[9] Spirito P, Bellone P, Harris KM, Bernabo P, Bruzzi P, Maron BJ. Magnitude of left ventricular hypertrophy and risk of sudden death in hypertrophic cardiomyopathy. *N Engl J Med* 2000; 342:1778-85.

[10] Devlin AM, Moore NR, Ostman-Smith I. A comparison of MRI and echocardiography in hypertrophic cardiomyopathy. *Br J Radiol* 1999; 72:258-64.

[11] Maron MS, Olivotto I, Betocchi S, Casey SA, Lesser JR, Losi MA *et al.* Effect of left ventricular outflow tract obstruction on clinical outcome in hypertrophic cardiomyopathy. *N Engl J Med* 2003; 348: 295-303.

[12] Autore C, Quarta G, Spirito P. Risk stratification and prevention of sudden death in hypertrophic cardiomyopathy. *Curr Treat Options Cardiovasc Med* 2007; 9:431-5

[13] Miller MA, Gomes JA, Fuster V. Risk stratification of sudden cardiac death in hypertrophic cardiomyopathy. *Nat Clin Pract Cardiovasc Med* 2007; 4:667-76.

[14] Li M, Wang QB, Cheng K. Long term follow-up results of 199 patients with hypertrophic cardiomyopathy. *Zhonghua Xin Xue Guan Bing Za Zhi (in Chinese)* 2007; 35:988-91.

[15] 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; 281:650-5

[16] Maron MS, Olivotto I, Betocchi S, Casey SA, Lesser JR, Losi MA *et al.* Effect of left ventricular outflow tract obstruction on clinical outcome in hypertrophic cardiomyopathy. *N Engl J Med* 2003; 348: 295-303.

[17] Wigle ED, Rakowski H, Kimball BP, Williams WG. Hypertrophic cardiomyopathy. Clinical spectrum and treatment. *Circulation* 1995; 92:1680-92.

[18] Maron BJ, Shen WK, Link MS, Epstein AE, Almquist AK,Daubert JP *et al.* Efficacy of implantable cardioverter-defibrillators for the prevention of sudden death in patients with hypertrophic cardiomyopathy. *N Engl J Med* 2000; 342:365-73.

[19] Adabag AS, Kuskowski MA, Maron BJ. Determinants for Clinical Diagnosis of Hypertrophic Cardiomyopathy. *Am J Cardiol* 2006; 98:1507-11.

[20] 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; 281:650-5.

[21] Ho HH, Lee KL, Lau CP, Tse HF. Clinical Characteristics of and Long-term Outcome in Chinese Patients with Hypertrophic Cardiomyopathy. *Am J Med* 2004; 116:19-23.

[22] Monserrat L, Elliott PM, Gimeno JR, Sharma S, Penas-Lado M, Mckenna WJ. Non-sustained ventricular tachycardia in hypertrophic cardiomyopathy: an independent marker of sudden death risk in young patients. *J Am Coll Cardiol* 2003; 42:873-9.