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Clinical Profile of Hypertrophic Cardiomyopathy Identified De Novo in Rural Communities

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OBJECTIVES The purpose of this study was to assess the extent to which hypertrophic cardiomyopathy (HCM) exists unsuspected and undetected in the general population.

BACKGROUND Hypertrophic cardiomyopathy is a disease with diverse natural history for which the potential to produce adverse consequences has been emphasized. However, the possibility of this disease remaining clinically dormant for many years has not been as widely appreciated. Certainly, the clinical recognition of previously undiagnosed patients with HCM may be advantageous by permitting risk stratification for sudden cardiac death or for timely pharmacologic therapy when symptoms intervene.

METHODS We prospectively conducted an echocardiographic survey in 64 primarily rural communities within Minnesota (populations <10,000) over a 33-month period.

RESULTS A total of 15,137 echocardiograms were performed at the request of primary care physicians for the purpose of excluding cardiovascular abnormalities. Hypertrophic cardiomyopathy was identified in 44 patients during the survey (0.29%), and 29 of these patients (0.19% of the 15,137 echocardiograms) had not been previously identified as having cardiac disease or HCM. At diagnosis, ages were 16 to 87 years (mean 57); 14 patients were ≥60 years of age, and only two were <30 years. Twenty-four patients (83%) had either no or only mild or transient symptoms; 5 (17%) evidenced severe functional limitation; in eight patients the onset of symptoms had been deferred until ≥70 years of age. Basal left ventricular outflow obstruction (gradients 20 to 82 mm Hg) was evident in 11 patients (38%). Relatively mild phenotypic expression of the disease was substantiated by localized patterns of left ventricular wall thickening occurring more commonly than diffusely distributed hypertrophy (48% vs. 7%, respectively), and electrocardiograms that were frequently normal (about 25%) and rarely showed evidence of left ventricular hypertrophy (10%).

CONCLUSIONS These prospectively assembled data show that HCM may remain clinically dormant and undetected within community-based rural populations for many years (often to advanced ages) with a not inconsequential prevalence similar to that of HCM in the general population. (J Am Coll Cardiol 1999;33:1590–5) © 1999 by the American College of Cardiology

Hypertrophic cardiomyopathy (HCM) is a primary and heterogeneous cardiac disease that may result in premature cardiovascular death, but is also consistent with normal longevity with little or no disability (1–10). The extent to which HCM can remain clinically occult and undetected for many years remains unresolved (6–10). Indeed, the occurrence of unsuspected HCM in the general population has recently been reported to be 0.17% (about 1:500) (11), suggesting that this disease may be more common than previously thought. However, many of the clinical data available in HCM have been generated from a few tertiary referral centers in urban settings, largely comprising highly selected and preferentially referred patient populations (1,2,12,13). Therefore, in the present study, we took advantage of a unique circumstance at our institution in which echocardiographic services are routinely performed in rural areas of Minnesota (and Wisconsin) for patients suspected of having cardiac disease. This circumstance permitted us to prospectively assemble data relevant to the occurrence and clinical profile of HCM in community-based rural populations.

METHODS

Patient selection. The present data acquisition took advantage of a long-standing outreach cardiology program administered by the Minneapolis Heart Institute. Mobile

From Cardiovascular Research Division, Minneapolis Heart Institute Foundation, Minneapolis, Minnesota. Each of the authors contributed significantly to the submitted work including: 1) conception and design of the project and/or interpretation of data; 2) drafting and/or revising the manuscript, and 3) final approval of the submitted manuscript.

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Abbreviations and Acronyms

CI = confidence interval
ECG = electrocardiogram
HCM = hypertrophic cardiomyopathy

vans equipped with two-dimensional echocardiographic instruments systematically make scheduled visits on request to 64 primary care nonspecialty clinics, offices and hospitals (which are without echocardiographic capability), to perform diagnostic studies. These echocardiographic studies are performed on a daily basis largely in rural regions throughout Minnesota and also Wisconsin (primarily communities of <10,000 in population). Patients at these sites were scheduled in advance for complete diagnostic echocardiographic studies for the purpose of excluding cardiovascular abnormalities, at the discretion of primary care physicians, general internists, pediatricians and occasionally clinicians with training specifically in cardiovascular diseases.

The present study represents a prospectively conducted survey of echocardiographic studies obtained at all outreach sites over the 33-month period from December 1993 to March 1996. This diagnostic echocardiography program involved 30 Minnesota counties with a combined population of 2,700,000 constituting 60% of the overall state population. Also included were five adjacent counties in Western Wisconsin with a combined population of 190,000. Studies were performed by six highly experienced echocardiography technicians (cumulative 75 years of imaging experience), each of whom had received specific advance training focused on recognition of the HCM phenotype (14,15). Those echocardiographic studies that were judged on site to be potentially diagnostic or suggestive of HCM were subsequently reviewed by the senior investigator (B.J.M.) in Minneapolis.

Echocardiography. Echocardiographic studies were performed with commercially available Hewlett-Packard Sonos 1000 or 2000 series instruments using 2.5-MHz transducers (Andover, Massachusetts) in a standard fashion (14). Hypertrophic cardiomyopathy was diagnosed (with two-dimensional echocardiography) by virtue of a hypertrophied, nondilated left ventricle (wall thickness, >13 mm) in the absence of another cardiac or systemic disease capable of producing the magnitude of left ventricular hypertrophy observed (14,16). Extent and distribution of left ventricular hypertrophy were assessed from the two-dimensional image with the site of maximum wall thickness identified, as previously described (14). Peak instantaneous left ventricular outflow tract gradient was estimated with continuous wave Doppler imaging under basal conditions (17).

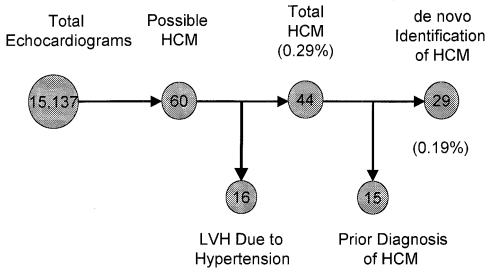

Figure 1. Flow diagram summarizing the echocardiographic findings and identification of hypertrophic cardiomyopathy (HCM) in the overall patient study group from rural, primary medical practice. LVH = left ventricular hypertrophy.

RESULTS

Echocardiographic diagnosis of HCM. Over the 33-month study period, 15,137 echocardiograms were obtained, and 60 were initially judged on site to be possibly diagnostic of HCM (Fig. 1). Of these 60 patients, 16 were excluded after careful inspection of the clinical record revealed a history of systemic hypertension, judged sufficient in magnitude and duration to account for the extent of left ventricular wall thickening evident in that patient (18). Of the remaining 44 patients (0.29%; 95% confidence interval [CI]: 21, 39), 15 proved to have a prior diagnosis of HCM upon retrospective review of the case records. Therefore, the final 29 patients (0.19% of the overall study group; 95% CI: 13, 27) were patients in whom HCM was identified de novo as part of the present study (Table 1, Fig. 1).

Patients with HCM identified de novo

INDICATIONS FOR ECHOCARDIOGRAPHIC STUDY. The 29 HCM patients identified for the first time in this study had their diagnostic echocardiograms performed for a variety of reasons. The primary clinical indications were: 1) recent and initial onset of symptoms or a clinical event presumed to be cardiovascular-related (16 patients; 55%), including three with a cerebrovascular accident; 2) a heart murmur (11 patients; 38%), or 3) an abnormal 12-lead electrocardiogram (ECG) performed as part of a routine examination (two patients; 7%). Of note, of the 11 patients in whom identification of a murmur played a major role in the initial diagnosis, five proved to have no outflow gradient on the diagnostic echocardiogram.

CLINICAL PROFILE. At diagnosis, the patients were 16 to 87 years of age (mean 57); 14 were ≥60 years of age, and only two were <30 years (Fig. 2). Fifteen patients (51%) were female, and all were white. At the time of diagnosis, 12 patients (41%) were judged to have no functional limitation, although four of these had experienced transient symptoms such as presyncope or syncope (Fig. 2); 12 others (41%) had mild exertional symptoms (functional class II), and five (18%) had severe symptoms and functional limitation (class III). In eight of the latter 17 functionally limited patients,

Table 1. Clinical, Demographic, Echocardiographic and Electrocardiographic Findings in 27 Patients Identified with HCM De Novo in Rural Communities

No.	Age (yr)/ Gender	Indication for Echocardiogram	NYHA FC	Age at Onset of Symptoms (yr)	Echocardiogram							Electrocardiogram						Family History of HCM
					LV Segments (mm)			Proximal (P)/ Distal (D)*	LVOTG† (mm Hg)	LVID (mm)	LA (mm)	NL	AF	LVH	ST-T	Q Waves	Mild HPT	
					AVS	PVS	ALFW											
1	45/M	Routine ECG	1	None	17	—	17	P = D	0	40	38	0	0	0	0	+	0	0
2	54/M	Symptoms	1	None	20	17	—	P = D	0	45	41	0	0	0	+	0	0	0
3	49/F	Murmur	2	25	18	17	—	D > P	25	37	44	0	0	0	0	+	0	+‡
4	36/M	Murmur	2	11	18	—	—	P > D	82	48	41	+	0	0	0	0	0	+
5	64/M	Murmur	1§	None	22	—	—	P > D	58	56	45	0	0	0	+	+	0	0
6	82/F	Murmur	3	81	19	—	—	P > D	64	44	42	0	0	0	0	+	+	0
7	46/M	Murmur	1§	None	15	23	—	D > P	0	46	45	0	0	+	0	0	0	+
8	23/F	Murmur	2	21	30	29	—	D > P	0	31	42	0	0	0	+	0	0	+‡
9	60/M	Murmur	1	None	19	17	—	P > D	20	55	41	+	0	0	0	0	+	0
10	77/F	Symptoms	2	75	20	—	—	D > P	0	44	54	0	+	+	+	0	0	0
11	73/F	Symptoms	2	68	18	—	—	P > D	28	37	47	0	0	0	+	0	+	0
12	37/F	Symptoms	3	27	19	28	—	D > P	0	35	27	0	0	+	0	+	0	+‡
13	72/F	CVA	2	72	20	—	—	P > D	33	35	28	0	0	0	+	0	0	0
14	36/M	Murmur	1	None	20	17	17	P = D	0	40	40	0	0	0	0	+	+	0
15	41/F	Symptoms	1	None	18	—	—	P = D	0	43	34	0	0	0	+	0	0	+
16	36/F	Symptoms	2	None	18	30	—	D > P	0	40	39	0	0	0	+	+	0	+‡
17	58/M	Symptoms	2	54	18	—	—	P > D	0	43	35	+	0	0	0	0	0	0
18	86/F	CVA	3	83	28	—	18	P = D	0	36	48	0	+	0	+	+	+	0
19	78/F	CVA	2	71	28	—	20	D > P	53	38	50	0	+	0	+	0	+	0
20	16/M	Murmur	1	None	18	—	—	P > D	0	55	43	+	0	0	0	0	0	0
21	63/M	Symptoms	3	62	22	22	18	P = D	0	51	49	0	+	0	+	0	0	+
22	78/F	Symptoms	1	None	14	—	14	P = D	0	31	40	+	0	0	0	0	0	0
23	84/F	Symptoms	3	80	18	19	—	P = D	0	36	37	+	0	0	0	0	0	0
24	87/F	Symptoms	2	Unknown	19	—	—	P > D	60	31	32	0	0	0	0	0	+	0
25	72/M	Symptoms	2	70	22	—	—	P > D	35	40	41	0	0	0	+	+	+	0
26	53/M	Murmur	1	None	13	—	17	P = D	35	47	48	0	0	0	0	+	0	0
27	54/M	Murmur	1§	None	15	—	—	P = D	0	49	37	+	0	0	0	0	0	0
28	33/M	Routine ECG	1§	None	20	—	—	D > P	0	47	39	0	0	0	+	+	0	0
29	83/F	Symptoms	2	80	20	—	—	P = D	0	45	45	0	0	0	+	0	0	0

*Assessment of whether hypertrophy is predominant in the distal portion of left ventricle below mitral valve level or proximal portion cephalad to mitral valve. †Peak instantaneous left ventricular outflow gradient estimated with continuous wave Doppler color flow imaging (17) and due to mitral valve systolic anterior motion with mitral–septal contact. ‡Includes a family history of sudden cardiac death due to hypertrophic cardiomyopathy. §Transient and occasional symptoms of syncope or presyncope. + = present; 0 = absent; — = left ventricular wall thickness regarded as normal (≤12 mm).

AF = atrial fibrillation; ALFW = anterolateral free wall; AVS = anterior ventricular septum; CVA = cerebrovascular accident; ECG = electrocardiogram; FC = functional class; HCM = hypertrophic cardiomyopathy; HPT = (systemic) hypertension; LA = left atrium; LV = left ventricle; LVH = left ventricular hypertrophy; LVID = left ventricular internal dimension at end-diastole; LVOTG = left ventricular outflow tract gradient; NL = normal; NYHA = New York Heart Association; PVS = posterior ventricular septum.

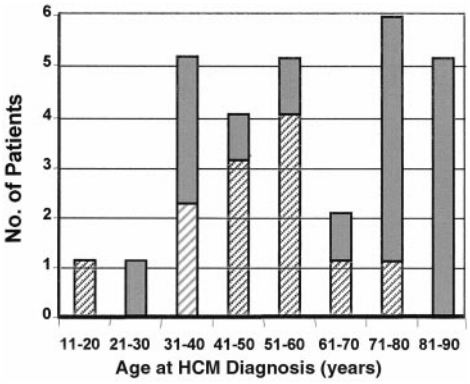

Figure 2. Age distribution in years at the time of initial hypertrophic cardiomyopathy diagnosis. Those 12 patients without functional limitation when recognized clinically are shown as stippled portions of the bars.

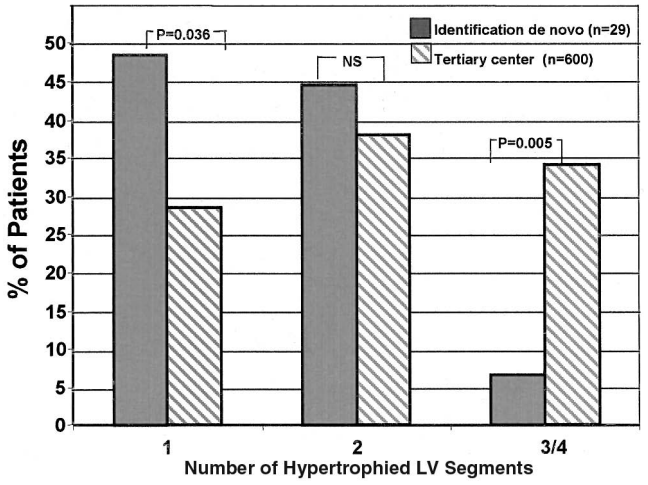

Figure 3. Extent of left ventricular hypertrophy (assessed by two-dimensional echocardiography) expressed as the number of hypertrophied left ventricular segments in each patient. The present study patients with HCM are compared with a previously reported hospital-based tertiary center HCM population (14).

the onset of symptoms had been delayed until ≥70 years of age (with the oldest 83 years).

Eight of the 29 HCM patients had a history of mild systemic hypertension judged to be insufficient to produce the pattern or degree of left ventricular wall thickening (≥18 mm) that was evident (14,16,18) (Table 1). In addition, each of the 8 patients with associated hypertension had clinical features consistent with HCM, such as basal left ventricular outflow tract gradients ≥20 mm Hg in 6; the other 2 nonobstructive patients had marked left ventricular wall thicknesses of 20 mm and 28 mm. Two patients had documented coronary artery disease, including one of those with hypertension. Only three of the 29 patients were known to have a family history of HCM, but systematic pedigree analyses (3,19) were not part of this investigation.

OUTFLOW OBSTRUCTION. Based on continuous wave Doppler examination, 11 of the 29 study patients (38%) had subaortic obstruction under basal conditions (peak instantaneous outflow gradients of 20 to 82 mm Hg), due to systolic anterior motion of the mitral valve and mitral–septal contact in 10 (anterior leaflet in 9 and posterior leaflet in 1); 8 of these patients had gradients ≥30 mm Hg, and 5 of these had marked outflow obstruction (i.e., with gradients ≥50 mm Hg). Eight other patients had mild-to-moderate degrees of mitral systolic anterior motion without mitral–septal contact which did not produce outflow obstruction (anterior leaflet in 6 and posterior leaflet in 2). Mitral valve leaflets were judged to be greatly elongated in 8 patients (20), including 5 with documented outflow gradients.

LEFT VENTRICULAR HYPERTROPHY. Maximum left ventricular wall thicknesses were 14 to 30 mm (mean 21), and were ≥28 mm in 5 patients (17%). Analysis of the patterns of left ventricular hypertrophy showed wall thickening confined to one segment of the wall (i.e., anterior ventricular septum) in 14 patients (48%), involving two segments (anterior and posterior septum or anterior septum and anterolateral free wall) in 13 patients (45%) and diffusely involving three or four segments (substantial portions of anterior and posterior septum as well as anterolateral free wall) in only two patients (7%) (Fig. 3).

The magnitude and extent of left ventricular hypertrophy in the 29 HCM patients was compared with those of a previously reported tertiary center HCM population (14). With respect to the number of left ventricular wall segments involved, the present study patients with HCM less commonly demonstrated diffuse hypertrophy (7% vs. 34%; $p = 0.005$), and more frequently showed a mild phenotypic expression with hypertrophy confined to one segment (48% vs. 28%; $p = 0.036$) (Fig. 3). Maximum left ventricular wall thickness was similar in the present cohort and the tertiary center HCM population presented for comparative purposes (21 ± 4 mm and 22 ± 5 mm, respectively).

OTHER ECHOCARDIOGRAPHIC FINDINGS. Left atrial dimension was 27 to 54 mm (mean 40), and cavity enlargement (>40 mm) was evident in 17 of the 29 patients (60%). Left ventricular end-diastolic dimension was 31 to 56 mm (mean 42), and >55 mm in only one patient. Mitral regurgitation was identified by color flow imaging in 13 patients (44%) and was judged as mild in eight and moderate in five.

ELECTROCARDIOGRAMS. A variety of abnormal patterns and abnormalities were evident on the 12-lead ECG, either alone or in combination: 1) ST segment and T wave alterations (n = 14); 2) abnormally deep Q waves in inferior and lateral leads, (n = 9); 3) conduction abnormalities including left or right bundle branch block and left or right anterior hemiblock (n = 5); 4) reduced R wave in the right precordial leads (n = 3), and 5) Wolff–Parkinson–White syndrome (n = 1). Atrial fibrillation was present in 4 patients, including 2 who presented with an embolic stroke.

Increased precordial voltages consistent with a pattern of left ventricular hypertrophy (R or S wave ≥25 mm; range to 38 mm) were present in only 3 patients (10%). Of note, 7 patients (24%) had ECGs judged to be within normal limits; each of these had mild-to-moderate hypertrophy with maximum left ventricular wall thickness <20 mm, most prominent in the basal portion of the wall.

Family history of HCM. Systematic pedigree analysis with echocardiography was not performed. However, in 8 (28%) of the 29 patients familial occurrence of HCM had been documented in 1 or 2 relatives. In 4 of those 8 families, 1 to 3 relatives had died prematurely of HCM.

Clinical follow-up. Longitudinal clinical evaluation 3 months to 3.8 years after initial HCM diagnosis showed that 25 of the 29 patients were alive. Of the 4 other patients, 3 died of causes definitely or probably related to HCM, including 2 of stroke with atrial fibrillation (patients #18 and #19) and one suddenly with coexistent coronary artery disease (patient #12); the remaining patient died of cancer.

DISCUSSION

Patient selection and HCM disease spectrum. Our overall perception of the clinical spectrum of HCM has been greatly skewed by the experience of large tertiary referral institutions located in urban centers which have dominated the available published data (1,2,12,13). These traditional HCM referral patterns have preferentially directed high risk patients to such institutions, and as a result certain subgroups with this disease have not been adequately represented either in the published reports or within the prevailing concepts of the disease spectrum. For example, asymptomatic or mildly symptomatic older patients have been largely absent from many published reports on HCM (6–8). These considerations legitimately raise questions regarding the extent to which some HCM patients may remain unrecognized within the community. Indeed, in a prior study (11), previously unsuspected HCM was identified by echocardiography in 0.17% of 4,111 subjects (or about 1:500) from the general population, although the prevalence of HCM has been reported to be much less when limited to cases recognized clinically or at autopsy (21). In addition, genotyping of selected HCM pedigrees has demonstrated many asymptomatic patients with mild phenotypic expressions of HCM detectable only by echocardiography (3,19,22) who otherwise might not be easily identifiable clinically.

Identification of HCM in the study population. We designed the present prospective investigation to extend these observations and study the frequency with which clinically unsuspected HCM could be detected by echocardiography in rural and general medical practice from over 60 communities within Minnesota (and Wisconsin). It has been the mandate of our institution over the last 18 years to provide diagnostic services to rural hospitals and clinics as part of an outreach program, utilizing mobile units equipped with echocardiographic instruments. Over the 17-month study period described here we identified 29 previously undiagnosed patients with HCM in about 15,000 echocardiograms. Of note, these newly recognized patients accounted for 0.19% of the overall study group, a figure remarkably similar to that previously reported in the general population (11), as well as in referrals to an echocardiography laboratory in an urban primary care setting for the purpose of excluding cardiovascular disease (23). The proportion of patients with the obstructive form of HCM (i.e., 27% with left ventricular outflow gradients ≥30 mm Hg) was similar to that generally reported in this disease (1,2).

The majority of patients in this series had symptoms or cardiovascular events that brought them to clinical recognition and consequently stimulated an echocardiographic study which resulted in the diagnosis of HCM for the first time. Therefore, identification of our patient group involved some selection bias due to the fact that most patients had overt disease expression. However, in about 40% of our patients it was only the fortuitous identification of a heart murmur that triggered the diagnostic echocardiographic studies. Therefore, it is possible that if the mobile echocardiography services available through our outreach program to small rural communities had not been readily available, the diagnosis of HCM may have been significantly delayed or conceivably never documented in some of these cases.

Demographics and phenotypic expression. The present HCM patients diagnosed for the first time showed a relatively mild expression of their disease with clinical and demographic features consistent with HCM in populations removed from the selection bias characteristic of tertiary referral centers (14,15,24,25). For example, 80% of the unselected HCM patients who comprise the present study group had experienced no functional limitation from their disease, were 60 years of age or older at the time of diagnosis, or both. Of those patients who developed symptoms, about one half were asymptomatic until ≥70 years of age. Indeed, the study group is of relatively advanced age with only 7% less than age 30 and an average age of 57 years. These observations all underline the importance of recognizing HCM as a disease compatible with advanced age and normal longevity, and often associated with little or no disability. Such a perspective is largely unappreciated in the available HCM published data (1,2,26–29).

Also, in contrast to referral center populations (14), our patients showed relatively mild phenotypic expression. Hypertrophy was most frequently confined to a single segment of the left ventricular wall (in almost 50%); more substantial and diffusely distributed wall thickening was uncommonly observed in <10%. Furthermore, phenotypic expression on the 12-lead ECG (24) was also considered to be relatively mild, with about 25% of patients showing normal 12-lead ECG patterns, and only about 10% demonstrating evidence of left ventricular hypertrophy.

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REFERENCES

1. Maron BJ. Hypertrophic cardiomyopathy. Lancet 1997;350:127–33.
2. Spirito P, Seidman CE, McKenna WJ, Maron BJ. The management of hypertrophic cardiomyopathy. N Engl J Med 1997;336:775–85.
3. Niimura H, Bachinski LL, Sangwatoraj S, et al. Human cardiac myosin binding protein C mutations cause late-onset familial hypertrophic cardiomyopathy. N Engl J Med 1998;338:1248–57.
4. 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;287:650–5.
5. Cecchi F, Olivotto I, Montereggi A, et al. Hypertrophic cardiomyopathy in Tuscany: clinical course and outcome in an unselected regional population. J Am Coll Cardiol 1995;26:1529–36.
6. Lever HM, Karam RF, Currie PJ, Healy BP. Hypertrophic cardiomyopathy in the elderly: distinctions from the young based on cardiac shape. Circulation 1989;79:580–9.
7. Lewis JF, Maron BJ. Elderly patients with hypertrophic cardiomyopathy: a subset with distinctive left ventricular morphology and progressive clinical course late in life. J Am Coll Cardiol 1989;13:36–45.
8. Lewis JF, Maron BJ. Clinical and morphologic expression of hypertrophic cardiomyopathy in patients ≥ 65 years of age. Am J Cardiol 1994;73:1105–11.
9. Fay WP, Taliercio CP, Ilstrup DM, et al. Natural history of hypertrophic cardiomyopathy in the elderly. J Am Coll Cardiol 1990;16:821–6.
10. Maron BJ, Poliac LC, Casey SA. Hypertrophic cardiomyopathy compatible with survival to advanced age: a congenital disease associated with normal longevity and occurrence in very elderly patients (abstr). Circulation 1996;94:I-246.
11. Maron BJ, Gardin JM, Flack JM, et al. Assessment of the prevalence of hypertrophic cardiomyopathy in a general population of young adults: echocardiographic analysis of 4111 subjects in the CARDIA Study. Circulation 1995;92:785–9.
12. Maron BJ, Spirito P. Impact of patient selection biases on the perception of hypertrophic cardiomyopathy and its natural history. Am J Cardiol 1993;72:970–2.
13. Spirito P, Chiarella F, Carratino L, et al. Clinical course and prognosis of hypertrophic cardiomyopathy in an outpatient population. N Engl J Med 1989;320:749–55.
14. 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.
15. Maron BJ, Gottdiener JS, Epstein SE. Patterns and significance of the distribution of left ventricular hypertrophy in hypertrophic cardiomyopathy: a wide-angle, two-dimensional echocardiographic study of 125 patients. Am J Cardiol 1981;48:418–28.
16. Maron BJ, Epstein SE. Hypertrophic cardiomyopathy: a discussion of nomenclature. Am J Cardiol 1979;43:1242–4.
17. Panza JA, Petrone RK, Fananapazir L, Maron BJ. Utility of continuous wave Doppler echocardiography in the noninvasive assessment of left ventricular outflow tract pressure gradient in patients with hypertrophic cardiomyopathy. J Am Coll Cardiol 1992;19:91–9.
18. Lewis JF, Maron BJ. Diversity of patterns of left ventricular wall thickening in patients with systemic hypertension and marked hypertrophy. Am J Cardiol 1990;65:874–81.
19. Watkins H, McKenna WJ, Thierfelder L, et al. Mutations in the genes for cardiac troponin T and α-tropomyosin in hypertrophic cardiomyopathy. N Engl J Med 1995;332:1058–64.
20. Klues HG, Maron BJ, Dollar AL, Roberts WC. Diversity of structural mitral valve alterations in hypertrophic cardiomyopathy. Circulation 1992;85:1651–60.
21. Codd MB, Sugrue DD, Gersh BJ, Melton LJ III. Epidemiology of idiopathic dilated and hypertrophic cardiomyopathy. A population-based study in Olmsted County, Minnesota, 1975–1984. Circulation 1989;80:564–72.
22. Maron BJ, Moller JH, Seidman CE, et al. Impact of laboratory molecular diagnosis on contemporary diagnostic criteria for genetically transmitted cardiovascular diseases: hypertrophic cardiomyopathy, long-QT syndrome, and Marfan syndrome. Circulation 1998;98:1460–71.
23. Maron BJ, Peterson EE, Maron MS, Peterson JE. Prevalence of hypertrophic cardiomyopathy in an outpatient population referred for echocardiographic study. Am J Cardiol 1994;73:577–80.
24. Maron BJ, Wolfson JK, Ciró 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;51:189–94.
25. Shapiro LM, McKenna WJ. Distribution of left ventricular hypertrophy in hypertrophic cardiomyopathy. A two-dimensional echocardiographic study. J Am Coll Cardiol 1983;2:437–44.
26. Cannan CR, Reeder GS, Bailey KR, et al. Natural history of hypertrophic cardiomyopathy. A population-based study, 1976 through 1990. Circulation 1995;92:2488–95.
27. McKenna WJ, Deanfield, Faruqui A, et al. Prognosis of hypertrophic cardiomyopathy: role of age and clinical, electrocardiographic and hemodynamic features. Am J Cardiol 1981;47:532–8.
28. McKenna WJ, Deanfield JE. Hypertrophic cardiomyopathy: an important cause of sudden death. Arch Dis Child 1984;59:971–5.
29. Maron BJ, Roberts WC, Epstein SE. Sudden death in hypertrophic cardiomyopathy: profile of 78 patients. Circulation 1982;65:1388–94.