Progression of hypertrophic cardiomyopathy

A cross sectional echocardiographic study

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SUMMARY The progression of hypertrophy was studied in 39 patients with hypertrophic cardiomyopathy by echocardiography at follow up from January 1979 to September 1983 (mean follow up 42 months). Thirty two patients were treated medically and 11 had had a septal myotomy-myectomy. Progression of the hypertrophy was noted in four patients treated with propranolol. An additional region in the left ventricular long axis plane was affected in two, extending to the apical region in one and to the basal region in the other, and an additional segment in the left ventricular short axis plane in two extending from the septum into the free wall. The electrocardiograms of these four patients showed a significant increase in QRS voltages (Sokolow-Lyon index increase >10 mm) and of the Romhilt-Estes score (increase ≥ 3 points) in two, development of a left bundle branch block in one, and no change in one. Progression of hypertrophy was seen in none of the 11 patients treated with myotomy-myectomy.

Thus echocardiography accurately detects the progression of hypertrophy in patients with hypertrophic cardiomyopathy, which may be prevented by septal myotomy-myectomy.

With echocardiography the familial occurrence of hypertrophic cardiomyopathy,¹⁻³ its morphological⁴⁻⁶ and functional aspects,⁷⁻⁹ and the effects of medical¹⁰⁻¹² and surgical treatment can be studied.^{13,14} Based on the patterns of distribution of the hypertrophy, classification into subtypes of hypertrophic cardiomyopathy has been proposed.^{15,16} The progression of hypertrophy has been assessed in patients by electrocardiography,¹⁷ but because of its low sensitivity and specificity in detecting hypertrophy in these patients¹⁸ this method may not be useful for studying its progression. The aim of this study was to investigate by serial electrocardiography and cross sectional echocardiography whether or not progression of hypertrophy occurs in hypertrophic cardiomyopathy.

Patients and methods

STUDY GROUPS

Two groups of patients with hypertrophic car-

diomyopathy were studied: 39 treated medically (25 men and 14 women, age range 16-70 (mean 44) years) and 11 treated with septal myotomy-myectomy (six men and five women, age range 17-65 (mean 46) years). They were selected from a group of 67 patients with hypertrophic cardiomyopathy because the quality of their cross sectional echocardiograms allowed the endocardial and epicardial borders of the left ventricular free wall and the endocardial boundaries of the interventricular septum to be identified.

The diagnosis was based on the history, typical clinical signs, and the established echocardiographic criteria for hypertrophic cardiomyopathy as proposed by Goodwin.¹⁹ Haemodynamic and angiographic studies were carried out in 25 of the 39 medically treated patients. A resting or provoked (isoproterenol infusion) left ventricular outflow gradient or both was noted in 13 of the 25 patients (range 20-155 mm Hg). Cardiac catheterisation was not performed in the 11 patients treated surgically. Table 1 shows the clinical data of the two groups. The indications for septal myotomy-myectomy were severe symptoms despite medical treatment with pronounced obstruction to left ventricular outflow at rest (≥ 50 mm Hg). Echocardiographic follow up data were available from

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Fig. 1 Diagram showing the principle of assessment of the regional distribution of the hypertrophy in hypertrophic cardiomyopathy from cross sectional echocardiograms in (a) the parasternal long axis view, (b) the apical four chamber view, and (c) the apical long axis view. The left ventricle (LV) is subdivided along its long axis into a basal region (B) and an apical region (A).

Table 1 Clinical data of the 50 patients with hypertrophic cardiomyopathy at the time of entry into the study. Figures are numbers of patients unless stated otherwise

Clinical data	Medically treated group (n=39)	Surgically treated group (n=11)
Male/female	25/14	6/5
Mean age (yr)	44	46
NYHA class		
I	18	7
II	17	4
III	4	0
IV	0	0
Drug treatment:		
Propranolol (80–240 mg/day)	30	7
Verapamil (160–320 mg/day)	2	0

January 1979 to September 1983 (mean follow up 42 months). Each patient underwent at least three echocardiographic and electrocardiographic studies. No patient died during the follow up period.

ECHOCARDIOGRAPHY

Cross sectional echocardiograms were obtained using a phased array system (Toshiba SSH-10 with a 2.25 MHz transducer and Toshiba SSH-40A with a 3.5 MHz transducer). In each patient the parasternal long axis and short axis views at multiple levels and the apical four chamber and apical long axis views were obtained. Standard M mode echocardiograms of the left ventricle were obtained from selected long axis

Fig. 2 Diagram showing the cross sectional echocardiographic short axis views used for evaluating the segmental distribution of the hypertrophy in hypertrophic cardiomyopathy. The basal region (a) is at mitral valve level (MV) and the apical region (b) at papillary muscle level. The left ventricle (LV) is subdivided into four segments and insertion of the free walls of the right ventricle is used as a landmark to separate the interventricular septum from free wall. The interventricular septum is divided into anterior (AVS) and posterior (PVS) segments. The left ventricular wall is also divided into two segments, an anterolateral free wall (ALFW) which includes the anterolateral papillary muscle and an inferoposterior free wall (IPFW).

Table 2 Distribution of the hypertrophy by cross sectional echocardiography in the long and short axis of the left ventricle in 39 patients with hypertrophic cardiomyopathy. Figures are numbers of patients

Short axis					
Long axis	Partial IVS	Entire IVS	IVS and partial FW	IVS and entire FW	Total (%)
Basal region	1	1	1	0	3 (8)
Apical region	0	0	0	2	2 (5)
Basal and apical regions	2	13	8	11	34 (87)
Total (%)	3 (8)	14 (36)	9 (23)	13 (33)	

IVS, hypertrophy of the interventricular septum; FW, hypertrophy of the left ventricular free wall; partial IVS, hypertrophy of one septal segment (anterior or posterior); entire IVS, hypertrophy of both septal segments (anterior and posterior); partial FW, hypertrophy of one segment of the free wall (anterolateral or inferoposterior); entire FW, hypertrophy of both segments of the free wall (anterolateral and inferoposterior).

and short axis views for accurate wall thickness measurements.

Analysis of the echocardiograms

The videotaped cross sectional echocardiograms were carefully and independently reviewed in a random order by two observers who did not know the name of the patient or the date of examination. Hypertrophy was considered to be present if the thickness of the left ventricular wall was ≥ 15 mm. Using guidelines proposed by Maron and coworkers,¹⁵ the segments of the left ventricular wall near to the lateral borders of the sector were considered hypertrophied when their thickness was ≥ 17 mm in order to avoid overestimation due to the limited lateral resolution.

The distribution of left ventricular hypertrophy was evaluated in both the long and short axis planes. In the long axis, the left ventricle was divided into two regions (Fig. 1): the basal region, from the cardiac base to a level just above the tips of the papillary muscles, and the apical region, from the papillary muscles to the cardiac apex. In the short axis plane (Fig. 2), at the level of the basal and apical region, the ventricular septum was divided in two segments, anterior and posterior. The left ventricular free wall was also divided into two segments at these levels, anterolateral and inferoposterior. A total of 1360 segments were analysed, and agreement between the observers in assessing the presence or absence of hypertrophy was obtained in 1331 (98%). For the remaining 19 segments, consensus was achieved with the help of a third observer.

The echocardiographic criteria used to detect progression of hypertrophy were (a) extension of the hypertrophy to another region, from the basal to the apical region and vice versa along the left ventricular long axis, and (b) extension of the hypertrophy to one or more segments of the same region along the left ventricular short axis.

ELECTROCARDIOGRAPHY

Standard 12 lead electrocardiograms were performed in all patients on the same day as the echocardiographic examination.

Tracings were recorded with the patients in the supine position during quiet respiration. Amplitude measurements were obtained from five consecutive complexes to reduce variation by respiration. The presence of left ventricular hypertrophy was diagnosed using the point score system proposed by Romhilt and Estes²⁰ (≥ 5 points) and the Sokolow-Lyon index ($SV1 + RV5 > 35$ mm).²¹ The electrocardiograms were analysed independently in random order by two observers who did not know the name of the patient or the date of examination.

Results

MEDICALLY TREATED GROUP

Table 2 shows the distribution of hypertrophy seen by cross sectional echocardiography in the 39 medically treated patients. Serial cross sectional echocardiographic studies showed progression of hypertrophy in four patients. In two patients it affected an additional region in the left ventricular long axis plane. In the first patient the initial septal hypertrophy in the basal region extended into the apical region and in the second it extended from the apical to the basal region. The extension of the hypertrophy into the basal region was also evident on M mode echocardiography (Fig. 3a and 3b). In two other patients progression of the hypertrophy affected another segment of the same region along the left ventricular short axis, the inferoposterior segment of the free wall in one patient (Fig. 4) and the anterolateral segment of the free wall in the other (Fig. 5). Progression of the hypertrophy was seen after two years of follow up and was confirmed in subsequent studies. Table 3 shows the clinical characteristics of the four patients.

The electrocardiograms showed an increase in the indices of left ventricular hypertrophy in two of these patients (Fig. 6). A third patient developed left bundle branch block, and no electrocardiographic changes were noted in the fourth.

The mean age and duration of follow up of these four patients did not differ from those without echocardiographic evidence of progression of hyper-

Fig. 3 M mode echocardiograms performed in 1979 (a) and 1982 (b) of a patient with hypertrophic cardiomyopathy and progression of hypertrophy present along the long axis from the apical to the basal regions of the inferoposterior wall. (a) The interventricular septum at the level of the basal region appeared to be considerably hypertrophied. The left ventricular posterior wall (LVPW) had a thickness of 12 mm. (b) After three years the thickness of the left ventricular posterior wall had increased to 15 mm.

Fig. 4 End diastolic cross sectional echocardiographic parasternal short axis views at the level of the basal region of a patient with hypertrophic cardiomyopathy, showing (a) hypertrophy of the entire septum and of the anterolateral segment of the free wall but normal thickness of the inferoposterior segment of the free wall and (b) hypertrophy in the inferoposterior segment of the free wall (arrows) three years later.

trophy. All four were initially asymptomatic (NYHA class I). Three remained asymptomatic, while one developed mild symptoms (NYHA class II). The cardiothoracic ratio increased in only one patient (from 0.51 to 0.57).

Cardiac catheterisation, performed in two of the four patients showed a resting outflow pressure gradient in both (60 and 100 mm Hg respectively). During the follow up period, all four patients were treated with propranolol (80–160 mg/day).

SURGICALLY TREATED GROUP

In the 11 patients who had undergone septal myotomy-myectomy, no progression of hypertrophy

Fig. 5 End diastolic cross sectional echocardiographic parasternal short axis views at the level of the basal region of a patient with hypertrophic cardiomyopathy showing (a) hypertrophy of the entire interventricular septum and of the inferoposterior segment of the free wall with normal thickness of the anterolateral segment of the free wall, and (b) hypertrophy of the anterolateral segment of the free wall three years later.

was noted on either their cross sectional echocardiograms or electrocardiograms; their clinical status remained unchanged.

Discussion

Our study represents the first observation of progres-

Table 3 *Clinical and electrocardiographic characteristics of the four patients with hypertrophic cardiomyopathy in whom cross sectional echocardiographic follow up showed progression of hypertrophy*

Case No	Sex/age (yr)	Duration of follow up (yr)	Family incidence hypertrophic cardiomyopathy	NYHA class		Treatment with propranolol (mg/day)	Electrocardiography			
				A	B		SV1+RV5 (mm)		Score* (points)	
							A	B	A	B
1	F/53	3	—	I	I	160	64	65	5	5
2	M/49	4	—	I	I	80	40	58	2	5
3	M/49	4	—	I	II	120	40	52	5	8
4	M/17	3	+	I	I	160	46	LBBB	4	LBBB

—, absent; +, present; A, initial evaluation; B, last evaluation; LBBB, left bundle branch block.
*Romhilt-Estes point-score system.²⁰

sion of hypertrophy in hypertrophic cardiomyopathy. Electrocardiographic evidence of progression of hypertrophy has been reported by McKenna *et al* in 20% of their patients with hypertrophic cardiomyopathy.¹⁷ The lower proportion of patients with progression of hypertrophy in our study may be explained by the shorter follow up period (3.5 years *vs* 8 years) and by the use of a different diagnostic technique. Indeed, previous studies have shown a poor correlation between the electrocardiographic and M mode echocardiographic changes seen in hypertrophic cardiomyopathy.^{22–24} Cross sectional echocardiography, by visualising the cardiac chambers and walls in multiple cross sectional planes and providing accurate information about the distribution of the hypertrophy, is superior to electrocardiography in detecting hypertrophy. Moreover, conduction disturbances, which are a common finding in these patients especially after septal myotomy-myectomy,^{14 25} further limit the use of electrocardiography in studying the progression of hypertrophy. In the present study elec-

trocardiography failed to detect the progression of hypertrophy in two of the four patients in whom this was clearly seen by cross sectional echocardiography. The good reproducibility of the cross sectional echocardiograms in identifying the areas of hypertrophy in our study is supported by the high rate of agreement obtained by the two observers (98%). These data agree with those of previous similar studies.^{15 16} For the assessment of the progression of the hypertrophy, thickness measurements obtained from M mode echocardiograms must be guided by cross sectional echocardiography, thus limiting the variability of these measurements.^{26–28} Age, sex, familial incidence of hypertrophic cardiomyopathy, and medical treatment do not seem to influence the potential progression of hypertrophy. McKenna *et al*, using electrocardiography in a larger patient population, found not relation between these factors and the increase of electrocardiographic indices of left ventricular hypertrophy.¹⁷ These authors noted worsening of symptoms in their patients with

Fig. 6 Electrocardiograms recorded in (a) 1979 and (b) three years later of a patient with cross sectional echocardiographic evidence of progressive hypertrophy showing a substantial increase in the voltage criteria of left ventricular hypertrophy (note different calibration).

the increase of hypertrophy, whereas this occurred in only one of our patients.

The absence of progression of hypertrophy in the patients who had had a septal myotomy-myectomy may indicate that in addition to symptomatic improvement²⁹⁻³¹ this intervention may prevent the progression of hypertrophy. This observation obviously needs further confirmation. We stress the importance of standardisation of the cross sectional echocardiographic evaluation of patients with hypertrophic cardiomyopathy. This would allow a better comparison between different studies, should greatly increase our knowledge about the morphological aspects of hypertrophic cardiomyopathy, and further determine the rate and clinical importance of the progression of hypertrophy in this disease.

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