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Association between high grade ventricular arrhythmia and extent of left ventricular hypertrophy in hypertrophic cardiomyopathy.

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Abstract

The association between the extent of left ventricular (LV) hypertrophy and severity of ventricular or atrial arrhythmias are examined. Two-dimensional echocardiography and 24-h Holter electrocardiography monitoring were performed in 60 patients with hypertrophic cardiomyopathy (HCM). According to the distribution of the LV hypertrophy, the patients were divided into three groups: 1. Apical hypertrophy (APH), 2. Septal hypertrophy, and 3. Extensive hypertrophy. Ventricular arrhythmias were found in 82% of the patients and supraventricular arrhythmias were detected in 70% of the patients. Lown grade III and IV arrhythmias occurred significantly more frequently in patients with extensive than with septal hypertrophy. Lown grade III to IV arrhythmias did not occur in patients with APH. Present results show a significant association between the extent of LV hypertrophy and the severity of ventricular arrhythmias in HCM.

KEYWORDS: hypertrophic cardiomyopathy, arrhythmia, echocardiography, Holter ECG

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Association between High Grade Ventricular Arrhythmia and Extent of Left Ventricular Hypertrophy in Hypertrophic Cardiomyopathy

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The association between the extent of left ventricular (LV) hypertrophy and severity of ventricular or atrial arrhythmias are examined. Two-dimensional echocardiography and 24-h Holter electrocardiography monitoring were performed in 60 patients with hypertrophic cardiomyopathy (HCM). According to the distribution of the LV hypertrophy, the patients were divided into three groups: 1. Apical hypertrophy (APH), 2. Septal hypertrophy, and 3. Extensive hypertrophy. Ventricular arrhythmias were found in 82% of the patients and supraventricular arrhythmias were detected in 70% of the patients. Lown grade III and IV arrhythmias occurred significantly more frequently in patients with extensive than with septal hypertrophy. Lown grade III to IV arrhythmias did not occur in patients with APH. Present results show a significant association between the extent of LV hypertrophy and the severity of ventricular arrhythmias in HCM.

Key words: **hypertrophic cardiomyopathy, arrhythmia, echocardiography, Holter ECG**

Arrhythmias are one of the most common clinical symptoms in patients with hypertrophic cardiomyopathy (HCM). The high incidence and prognostic value of serious ventricular arrhythmias in HCM have been well recognized (1-6). However, the mechamisms responsible for their genesis have not been totally clarified. Potentially useful information may come from results of morphologic studies of the distribution of hypertrophy, which have already proved useful in the evaluation of clinical, hemodynamic (2, 7), and ECG features (8, 9) of this disease. In paticular this method may help to clarify the still uncertain relationship between the extent of hypertrophy and arrhythmias. Although it has been hypothesized that marked left ventricular (LV) hypertrophy may predispose patients with HCM to serious ventricular arrhythmias (1), definitive evidence favoring this hypothesis is limited. This study investigates the potential relation in HCM between the extent of LV hypertrophy, assessed with two-dimensional (2-D) echocardiography, and the prevalence and severity of arrhythmias on 24-h Holter electrocardiography (ECG) monitoring.

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Subjects and Methods

Patients. On the basis of the satisfactory quality of 2-D echocardiograms and 24-h Holter ECG, we selected 60 patients with HCM. The criterion used to establish the diagnosis of HCM in the 60 patients was the demonstration, with M-mode and 2-D echocardiography, of a non-dilated, hypertrophied left ventricle (in the absence of other cardiac or systemic diseases that are capable of producing LV hypertrophy).

Fifty patients (83 %) were male and 10 (17 %) were female; their age ranged from 25 to 83 years (54 ± 13). Thirty-three patients had palpitation, 29 had chest pain or discomfort, 8 had dyspea, 2 had at least one episode of syncope. Coronary angiography was performed in 19 patients and none of them showed significant coronary artery narrowing. Outflow obstruction was detected by doppler echocardiography in 12 patients.

Echocardiographic measurements. 2-D echocardiograms were obtained using a electrical sector scanner (Toshiba Sonolayer SSH 65-A with a 3.75 or 2.5 MHz transducer). In each patient the parasternal long axis and short axis views at multiple levels and apical four chamber and apical long axis views were obtained. Standard M mode echocardiagrams of the LV were obtained from selected long axis and short axis views for accurate wall thickness measurements. The 2-D echocardiograms, recorded on a video recorder (National TQ-2300 FA), were reviewed.

Hypertrophy was considered to be present if the thickness of the LV wall was ≧ 15 mm. According to the distribution of the LV hypertrophy, we divided the patients into three groups: 1. Apical hypertrophy (APH): predominatly localized at the apical region of the ventricle; 2. Septal hypertrophy: localized at the anterior and/or posterior segment of the septem; 3. Extensive hypertrophy: involving both the septem and free wall.

Holter ECG monitoring recording. All cardioactive mediation were discotinued 24 to 48 h before monitoring in most of the patients with the exception of the 6 patients who were treated with nothing other than β-adrenargic blockers or calcium antagonist. Continuous 24-h Holter ECG recordings were obtained using a portable cassette tape recorder and modified V1 and V5 leads. Analysis of the 24-h ECG recordings was performed using a high-speed digital computer system (Dynamic Electrocardiosanner model DCG VII, DEL MAR AVIOMCS). Ventricular arrhythmias were classified according to the grading system proposed by Lown (See Ryan *et al.* (10)). Supraventricular arrhythmias were classified as supraventricular premature contractions (SVPC), supraventricular tachycardia (SVT) and atrial fibrillation (Af).

Statistical analysis. Appropiate chi-squre test, Student's *t*-test and multiple regression analysis were used to assess statistical significance. $p < 0.005$ was considered significant.

Results

Extent of hypertrophy. LV hypertrophy was localized at apical region (APH) in 11 patients (18 %); in 33 patients (55 %) it was limited to the septum (septal hypertrophy), and in sixteen (27 %) it involved both the septum and free wall (extensive hypertrophy).

Ventricular arrhythmias. Table 1 summarizes the ventricular arrhythmias detected during 24 h of Holter ECG monitoring. Forty-nine of 60 patients (82 %) had ventricular arrhythmias. Of these, 35 % had Lown grade I ventricular pre-

Table 1 Ventricular arrhythmias detected during 24-h Holter monitoring

Arrhythmia grade*	No. of patients	%
0	11	18
I (< 30 VPC/h)	21	35
II (≧30 VPC/h)	1	2
III (multiform VPC)	8	13
IV_a (couplets)	7	12
IV_b (VT)	12	20

VPC, ventricular premature contraction; VT, ventricular tachycardia. * Classification of Ryan and Lown *et al.* (10).

Table 2 Supraventricular arrhythmias detected during 24-h Holter monitoring

Arrhythmias	No. of patients	%
None	18	30
SVPC	18	30
SVT	20	33
Af	4	7

SVPC, supraventricular premature contraction; SVT, supraventricular tachycardia; Af, atrial fibrillation

mature contraction (VPC), 2 % had grade II, 13 % had multiform, and 12 % had couplets. Remaining twelve patients (20 %) had ventricular tachycardia (VT).

Supraventricular arrhythmias. Table 2 summarizes the supraventricular arrhythmias detected during Holter monitoring. Atrial arrhythmias were found in 42 patients (70 %), 18 had SVPC, 20 had SVT and 4 had Af.

Ventricular arrhythmias and LV hypertrophy. Table 3 shows the severity of ventricular arrhythmias in three different types of LV hypertrophy: apical, septal and extensive. The presence of less serious arrhythmias (Lown grades I and II) was significantly more common in patients with APH and septal hypertrophy than in those with extensive hypertrophy ($p < 0.05$). On the other hand, more serious arrhythmias (Lown grades III to IV_b) occurred significantly more frequently in patients with extensive hypertrophy than in those with septal hypertrophy ($p < 0.05$). Lown grades III and IV VPCs did not occur in APH. We also compared an incidence of grades III and IV in the hypertrophic obstructive cardiomyopathy (HOCM) with that in non-obstructive form (Table 4). Serious ventricular arrhythmias were more common in HOCM than in non-obstructive form ($p < 0.01$) independent of the extent of LV hypertrophy (5 of six patients with only septal hypertrophy had Lown grades III-IV VPCs). Multiple regression analysis showed no ralationship between the severity of ventricular arrhythmias and other variables such as age, sex, left atrial dimension, LV diastolic and LV ejection fraction (Table 5).

Atrial arrhythmias and LV hypertrophy. Table 6 shows the ralationship between atrial

Table 3 Relationship between severity of ventricular arrhythmias and distribution of hypertrophy

Arrhythmia grade	Number of patients (%)		
	APH	Septal H	Extensive H
0	4 (36)	7 (21)	0 (0)
I-II	8 (64)	13 (39)	2 (13)*
III-IV_a-IV_b	0 (0)	13 (40)	14 (87)*

APH, apical hypertrophy; H, hypertrophy, * $p < 0.05$ vs septal hypertrophy group. For classification of arrhythmia grades see Table 2. Figrures in parentheses indicate percentages of 11, 33 and 16 patients with APH, Septal H, and Extensive H, respectively.

Table 4 The prevalence of arrhythmias occurred in obstructiue and non-obstructive hypertropic cardiocyopathy

Arrhythmia	Number of patients (%)		p
	obstructive	non-obstructive	
Lown grades III-IV	11 (92)	16 (43)	< 0.01
Atrial arrhythmias	9 (75)	28 (76)	NS

NS, not significant. Figures in parenthese indicate percentages of 12 obstructive and 37 non-obstructive hypertrophic cardiomyopathy.

Table 5 Relationship between severity of ventricular arrhythmias and clinical features

Clinical features	Grade 0	Grades I-II	Grades III-IV
Age (year)	50 ± 15	57 ± 11	56 ± 11
Sex (% male)	82	90	81
Mean LVEF (%)	78 ± 8	70 ± 15	73 ± 9
Mean LVDd (mm)	46 ± 2	45 ± 7	42 ± 6
Mean LAD (mm)	38 ± 7	33 ± 7	37 ± 7

LVEF, left ventricular ejection faraction; LVDd, left ventricular diastolic dimension; LAD, left atrial dimension. Number of patients in Grades 0, I-II, and III-IV are 11, 22, and 27, respectively.

Table 6 Relationship between supraventricular arrhythmias and distribution of hypertrophy

Arrhythmias	Number of patients (%)			p
	APH	Septal H	Extensive H	
SVPC	4 (36)	12 (36)	2 (13)	NS
SVT	1 (9)	12 (36)	6 (38)	NS
Af	0 (0)	2 (6)	2 (13)	NS

APH, apical hypertrophy; H, hypertrophy; SVPC, supraventricular premature contraction; SVT, supraventricular tachycardia; Af, atrial fibrillation; NS, not significant. Figures in parentheses indicate percentages of 11, 33, and 16 patients with APH, Septal H, and Extensive H, respectively.

arrhythmias and the three morphologic types of hypertrophy. No association was observed between these patterns of LV hypertrophy and the prevalence of supraventricular arrhythmias. Although Af was more common in extensive hypertrophy group than in APH and septal hypertrophy groups (2/16 *vs* 2/33 *vs* 0/11), there was no statistically significant correlation between them. No relation was observed between obstructive form and non-obstructive form in the occurrence of supraventricular arrhyhmias (9/12 vs 28/37, p = NS, Table 6).

Discussion

The major finding of this study was the high grade ventricular arrhythmias (Lown grades III and IV) occurred in patients with extensive hypertrophy involving both the septum and free wall. Our data show a strong relation between the extent of LV hypertrophy, assessed with M-mode and 2-D echocardiography, and high grade ventricular arrhythmias, detected by Holter monitoring. Recently, Spirito *et al.* (11) have also investigated the relationship between the extent of hypertrophy and arrhythmias. Although in their study the 2-D echocardiographic method was used to appreciate LV hypertrophy, results did not differ greatly from those of this study. They did demonstrate a relationship between the extent of hypertrophy and ventricular tachycardia (grade-IV_b). In our investigation, we found a correlation not only with VT but also with multiform VPC and couplet VPC (grades III and IV_a).

In our study, no complex VPCs (grades III to IV_b) were detected in 11 patients with APH. Similarly, Webb *et al.* (12) followed 26 patients with APH for an average of 7.3 years. Only one patient was found to have documented life-threatening ventricular arrhythmias. It may be that because patients with APH have the least extensive LV hypertrophy, the prognosis in these patients appears relatively favorable. These results also clarify the relationship between extent of LV hypertrophy and severity of VPC in other hand.

Our data support the concept that a more extensive hypertrophy process, involving both the septum and free wall, enhances the development of arrhythmias. The explanation for this finding is only speculative. It seems possible to hypothesize that the electrophysiologic substrates of arrhythmias may be the histologic or functional alterations associated with hypertrophy, that is, myocardial disarray, ischemia, and fibrosis. Thus it would seem that diverse grades of these disorders could be raleted to different degrees of severity for arrhythmias.

The occurrence of arrhythmias has been shown to increase progressively with time (13), and a progression of LV hypertrophy has also been demonstrated in a percentage of patients with this disease (14, 15). Results of the present study raise the possibility that increases in the occurrence of hypertrophy and arrhythmias may be related, representing two different expressions of a common phenomenon, that is, the progressive pathologic change involving the myocadium. This hypothesis is an attractive one, but needs confirmation.

We also found that complex VPCs occurred significantly more commonly in the obstructive form than in the non-obstructive form, independent of the extent of LV hypertrophy. This finding is contrary to previous reports (1). But, Savage *et al.* (1) found that during treadmill exercise tests, patients with obstruction were significantly more likely to have high grade VPC than non-obstructed patients. The mechanism is not clear and needs further exploration.

Af is an adverse event in the evolution of HCM (5). It causes a sudden decrease in the atrial contribution to the filling of a non-compliant LV (16). This arrhythmia usually produces a decline in the clinical condition, so as to be considered as potentially life-threatening by some investigators (16). In this study, Af occurred more commonly in extensive hypertrophy but was

not statistically significant. This may be due to the small sample size.

Idetification of serious arrhythmia is an important goal in the management of patients with HCM (13, 16). Because of the poor positive accuracy of symptoms for indicating the presence of serious arrhythmia (13, 16), we think that an echocardiographic finding of extensive hypertrophy may represent a useful marker for detecting patients at increased risk for potentially life-threating arrhythmias. In these cases more frequent Holter monitoring and a more aggresive treatment than in patients with less extensive LV hypertrophy may be appropriate.

In this study, there are some limitations inherent that could influence the interpretation of our data. First, substantial spontaneous variation in ventricular arrhythmias may occur during Holter ECG monitoring, so that, a single 24-h ECG may not have identified all patients having episodes of high grade ventricular arrhythmias. Second, beta-adrenergic blockers or calcium antagonists were not discontinued in six patients during Holter ECG monitoring, which may influence the natural occurrence of arrhythmias in these patients, although among them, three still had Lown grade III VPC. Third, the outflow obstruction was judged only by doppler echocardiography. It would be better to identify the obstructive form by catheterazition.

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