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Clinical significance of left ventricular hypertrophy in dilated cardiomyopathy: An echocardiographic follow-up of 50 patients

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Summary

To evaluate the significance of left ventricular (LV) hypertrophy in patients with dilated cardiomyopathy (DCM), 50 patients seen between 1976 and 1983 were studied echocardiographically. We categorized the patients as four groups according to the degree of LV dilatation or hypertrophy. Group consisted of 17 patients with mild to moderate LV dilatation without hypertrophy (LV end-systolic I dimension: Ds$<$60 mm, LV wall thickness at end-systole: WTs$<$15 mm). Group II, 12 with mild to moderate LV dilatation and hypertrophy (Ds$<$60 mm, WTs$\geqq$15 mm). Group III, eight with marked LV dilatation and hypertrophy (Ds$\geqq$60 mm, WTs$\geqq$15 mm), and Group IV, 13 with marked LV dilatation without hypertrophy (Ds$\geqq$60 mm, WTs$<$15 mm). Twenty patients had LV hypertrophy and 30 patients were without LV hypertrophy at the start of this study. New York Heart Association functional classes, cardiothoracic ratio and ECG findings at the first study did not show any statistically significant differences among the four groups.

During the prospective follow-up of 2.7 years in average, eight patients died of congestive heart failure including five of Group IV, and three of Group I who had progressive LV dilatation. Three

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patients of Group I, II and III died suddenly. Ambulatory ECGs showed life-threatening ventricular arrhythmias in all 32 patients studied.

In conclusion, the presence of wall hypertrophy in DCM may be an important protective factor to the fatal congestive heart failure, whereas sudden and unexpected death due to serious arrhythmias may occur in any patient with DCM irrespective of the wall thickness. Thus, intensive antiarrhythmic therapy is mandatory in any category of DCM.

Key words

Dilated cardiomyopathy Echocardiography Left ventricular hypertrophy Prognosis

Cardiomyopathy is defined as heart muscle diseases of unknown cause and Goodwin's classification into congestive, hypertrophic and restrictive cardiomyopathy has been widely accepted[1]. More recently, the term "dilated" has been substituted for "congestive" as the preferred terminology, that is, dilated cardiomyopathy[2] (DCM). DCM remains a clinical challenge because the cause is unknown, the natural history is ill-defined and the response to therapy is generally unsatisfactory. There have been several studies comparing the clinical features and hemodynamic findings with prognosis in DCM[3~12]. We evaluated the role of echocardiography in detecting deteriorated left ventricular (LV) performance[13] in DCM and elucidated a factor influencing its prognosis.

Materials and Methods

The study population consisted of 50 patients who were referred to our hospital for the evaluation of heart disease between January 1976 and January 1983. There were 41 male and 9 female patients, and their ages ranged from 16 to 64 years. Diagnoses were recorded according to the report of the WHO/ISFC task force on the definition and classification of cardiomyopathies[2]. Thirty-three patients underwent left and right cardiac catheterization, left ventriculography and coronary cineangiography. Resting intracardiac pressures were recorded. The cardiac index was determined by the Fick method. LV ejection fraction was obtained by planimetric volume calculation from single plane left ventriculogram. Coronary cineangiograms were taken in multiple projections. Diagnoses were confirmed by autopsy in 11 patients. Patients with systemic hypertension, coronary artery disease and specific heart muscle disease were excluded from this study. Treatment with digitalis and diuretics was started in all 50 patients after the initial data acquisition. Vasodilator therapy was offered to 12 patients with congestive heart failure (CHF) who were severely compromised despite the treatment with digitalis and diuretics. All patients were subjected to a prospective follow-up study including physical examinations, 12-lead ECG, chest X-ray, 24-hour ambulatory ECG monitoring and echocardiography. Functional status was classified according to the criteria of the New York Heart Association (NYHA)[14]. The follow-up period was from 1 to 7 years and 2.7 years in average.

Echocardiograms were recorded with either a Toshiba Sonocardiograph 01A or a Toshiba SSH-11A two-dimensional echocardiograph interfaced with a Honeywell line-scan recorder Model FR-06A. We measured LV end-diastolic dimension and end-systolic dimensions (Dd and Ds) at the peak of the R wave and at the onset of aortic component of the second heart sound, respectively, and calculated LV percent fractional shortening (ΔD), an echocardiographic ejection index of LV performance, as follows: $\Delta D = [(Dd - Ds)/Dd] \times 100\%$. Interventricular septal thickness (IVST) and LV posterior wall thickness (PWT) were measured at both end-diastole and end-systole. LV wall thickness at end-diastole (WTd) and at end-systole (WTs) were calculated as follows: $WTd = (IVSTd + PWTd)/2$, and $WTs = (IVSTs + PWTs)/2$. LV relative wall thickness, expressed as the ratio of Ds to WTs (Ds/WTs), was calculated. We

made efforts during echocardiographic examinations to minimize the variability in LV measurements[15]. First, the left ventricle was always recorded from the same interspace. Second, the patient's upper body was always positioned in the same degree of left lateral tilt. Third, recordings were made at the same respiratory phase. Finally, by reviewing records, similar places within the left ventricle were selected for the serial measurements.

Thirty-two patients underwent 24-hour ambulatory ECG monitoring during the follow-up periods. A precordial bipolar ECG was recorded continuously for 24 hours on a magnetic tape system (Avionics, Model 447) without the use of antiarrhythmic agents. The recorded tapes were analyzed using an Avionics Dynamic Electrocardioscanner (Model 9500). A Lown's grading system[16] was used for classifying ventricular arrhythmias. Grade 1, <30 uniform premature ventricular contractions (PVCs) in any hour of monitoring, Grade 2, ≧30 uniform PVCs in any hour of monitoring, Grade 3, multiform PVCs, Grade 4A, couplets, Grade 4B, ventricular tachycardia, and Grade 5, R on T, defined as having a prematurity index RR'/QT <1. The values were expressed as mean±S.D. and the results were tested by student's test.

Echocardiographic classification of DCM

We categorized the patients as four groups according to the initial echocardiographic parameters (**Fig. 1**) based on our preliminary study[17], in which the echocardiographic LV dimensions, particularly Ds were regarded as good parameters in leading fatal congestive heart failure.

Group I: 17 patients with mild to moderate LV dilatation without hypertrophy (Ds<60 mm, WTs<15 mm); Group II: 12 with mild to moderate LV dilatation and hypertrophy (Ds <60 mm, WTs≧15 mm); Group III: 8 with marked LV dilatation and hypertrophy (Ds ≧60 mm, WTs≧15 mm); and Group IV: 13 with marked LV dilatation without hypertrophy (Ds≧60 mm, WTs<15 mm). LV hypertrophy (WTs≧15 mm) was found in 20 patients, and none in 30. Twenty-one patients had marked LV dilatation (Ds≧60 mm), and it was mild to moderate in 29 (Ds<60 mm).

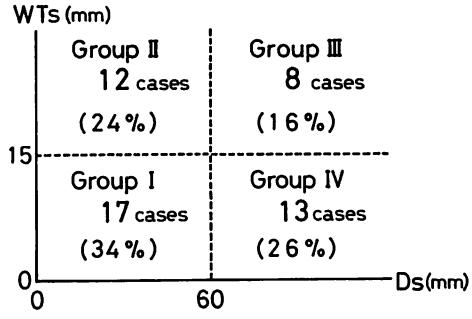

Fig. 1. Relation between Ds and WTs in 50 patients with dilated cardiomyopathy at the initial study.

Ds=LV end-systolic dimension; WTs=LV wall thickness at end-systole.

Results

1. Clinical and angiographic findings at the entry of this study

Twenty-eight patients were in NYHA functional class II, 19 in class III and 3 in class IV (**Fig. 2**). In Group I, 12 of 17 patients were in class II. Cardiothoracic ratios (CTR) were 60±7% in the study population, and CTRs in the first study in each Group were 56±7 (mean ±SD), 62±6, 61±7, and 61±8%, respectively. Numbers of ECG lead showing abnormal Q waves in the study population in each were 0.9±1.6, 1.4±2.4, 0.8±1.3, 0.3±0.5, and 0.7±1.1 leads, respectively. The voltage of Sv_1+Rv_5 in the study population and each Group was averaged 3.4±1.7, 3.3±1.8, 3.4±1.4, 4.3±1.8, and 2.9±1.7 mV, respectively. Thus NYHA functional class, CTR and ECG findings had no statistically significant difference among 4 groups. Cardiac catheterization and angiography revealed that cardiac index of 2.8±0.9 *l*/min/m^2, pulmonary capillary wedge pressure of 16±10 mmHg, and LV ejection fraction of 37±12% in 33 patients. There were no statistically significant differences among four groups.

2. Echocardiographic findings at the entry of this study

Echocardiographic results are summarized in

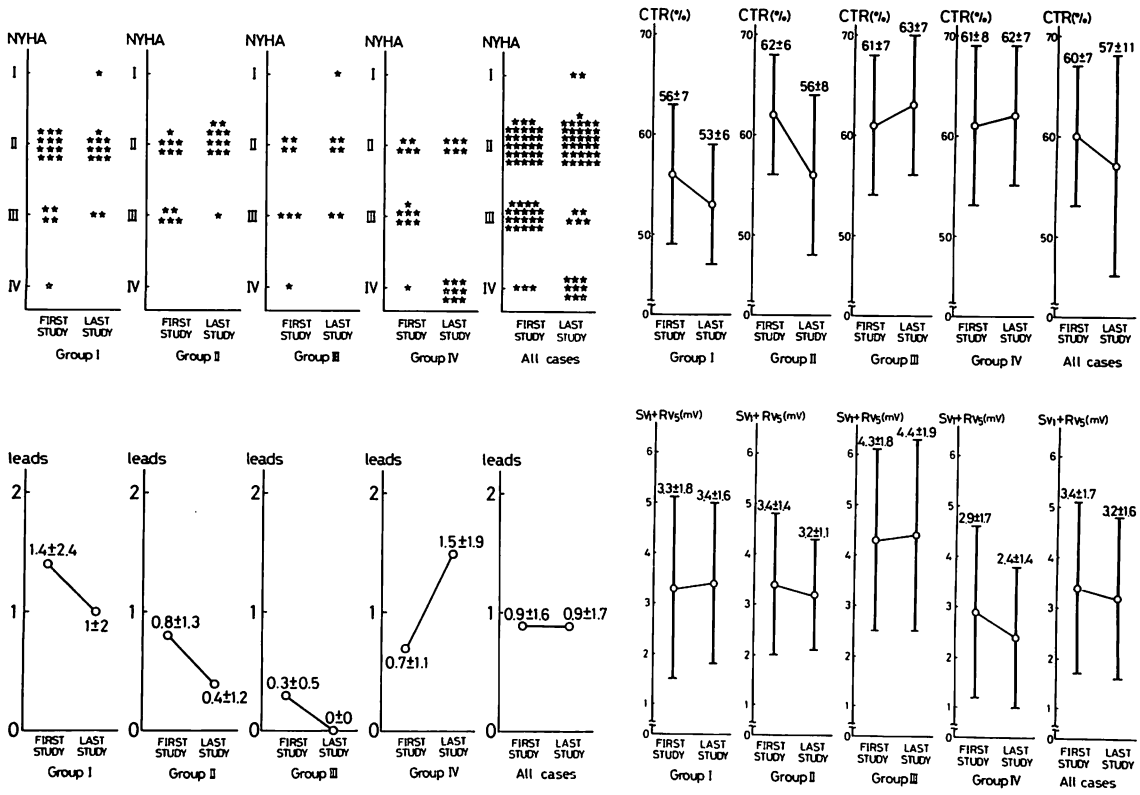

Fig. 2. NYHA functional class, CTR, number of ECG leads showing abnormal Q wave and Sv_1+Rv_5 voltage at the initial and last study.

Table 1. By definition, Dd of Group III and IV were significantly greater than that of Group I and II. Ds of Group III and IV was significantly greater than that of Group I and II. ⊿D of Group III and IV was significantly smaller than that of Group I and II. WTd of Group II and III was significantly greater than that of Group I and IV. WTs of Group II and III was also significantly greater than that of Group I and IV. In general, Ds/WTs in Group I, II, III, and IV was significantly different each other.

3. Ambulatory ECG findings

Prevalence of ventricular arrhythmias was shown in **Fig. 3**. All 32 patients had complex PVCs (Lown grading 3 or 4). Twenty-eight patients had couplets or ventricular tachycardias (Grade 4) and four patients had multifocal PVCs (Grade 3). The prevalence of Grade 4 arrhythmias in Group I, II, III, and IV was 89, 100, 75 and 75%, respectively.

4. Follow-up data

Changes in echocardiographic parameters were observed in nine patients (**Fig. 4**). Three patients in Group I and two in Group II had progressive LV dilatation. Two patients in Group III and one in Group IV had regression of LV dilatation. On the other hand, no patients had progression or regression of LV hypertrophy except one patient in Group I, who showed progressive LV hypertrophy and was finally categorized as Group II. Eight patients who died of congestive heart failure during the follow-up period included five patients in Group IV and three in Group I. The latter three progressed to Group IV and died. No patient with LV hypertrophy (Group II and III) died of

Table 1. Echocardiographic findings at the entry of this study

		Group I	Group II	Group III	Group IV	All cases	p value	
Dd	(mm)	63±3	64±8	76±6	72±6	68±8	p<0.001	I vs III, I vs IV
							p<0.005	II vs III
							p<0.01	II vs IV
Ds	(mm)	51±5	50±7	66±4	64±8	57±9	p<0.001	I vs III, I vs IV
								II vs III, II vs IV
⊿D	(%)	19±6	21±8	13±4	11±4	17±7	p<0.005	I vs IV, II vs IV
							p<0.05	I vs III, II vs III
WTd	(mm)	10±1	13±2	12±2	9±1	11±2	p<0.001	I vs II, I vs III
								II vs IV, III vs IV
WTs	(mm)	13±2	17±3	17±2	12±2	14±3	p<0.001	I vs II, I vs III
								II vs IV, III vs IV
Ds/WTs		4.0±0.4	3.1±0.8	4.2±0.8	5.7±1.4	4.3±1.3	p<0.001	Ivs II, I vs IV, II vs IV
							p<0.01	III vs IV
							p<0.02	II vs III

Db=LV end-diastolic dimension; Ds=LV end-systolic dimension; ⊿D=LV percent fractional shortening; WTd=LV wall thickness at end-diastole; WTs=LV wall thickness at end-systole.

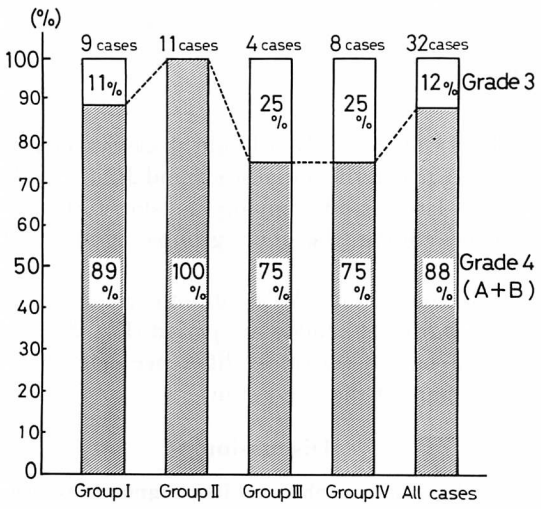

Fig. 3. Ambulatory ECG findings in 32 patients.
For classifying ventricular arrhythmias, Lown's grading system is used.

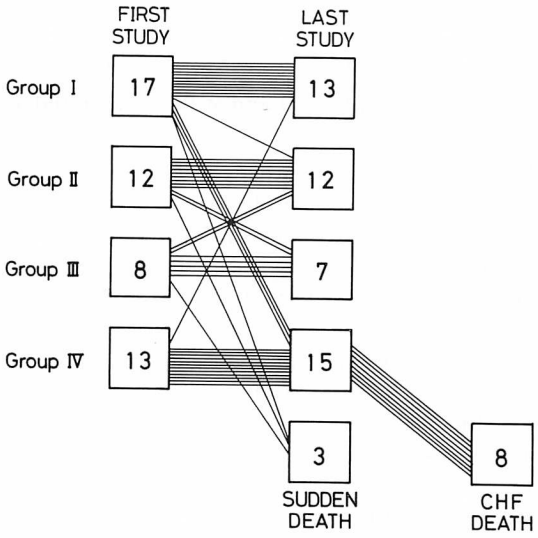

Fig. 4. Breakdown of 50 patients during the follow-up period.
CHF=congestive heart failure.

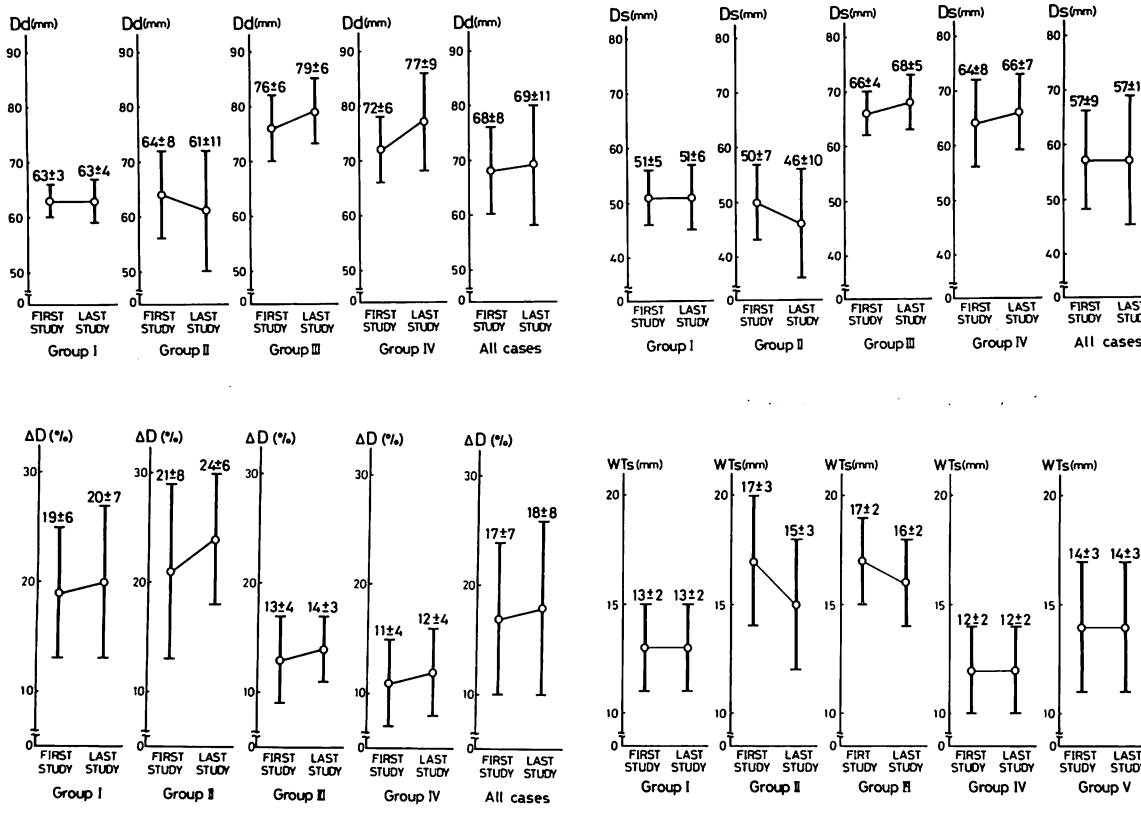

Fig. 5. Dd, Ds, ⊿D and WTs at the initial and last studies.

heart failure. Three patients of Group I, II and III experienced sudden deaths.

Two patients were in NYHA functional class I, 31 in class II, five in class III, and nine in class IV in the latest study (**Fig. 2**). Seven patients initially in functional class III in Group IV experienced deterioration and progressed to class IV in the latest study.

CTR in all cases averaged 60±7 and 57±11% at the initial and the latest study, and no significant changes were observed. At the latest study, the CTR among four groups had no significant difference.

The number of ECG leads with abnormal Q waves in all cases was 0.9±1.6 at the initial study and 0.9±1.7 leads at the last study, and there was no statistical difference among the four groups at the last study.

ECG voltages of Sv_1+Rv_5 in all cases averaged 3.4±1.7 mV at the initial study and 3.2±1.6 mV at the latest study, giving no statistical difference among the four groups at the last study.

Dd, Ds, ⊿D and WTs did not change significantly during the follow-up period (**Fig. 5**), and did not have a statistical difference among the four groups at the latest study.

Discussion

1. LV hypertrophy and its prognostic significance

Most of the previous studies emphasized exclusively the significance of LV dilatation in terms of the cardiac dysfunction in DCM, but did not focus the potential importance of LV hypertrophy. However, the development of hy-

pertrophy was regarded as one of the important factors for predicting prognosis by Feild et al[4], who assessed LV function and hypertrophy using invasive technique in 36 patients with DCM and concluded that not only LV ejection fraction but also ratio of LV mass/volume, a relative degree of LV hypertrophy, closely related to the postcatheterization course. Hatle et al[6] reported that an angiographical increase in LV wall thickness was closely related to better prognosis. Das et al[10] also reported a favorable response to vasodilators in DCM with LV hypertrophy using echocardiography. The pathologic study by Benjamin et al[18] revealed that patients of DCM with compensatory LV hypertrophy had more favorable prognosis.

LV relative wall thickness, expressed as the LV volume/mass or LV dimension/wall thickness ratio, has provided important diagnostic and prognostic informations in patients with heart diseases[19]. This parameter has a constant relation with LV systolic pressure in subjects with a normal heart and physiologic forms of cardiac hypertrophy. Greatly increased values, suggesting inadequate hypertrophy, indicate a poor prognosis, as in the cases of chronic aortic regurgitation.

The follow-up results in the present study indicate the importance of LV hypertrophy to the prognosis of DCM. Eight patients who died of congestive heart failure did not have LV hypertrophy throughout the follow-up period and the patients with LV hypertrophy (Groups II and III) never died of heart failure. It was, therefore, postulated that patients with acquired compensatory hypertrophy may survive longer than those without LV hypertrophy, and that the increased wall stress might be an important factor to the prognosis. This, in turn, indicates that the echocardiography is highly recommended in the early detection and management of high risk patients.

2. Ventricular arrhythmia and prognosis

Ambulatory ECG monitoring has been useful in detecting and evaluating the significance of cardiac arrhythmias in terms of the prognostic significance of patients with coronary artery disease or hypertrophic cardiomyopathy[16,20,21]. However, in patients with DCM, little is known about the incidence of ventricular arrhythmias and their significance. Huang et al[22] reported that 77% and 60% of 35 patients with DCM had multifocal PVCs and ventricular tachycardias, respectively. Our study demonstrated life-threatening ventricular arrhythmias in all patients studied, and a higher prevalence of complex PVCs than that of Huang et al. Three patients experienced unexpected, sudden death during the follow-up period. Each patient was in Group I, II and III, at the initial study and sudden death was considered independent of the various echocardiographic findings. Thus, intensive antiarrhythmic therapy is mandatory in all patients with DCM.

拡張型心筋症における左室壁肥厚の臨床的意義：心エコー図法による検討

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本研究の目的は，心筋収縮不全を基本病態とし，種々の程度の左室の拡張・肥大を有する症例を含む拡張型心筋症 (dilated cardiomyopathy) における，左室壁肥大の臨床的意義を明らかにすることにある．

症例は 1976 年から 1983 年までの 50 例(男性 41 例，女性 9 例)で，これを初診時の心エコー図所見のうち，収縮末期左室短径 Ds および収縮末期左室壁厚 WTs の 2 指標に基づき，Group I (Ds＜60 mm，WTs＜15 mm) 17 例，Group II (Ds＜60 mm，WTs≧15 mm) 12 例，Group III (Ds≧60 mm，WTs≧15 mm) 8 例，および Group IV (Ds≧60 mm，WTs＜15 mm) 13 例の 4 群に分類し，最長 7 年，平均 2.7 年の follow-up を行った．壁肥厚例 (Group II, III) は 20 例，非壁肥厚例 (Group I, IV) は 30 例であった．

経過観察中，Group IV の 5 例と Group I よ

り Group IV に移行した3例の計8例が心不全死したが，Group II および Group III には心不全死例は認められなかった．Group I～III の3群のうち計3例は突然死を遂げ，長時間心電図検査を施行した32例全例に，心室頻拍を含む重篤な心室性不整脈が検出された．

本症における左室壁肥大の有無は，心不全死に関する予後と密接な関連を有し，壁肥厚は心筋収縮不全に対する代償的機序を果していると考えられる．一方，突然死や致死的不整脈は左室拡張・壁肥大の軽度な症例にも認められ，本症では全例に強力な抗不整脈療法が必要であると考えられた．

文　献

1) Goodwin JF: Congestive and hypertrophic cardiomyopathies. A decade of study. Lancet **1**: 731, 1970
2) Brandenburg RO, Chazov E, Cherian G, Falase AO, Grosgogeat J, Kawai C, Loogen F, Martin Judez V, Orinius E, Goodwin JF, Olsen EGJ, Oakley CM, Pisa Z: Report of the WHO/ISFC task force on definition and classification of cardiomyopathies. Circulation **64**: 437A, 1981
3) Shugoll GI, Bowen PJ, Moore JP, Lenkin ML: Follow-up observations and prognosis in primary myocardial disease. Arch Intern Med **129**: 67, 1972
4) Feild BJ, Baxley WA, Russell RO, Hood WP, Holt JH, Dowling JT, Rackley CE: Left ventricular function and hypertrophy in cardiomyopathy with depressed ejection fraction. Circulation **47**: 1022, 1973
5) Hatle L, Örjavik O, Storstein O: Chronic myocardial disease. I. Clinical picture related to long-term prognosis. Acta Med Scand **199**: 399, 1976
6) Hatle L, Stake G, Storstein O: Chronic myocardial disease. II. Haemodynamic findings related to long-term prognosis. Acta Med Scand **199**: 407, 1976
7) Oakley C: Diagnosis and natural history of congested (dilated) cardiomyopathies. Postgrad Med J **54**: 440, 1978
8) Shirey EK, Proudfit WL, Hawk WA: Primary myocardial disease: Correlation with clinical findings, angiographic and biopsy diagnosis. Follow-up of 139 patients. Am Heart J **99**: 198, 1980
9) Unverferth DV, Magorien RD, Lewis RP, Leier CV: Long-term benefit of dobutamine in patients with congestive cardiomyopathy. Am Heart J **100**: 622, 1980
10) Das SK, Randall OS, Steffens TG: Ventricular wall thickness. A predictor of response to vasodilators in cardiomyopathy. Eur J Cardiol **12**: 103, 1980
11) Fuster V, Gersh BJ, Giuliani ER, Tajik AJ, Brandenburg RO, Frye RL: The natural history of idiopathic dilated cardiomyopathy. Am J Cardiol **47**: 525, 1981
12) Lengyel M, Kökény: Follow-up study in congestive dilated cardiomyopathy. Acta Cardiol **36**: 35, 1981
13) Hayakawa M, Inoh T, Kawanishi H, Kaku K, Kumaki T, Yokota Y, Fukuzaki H: Evaluation of left ventricular function in patients with dilated cardiomyopathy by exercise echocardiography. J Cardiography **12**: 605, 1982 (in Japanese)
14) The Criteria Committee of the New York Heart Association. Nomenclature and Criteria for Diagnosis of Diseases of the Heart and Great Vessels. 8th ed, Little Brown, Boston, 1979, p 290
15) Clark RD, Korcuska K, Cohn K: Serial echocardiographic evaluation of left ventricular function in valvular disease, including reproducibility guidelines for serial studies. Circulation **62**: 564, 1980
16) Lown B, Wolf M: Approaches to sudden death from coronary heart disease. Circulation **44**: 130, 1971
17) Hayakawa M, Inoh T: Study of dilated cardiomyopathy with special reference to the observation of mitral apparatus and long-term follow-up by two-dimensional echocardiography. Abstract of 3rd Meeting of the World Federation for Ultrasound in Medicine and Biology, 1982, p 76
18) Benjamin IJ, Schuster EH, Bulkley BH: Cardiac hypertrophy in idiopathic dilated congestive cardiomyopathy : A clinicopathologic study. Circulation **64**: 442, 1981
19) Gaasch WH: Left ventricular radius to wall thickness ratio. Am J Cardiol **43**: 1189, 1979
20) McKenna WJ, England D, Doi YL, Deanfield JE, Oakley C, Goodwin JF: Arrhythmia in hypertrophic cardiomyopathy : I. Influence on prognosis. Br Heart J **46**: 168, 1981
21) Maron BJ, Savage DD, Wolfson JK, Epstein SE: Prognostic significance of 24-hour ambulatory electrocardiographic monitoring in patients with

hypertrophic cardiomyopathy: A prospective study. Am J Cardiol **48**: 252, 1981
22) Huang SK, Messer JV, Denes P: Significance of ventricular tachycardia in idiopathic dilated cardiomyopathy: Observations in 35 patients. Am J Cardiol **51**: 507, 1983