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Clinical characteristics of cardiomyopathy with mild dilatation

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Summary

The clinical features of 20 patients with mildly dilated cardiomyopathy (MDCM) were investigated by electrocardiography and echocardiography. MDCM was defined as conditions with : 1) left ventricular end-diastolic dimension between 55 and 65 mm and 2) left ventricular fractional shortening between 10 and 25%.

Nine patients (45%) had no histories of congestive heart failure. Eight patients had atrial fibrillation, and the other 12 patients were in regular sinus rhythm. Two patients had supraventricular premature contractions and five patients had ventricular premature contractions. One patient had paroxysmal atrial tachycardia. During the 40-months' span of this echocardiographic study, left ventricular end-diastolic dimension (60.8 ± 3.8 mm to 57.3 ± 4.6 mm) and left ventricular fractional shortening (17.2 ± 4.6% to 22.7 ± 7.1%) did not change significantly. One patient died suddenly.

These results suggest that 1) some patients with MDCM have neither definite histories nor symptoms to suggest heart failure ; 2) the hemodynamic conditions of patients with MDCM do not always deteriorate, but rather stabilize, and even improve during follow-up periods ; 3) several types of arrhythmias can be observed, even in standard resting electrocardiograms ; and 4) patients with MDCM may die suddenly.

Key words

Dilated cardiomyopathy Echocardiography Electrocardiography Clinical course

Introduction

Dilated cardiomyopathy (DCM) consists of disease of the heart muscle which is characterized by ventricular dilatation, poor systolic function and greatly reduced ejection fraction[1~5]. Previous studies have shown that DCM usually meets grave prognosis[6~8]. However, the clinical course may vary among DCM patients : as progressively deteriorating, or stable, or even improving for varying periods[9,10]. Figulla et al. recently demonstrated that hemodynamic conditions improved or became stabilized in 22 of 56 DCM patients[11]. Important DCM characteristics other than hemodynamic conditions include various types of arrhythmias[7,12~14], and ventricular arrhythmias have reportedly been significantly associated with

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cardiac deaths[15].

Mild dilatation of the left ventricle and slight impairment of systolic function suggest early stages of DCM. This condition has been termed "mildly dilated cardiomyopathy (MDCM). We have observed these patients without complaints or symptoms. However, there have been few studies of MDCM with mild dilatation and slightly depressed function. The aim of this study was to investigate clinical characteristics and courses of patients with MDCM investigated using standard electrocardiograms and echocardiograms.

Methods

Patients

Among 48 consecutive patients with DCM observed at Tsukuba University Hospital, 20 had mild dilatation of the left ventricle and relatively poor systolic function (MDCM). DCM was diagnosed according to the definition of the WHO/ISFC[1]. The patients with MDCM fulfilled the following additional criteria : 1) left ventricular end-diastolic diameter (Dd) between 55 mm and 65 mm, and 2) left ventricular fractional shortening (FS) between 10 and 25%. The patients consisted of 17 men and three women and ranged in age from 18 to 76 years (mean±SD, 51±17). Patients with clinical evidence of systemic hypertension, cor pulmonale, valvular heart disease, congenital heart disease and systemic disease involving the heart were excluded from the study. In 11 patients whom selective coronary angiography was performed according to the Judkins technique, no significant stenosis was observed. The other patients had neither symptoms nor signs to suggest coronary artery disease. All patients' histories were taken and their physical examinations were performed by two physicians. The functional status of each patient at the initial examination was judged according to the classification of the New York Heart Association (NYHA). Four patients were in NYHA functional Class III ; six in Class II ; and 10 in Class I. According to their degrees of cardiac failure, 15 patients were treated with digitalis ; 13 with diuretics, and five with vasodilators. Seven patients were also treated with antiarrhythmic drugs.

Electrocardiograms and echocardiograms

Electrocardiograms were obtained at rest using a simultaneous six-channel recorder. All electrocardiographic findings were independently interpreted by two cardiologists. M-mode and cross-sectional echocardiograms were obtained using a Toshiba SSH-11A cross-sectional ultrasonoscope with a 2.4 MHz transducer. M-mode echocardiograms were recorded on light-sensitive paper (Kodak Linagraph, 1985) at a paper speed of 50 mm/s using a Honeywell 1956 strip chart recorder. All echocardiograms were obtained with the patients in a slight left lateral position. The transducer was placed at the third or fourth intercostal space near the left sternal border. Left ventricular M-mode echocardiograms were recorded at the level of the chordae tendineae just below the tip of the mitral leaflets during monitoring by two-dimensional echocardiograms. Electrocardiograms and phonocardiograms with a contact microphone placed at the second intercostal space near the left sternal border were recorded simultaneously with the echocardiogram. Recordings were made during suspended expiration and care was taken to avoid involuntary Valsalva maneuvers. The diameter of the left ventricle was measured as the distance between the echoes of the left ventricular posterior wall and the interventricular septum. Left ventricular end-diastolic diameter (Dd) was determined at the time of the R wave of the electrocardiogram, and the end-systolic diameter (Ds) was determined at the onset of the second heart sound on the phonocardiogram. All measurements were made with a centimeter scale superimposed on the echocardiogram. Fractional shortening (FS) was calculated as : $(Dd-Ds)/Dd \times 100$.

Echocardiographic findings and other clinical data of the individual case are listed in **Table 1**. Dd was 60±3 mm and FS was 17±4% (mean±SD).

Clinical course and prognosis

Follow-up studies during a mean of 40 months

Table 1. Study population and clinical data

Case	Age (y.o.)	Sex	History of CHF	NYHA	Dd (mm)	FS (%)
1	58	M	−	I	65	18
2	61	F	+	III	64	11
3	57	M	+	II	60	11
4	51	F	+	III	65	11
5	62	M	+	II	56	14
6	66	M	+	I	63	11
7	66	M	+	II	56	19
8	50	M	−	I	57	18
9	37	F	−	I	65	22
10	38	M	−	I	64	19
11	60	M	−	I	56	23
12	18	M	+	II	62	16
13	59	M	−	I	57	19
14	51	M	+	II	65	17
15	58	M	+	III	60	17
16	43	M	−	I	59	12
17	56	M	−	I	60	12
18	76	M	+	II	55	16
19	74	M	+	III	60	17
20	47	M	−	I	60	20

NYHA=New York Heart Association functional class; M=male; F=female; Dd=left ventricular end-diastolic diameter; FS=fractional shortening.

(range 25～60 months) were performed on the basis of echocardiographic data (Dd, FS) of the 12 patients. There were 10 men and two women whose average age was 53 years.

Statistical analysis

Differences in hemodynamic courses were evaluated using the Wilcoxon test, since a normal distribution could not be presumed because of the nonlinearity of the parameters.

Results

History of heart failure

Eleven patients (55%) had histories and symptoms typical of cardiac failure, such as orthopnea, dyspnea on exertion and peripheral edema. Their cardiac functional status was NYHA functional Class II or III at their initial examinations in our hospital. The other nine patients (45%) had neither symptoms nor histories to suggest heart failure. They were all in NYHA functional Class I at their initial examinations.

Electrocardiographic findings

All patients had electrocardiographic abnormalities. Eight (40%) had atrial fibrillation; the other 12 were in regular sinus rhythm. Among the 12 patients with sinus rhythm, two had supraventricular premature contractions and three had ventricular premature contractions. Two patients with atrial fibrillation had ventricular premature contractions too. One patient with regular sinus rhythm had also paroxysmal atrial tachycardia. ST or T wave abnormalities were observed in 19 of the 20 patients, regardless of their taking digitalis. One patient without ST or T wave abnormalities had atrial fibrillation. Fourteen patients had high voltage in their precordial leads; three patients had complete right bundle branch block.

Fig. 1 shows the electrocardiogram of a patient (Case 20) who had no history of heart failure. The patient did not complain of any symptoms such as dyspnea, while playing golf. His home doctor incidentally detected his electrocardiographic abnormality during a checkup. The patient visited our hospital because of his electrocardiographic abnormalities. His electrocardiogram at that time revealed paroxysmal atrial tachycardia, flat T waves in leads II, III, aVF, V_5 and V_6, and negative T waves in $V_{4\sim6}$. His echocardiogram showed mild dilatation of his left ventricle (Dd 60 mm, Ds 48 mm) and a slightly decreased left ventricular systolic function (FS 20%).

Clinical course and prognosis

Dd decreased significantly, on the average from 61 mm to 57 mm, and Ds decreased significantly from 51 mm to 44 mm during the follow-up period ($p<0.01$, $p<0.01$, respectively). FS tended to increase from $17.2\pm4.6\%$ to $22.7\pm7.1\%$, though the difference was not statistically significant. In **Fig. 2** serial changes of Dd of each of the 12 patients are shown according to time. In most cases there was a gradual decrease in Dd with time, though it increased slightly in one patient. In **Fig. 3**

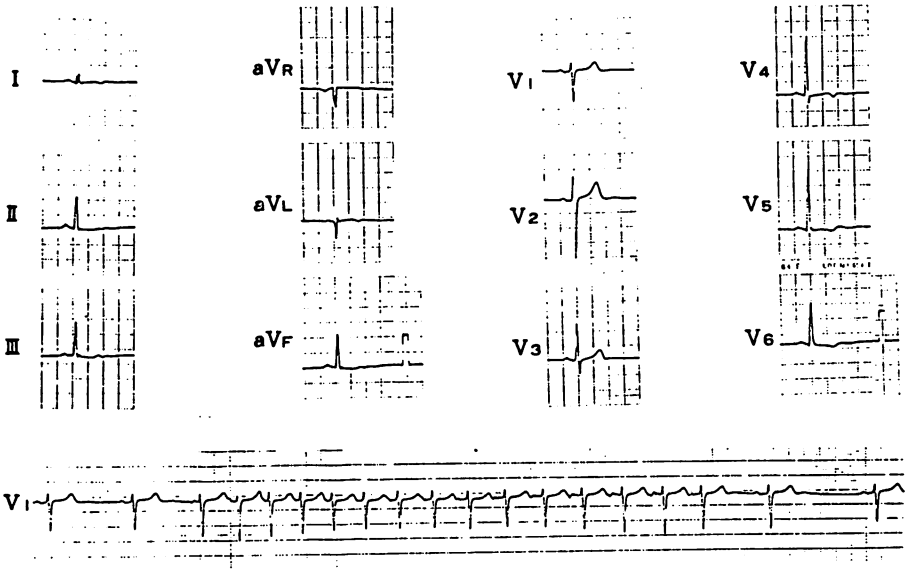

Fig. 1. Electrocardiogram of a patient (Case 20) **without history of heart failure.**
This electrocardiogram shows flat T waves in leads II, III, aV_F, V_5 and V_6, and negative T waves in $V_{4\sim6}$. The lower panel demonstrates paroxysmal atrial tachycardia.

FS of the individual patient is shown in relation to time. Significant fluctuations in FS, indicating great variability in the individual patient's contractility, were rare (except for one patient). One patient improved significantly (from 14% to 41% during a 45-month interval) and the conditions of the other patients were nearly stable, and no patient deteriorated significantly.

One patient (Case 2) died suddenly during the follow-up period after taking a bath, though his follow-up echocardiographic study did not show deterioration of his left ventricular systolic function (Dd 64 mm, Ds 57 mm, FS 11% at initial examination; Dd 64 mm, Ds 57 mm, FS 11% at final examination; interval, 60-months). His electrocardiogram at rest showed regular sinus rhythm and inverted T waves in the precordial leads, but no ventricular or supraventricular premature beats. Before his death, he did not complain of any serious symptoms.

Fig. 4 shows the echocardiograms at the initial examination (**Fig. 4** left) and the final examination (**Fig. 4** right) of Case. 14, whose chief complaint was dyspnea on exertion. The first echocardiogram showed Dd of 65 mm, Ds of 54 mm and FS of 17%. The last echocardiogram, which was recorded 32 months after the first visit, shows Dd of 60 mm, Ds of 48 mm and FS of 20%. These echocardiographic findings suggested that the patient's condition did not deteriorate during the long interval, though he took no prescribed cardiovascular drugs such as digitalis or diuretics, because he had fairly good systolic function during the follow-up period. His electrocardiogram showed atrial fibrillation and high voltage, but no ST-T wave abnormalities in the precordial leads.

Discussion

It may be possible that during long latent period in some individuals of DCM, cardiac disorders may remain obscure. Probably the disorders exist in milder forms and remain undetected in a number of individuals who are not examined. It seems that impairment

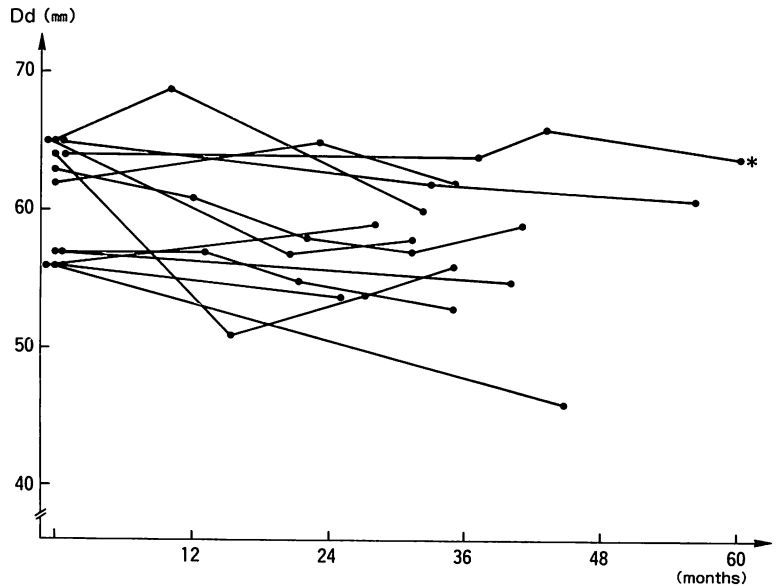

Fig. 2. The course of left ventricular end-diastolic diameters (Dd) **in 12 patients examined several times.**

In most of the cases there is a monotonic decrease in Dd with time.

*=patient who died suddenly.

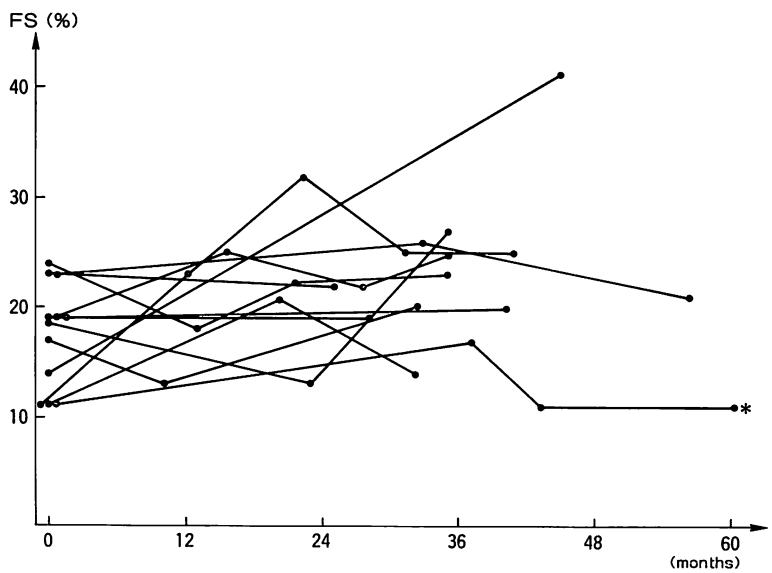

Fig. 3. The course of fractional shortening (FS) **in 12 patients examined several times.**

FS improved significantly in one patient and did not change in the other patients, but no patients deteriorated significantly.

*=patient who died suddenly.

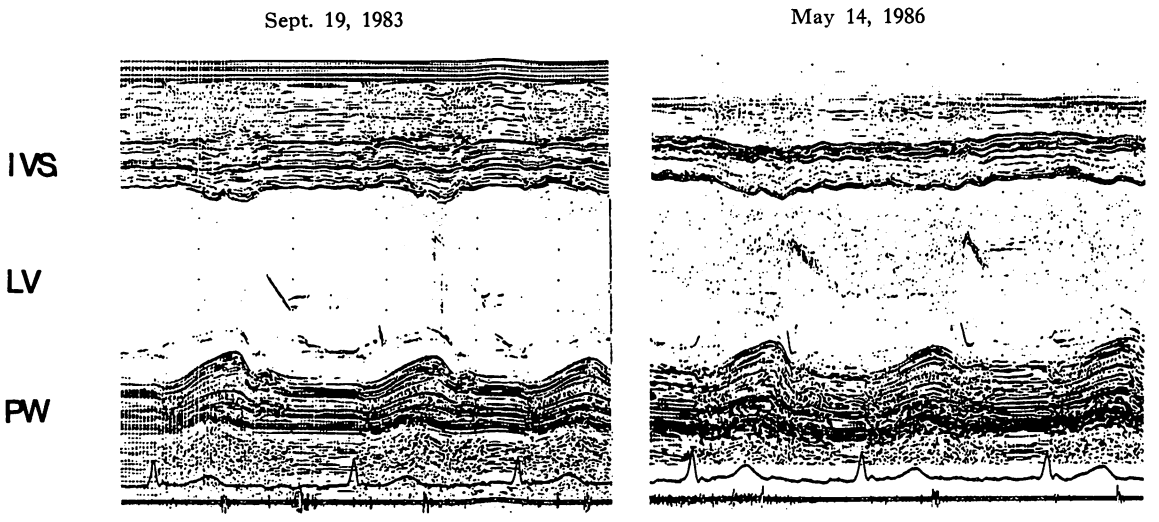

Fig. 4. Echocardiograms at the initial examination (left) **and the last examination** (right) **in a patient** (Case 14).

These echocardiographic findings suggest that the condition of the patient do not deteriorate during the long interval (32 months).

IVS=interventricular septum; LV=left ventricular cavity; PW=posterior wall of the left ventricle.

of left ventricular systolic function may be compensated for by increasing left ventricular end-diastolic volume. This does not permit early diagnosis of patients because they do not complain of cardiac symptoms. Curtius et al. demonstrated the existence of latent cardiomyopathy[16], and defined it by the normal thickness of the septum and the posterior wall of the left ventricle as measured by M-mode echocardiography, normal left ventricular end-diastolic volume, normal ejection fraction and no outflow tract obstruction of the left ventricle, but elevated left ventricular end-diastolic pressures at rest or, in most cases, on exercise. They suggested that latent cardiomyopathy could be a pre-stage of DCM and a pre-symptomatic and early manifestation of DCM[16]. Kurozumi et al. also reported that cardiac systolic performance deteriorated on angiotensin II loading in patients with latent DCM who had mildly dilated left ventricle and slightly decreased left ventricular function[17]. Previous studies emphasized that the clinical characteristics and the course of latent cardiomyopathy should be investigated[9,17,18].

Keren et al. demonstrated the clinical and morphologic data of patients in whom the characteristic features of DCM were noted without significant ventricular dilatation[19]. They also termed such DCM as "mildly dilated, congestive cardiomyopathy". But there are clear differences between our patients and theirs. Their patients underwent cardiac transplantation because of Class IV NYHA heart failure; whereas none of our patients belonged to NYHA Class IV. Dd of their patients was nearly the same as that of ours, but FS of their patients was significantly smaller than that of ours. They cited a group of patients with end-stage heart disease whose hearts were only mildly dilated. However, we wish to emphasize that this type of DCM should be an early form of DCM.

According to most reports of previous studies, the prognosis of DCM is poor[6~8]. The average yearly mortality of DCM is reportedly about

10%[7,8,11]. However, a recent study revealed that the condition of 22 of 42 patients with DCM (52%) improved, or at least, did not change[11]. Since the end-diastolic diameters of their patients were larger than those of ours, our patients may have an earlier stage of DCM than were theirs. That may be one of the reasons why the clinical courses of our patients were better than those of their patients.

Many numerous longitudinal studies have stressed correlations between the outcomes of DCM and numerous factors such as histories of alcohol consumption[7], cardiothoracic ratio[7,8], hemodynamic manifestations[7,8,14,20,21] or electrocardiographic abnormalities[8,21]. Fuster et al. followed up 104 patients with DCM and showed that their cardiothoracic ratios on chest radiograph, cardiac indices and left ventricular end-diastolic pressures were highly predictive of the clinical outcomes[7]. However, a recent study showed that cardiac deterioration may occur among some of the cases who had slightly depressed contractility of the left ventricle at the first admission[11]. The present study demonstrated that the hemodynamic conditions of all patients with MDCM did not deteriorate during the follow-up period. The reason why there was no deterioration among our patients is obscure, but may have depended on our patient selection. They included patients in the acute phase of DCM. In our study, the patients became already stabilized before their entry into this study, because 11 patients experienced heart failure and improved significantly on medical treatment after their entry. The other nine patients in our study did not manifest heart failure. This profile is different from that of their patients.

Several types of arrhythmias were observed in our patients, including supraventricular premature contractions, ventricular premature contractions, atrial fibrillation and paroxysmal atrial tachycardia. Supraventricular premature contractions are not thought to play a significant role in cardiac deaths, but they can lead to atrial fibrillation[22]. Atrial fibrillation has reportedly been a significant risk factor[10] and may have some predictive value for systemic emboli[7]. Unverferth et al. reported that there was an apparent relationship between mortality and an increase in malignancy of ventricular arrhythmias recorded by standard electrocardiography[21]. Meinertz et al. reported the prognostic significance of ventricular arrhythmias identified by 24-hour ambulatory electrocardiography[15]. Their study patients with DCM who died suddenly had significantly more frequent episodes of ventricular tachycardia, or greater numbers of ventricular pairs or total ventricular premature contractions as compared with survivors and those who died from congestive heart failure. The standard electrocardiogram of our patient who died suddenly showed no ventricular arrhythmias, but this does not exclude the possibility that 24-hour ambulatory electrocardiography might have demonstrated ventricular arrhythmias in this patient. Meinertz et al. also observed no correlation between clinical symptoms or the degree of left ventricular impairment and the number of ventricular pairs, or episodes of ventricular tachycardia[15]. In our study, ventricular arrhythmias were revealed even in patients with MDCM who had no histories of heart failure.

Several studies[23~26] of endocardial biopsies have shown that chronic inflammatory cells are present in five to 65% of patients with DCM. A correlation between viral infection and DCM has been suggested[23~26]. Hayakawa et al. followed up acute myocarditis and demonstrated that some of the patients with acute myocarditis resulted in left ventricular dilatation and dysfunction[27]. However, Vignola et al. reported the results of right ventricular endomyocardial biopsies in patients with ventricular arrhythmias but without apparent heart disease, and there was no ventricular dilatation and only normal systolic function[28]. Six of the 12 biopsies demonstrated clinically unsuspected lymphocytic myocarditis. Judging from these reports, myocarditis is thought to be one of the etiologic factors that causes mild dilatation of the left ventricle with various kinds of arrhythmias.

There are numerous reports of patients with DCM who died suddenly[5,10,12~15,21,29] as patients with hypertrophic cardiomyopathy[28,30]. The incidence of sudden death in DCM is estimated to be 14～100%[5,12~15,21,29]. Most of these sudden deaths are probably arrhythmic in origin. But the standard electrocardiogram of our patient who died suddenly showed no significant arrhythmias. A 24-hour ambulatory electrocardiogram was not obtained in our patient. The results of a standard electrocardiogram do not necessarily mean that 24-hour ambulatory electrocardiography cannot detect significant ventricular arrhythmias. We assume that the death might have been arrhythmic in origin, but we do not have to prove this point. In the study of Meinertz et al. the patients with DCM, in whom frequent episodes of ventricular tachycardia or ventricular pairs were detected by 24-hour Holter monitoring, were at high risk of sudden death and the severity of ventricular arrhythmias was unrelated to the impairment of left ventricular function[15]. Olshausen et al. reported that the correlation between ejection fraction and the occurrence of ventricular tachycardia was relatively poor in patients with DCM[13]. These reports support conclusions from our results that ventricular arrhythmias were observed in patients with MDCM, and our patient with MDCM died suddenly of arrhythmias.

In the present study, we evaluated the patients with MDCM only by echocardiography. Further studies are required to clarify the pathological significance of MDCM and metabolic abnormalities in patients with MDCM.

In conclusion : 1) some patients with MDCM have neither definite histories nor symptoms to suggest the presence of heart failure ; 2) the hemodynamic conditions of all patients with MDCM do not deteriorate, but stabilize, and even improve during the spans of the studies ; 3) various types of arrhythmias are observed during their standard resting electrocardiography ; and 4) patients with MDCM may die suddenly.

要　約

軽症拡張型心筋症の病態と予後

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拡張型心筋症において左室拡張終期径 (Dd) が 55～65 mm，かつ左室内径短縮率 (FS) が 10～25% の拡張型心筋症を軽症拡張型心筋症と定義し，それに当てはまる 20 例 (男性 17 例，女性 3 例，平均年齢 55 歳) を対象とした．心不全の既往歴および安静時心電図での不整脈について検討した．24 ヵ月以上の経過を観察し得た 12 例につき，心エコー図での Dd, FS の経時的変化ならびに予後を検討した．

20 例中 9 例 (45%) には明らかな心不全歴を認めなかった．上室性期外収縮 2 例，心室性期外収縮 5 例，発作性上室性頻拍 1 例，心房細動 8 例であった．平均観察期間 40 ヵ月において，Dd 60.8±3.8 mm から 57.3±4.6 mm へ，FS は 17.2±4.6% から 22.7±7.1% と変化し，明らかな悪化傾向を認めなかった．死亡は心不全を伴わない突然死 1 例のみであった．

以上より，軽症拡張型心筋症では心不全歴を認めない症例があり，平均 40 ヵ月の観察期間中，心拡張と心機能低下の増悪を認めないが，多彩な不整脈を認め，突然死の可能性があることが示唆された．

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