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Assessments of left ventricular function during exercise in patients with dilated cardiomyopathy: Comparison with ischemic cardiomyopathy

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Summary

Responses to supine bicycle ergometer exercise were assessed in a study population consisting of 26 patients with dilated cardiomyopathy (DCM) and 23 patients with ischemic cardiomyopathy (ICM). Left ventricular ejection fraction (LVEF) and regional wall motion were analyzed at rest and during supine bicycle ergometer exercise with radionuclide ventriculography. Although the same degree of LVEF between DCM (23±8%) and ICM (26±4%) occurred at rest, the left ventricular regional wall motion abnormality was more prominent in DCM. LVEF during the peak exercise stage in DCM was almost unchanged (24±8%), but in ICM it decreased significantly (22±5%). Exercise-induced regional wall motion abnormalities were detected in nine patients (35%) in DCM and 13 patients (57%) in ICM. Although patients with DCM are believed to have diffuse hypokinesis of the left ventricle, severe regional wall motion abnormalities (akinesis or dyskinesis) were frequently observed.

During the follow-up period of up to six years, eight patients with DCM died of congestive heart failure. In eight patients with DCM who showed decreased LVEF during exercise, five patients died. However, only three of 18 patients without decreased LVEF during exercise died.

Exercise-induced left ventricular dysfunction in DCM seems to be a poor prognostic sign.

Key words

Dilated cardiomyopathy　Ischemic cardiomyopathy　Left ventricular function　Exercise test
Prognosis　Regional wall motion

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Introduction

The left ventricle in patients with dilated cardiomyopathy (DCM) has contraction abnormalities although the myocardial cells still seem to be viable, and left ventricular dilatation occurs as a compensatory mechanism. In ischemic cardiomyopathy (ICM); however, myocardial necrosis takes place over wide areas in the left ventricle due to coronary artery disease, which leads to an advanced left ventricular disorder. Although both diseases are caused by different etiological factors, cardiac function is damaged to a similar degree, and some difficulties are encountered in patients in differentiating the two diseases clinically.

We evaluated left ventricular ejection fraction and regional wall motion abnormalities using radionuclide ventriculography at rest and during exercise in the two groups. Furthermore, in patients with DCM, the effects of the regional wall motion abnormalities and abnormal response of LVEF during exercise on the prognosis were studied.

Methods

Patient population

The subjects consisted of 26 patients with DCM who had resting left ventricular ejection fraction (LVEF) less than 35%[1] and sinus rhythm applicable to multigate radionuclide ventriculography. The follow-up period was over a year. Patients with left bundle branch block and significant valvular dysfunction or coronary artery disease were excluded. The 26 patients comprised 21 men and five women, between 27 and 72 (average 50 ± 11) years of age.

Among patients with consecutive 23 patients with significant coronary artery disease and LVEF of 35% or less were selected. Coronary arteriographic findings were one vessel disease in six patients and multivessel disease in 17 patients. There were 20 men and three women, whose ages ranged from 47 to 69 years (average 57 ± 6 years), and their ages were significantly higher ($p<0.05$) than those of the DCM group.

Exercise radionuclide ventriculography

The patients were not being treated with digitalis, diuretics, vasodilators or inotropic agent for 24 hours before radionuclide ventriculography. A 12-lead electrocardiogram and blood pressures were monitored during exercise at regular intervals.

All patients underwent ECG-gated radionuclide ventriculography at rest following in vivo red blood cell labeling with 30 mCi technetium-99 m[2]. Cardiac imaging was performed in a modified left anterior oblique projection using a gamma camera equipped with an all-purpose collimator. Data acquisition was at 28 frames per beat for 5 minutes. Camera data were acquired in a 64×64 matrix frame format and were stored in a Toshiba data processor 90A system. Supine ergometer multistage exercise was performed at a work load of 25 watts. The work load was increased by 25 watts every three minutes. Cardiac imaging was performed at each exercise stage for 2.5 minutes in the same manner as at rest. The exercise test was terminated at the onset of symptoms of dyspnea, chest discomfort, chest pain, or the occurrence of premature ventricular beats. None of the patients in the present study completed the exercise up to the target heart rate.

LVEF was measured using an established method[3]. As shown in **Fig. 1**, the left ventricular image was divided into four segments:

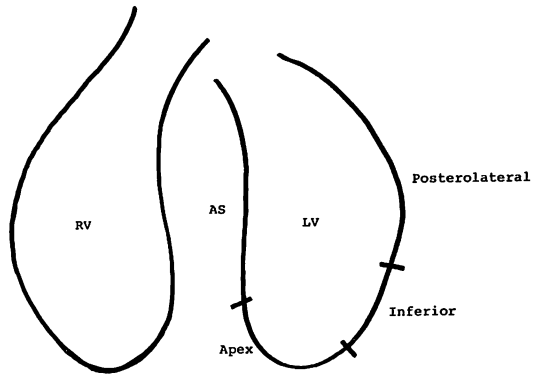

Fig. 1. Blood pool image in left anterior oblique view.

the anteroseptal (AS) wall, apex, inferior wall and posterolateral wall. The regional wall motion of each segment was evaluated using phase analysis[4,5], and moving images were divided into normokinesis, hypokinesis, akinesis or dyskinesis. The wall motion of each segment was scored from 4 to 0, from normokinesis to dyskinesis, and the sums of the scores of each segment were termed the wall motion scores (WMS).

Follow-up study

Twenty-six patients with DCM were observed for 1 to 6 years (average 2.9±1.7 years). Eight patients with DCM died of congestive heart failure.

Statistical analysis

Numerous values provided in this report were expressed as means±standard deviations; any significant difference was verified by either the paired or non-paired t-test. A significant diffference was noted if the p value was less than 0.05. For the patients with DCM, the relation between the prognosis and left ventricular response to exercise was evaluated by the chi square test, and the cumulative survival rate was determined by the Kaplan-Meier method, and any significant difference was decided by the Log-Rank test.

Results

1. Hemodynamic parameters during exercise

Heart rate, blood pressure, pressure rate products (PRP), exercise duration and other indices are shown in **Table 1**, but there were no significant differences between the two groups except index in age and resting wall motion scores. Symptoms of myocardial ischemia such as angina or chest oppression were not observed in patients with DCM, but they were observed in 10 patients with ICM (44%). The exercise was terminated due to arrhythmia in two patients with DCM (one patient with ventricular tachycardia and one patient with frequent ventricular premature beats). The remaining patients could not continue preforming the exercise test due to subjective symptoms, such as dyspnea or leg fatigue.

2. Response of LVEF during exercise (Table 1, Fig. 2)

In DCM, LVEF at rest (23±8%) did not differ significantly from the value of the peak exercise (24±8%). Among individual cases, LVEF was increased in 13, unchanged in four

Table 1. Patient profiles

	DCM	ICM	p value
No. of cases	26	23	
Age (years)	50±11	57± 6	<0.05
Resting HR (/min)	75±15	70±12	NS
Exercise HR (/min)	119±24	118±18	NS
Resting SBP (mmHg)	114±17	111±16	NS
Exercise SBP (mmHg)	144±48	144±21	NS
Resting PRP	8,608±2,338	8,008±1,962	NS
Exercise PRP	18,571±5,746	17,043±4,013	NS
Resting WMS	6.3±1.8	5.3±1.0	<0.05
Exercise duration (min)	7.1±1.9	7.3±1.7	NS
Resting LVEF (%)	23± 8	26± 4	NS
Exercise LVEF (%)	24± 8	22± 5	NS

HR=heart rate; SBP=systolic blood pressure; PRP=pressure rate product; WMS=wall motion score; LVEF=left ventricular ejection fraction; NS=not significant.

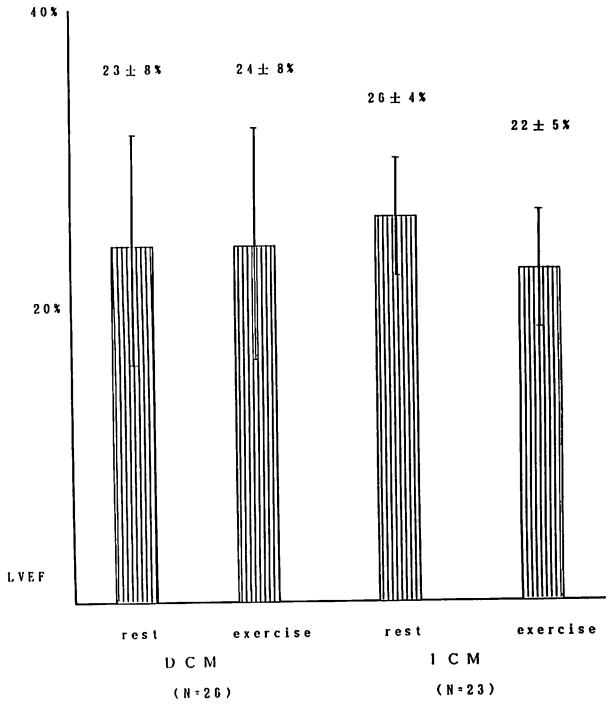

Fig. 2. Changes of LVFE during ergometer exercise.

and decreased in eight patients.

In ICM, the LVEF was 26±4% at rest, and decreased significantly during exercise to 22± 5% ($p<0.001$). Individually, LVEF was increased in three, unchanged in three and decreased in 17 patients. Compared with DCM, there were no significant differences in LVEF either at rest or during exercise.

3. Regional wall motion abnormalities

Regional wall motion at rest was analyzed in patients with DCM. Among a total of 104 segments in the 26 patients, normokinesis was observed in 14; hypokinesis in 48; akinesis in 25; and dyskinesis in 17 segments. As shown in **Table 2**, advanced wall motion abnormalities, including akinesis and dyskinesis were prominent among observations at the apex and inferior wall in DCM, while these abnormalities tendedto occur in the anteroseptal and apical regions (supplied by the left anterior descending artery) in ICM, without significant differences.

Table 2. Regional wall motion

	DCM				ICM			
	N	H	A	D	N	H	A	D
Anteroseptal	4	11	9	2	2	5	10	6
Apex	1	10	5	10	0	2	6	15
Inferior	1	9	11	5	3	4	9	7
Posterolateral	8	18	0	0	17	5	1	0

N=normokinesis; H=hypokinesis; A=akinesis; D=dyskinesis.

The wall motion score at rest was 6.3±1.8 (**Table 1**) in DCM, which was significantly higher ($p<0.05$) than the value (5.3±1.0) in ICM. Although the LVEF did not differ between the two groups, the degree of wall motion abnormality was greater in ICM. Exercise-induced regional wall motion abnormali-

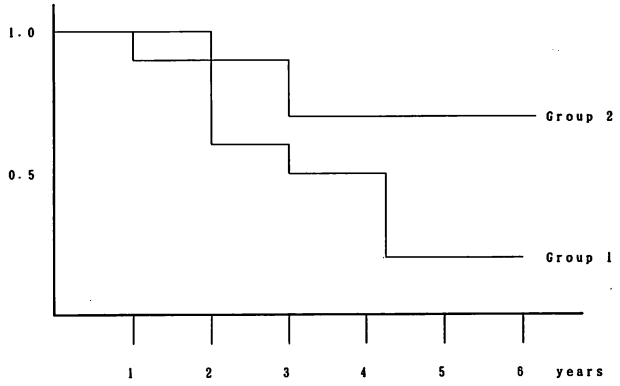

Fig. 3. Survival curve in DCM.
Group 1: 8 cases with decreased LVEF during exercise.
Group 2: 18 cases without decreased LVEF during exercise.

ties were noted in nine patients (35%) with DCM and in 13 (57%) in ICM. Of the nine patients with exercise-induced wall motion abnormalities, only three patients had decreased LVEF. The occurrence of exercise-induced regional wall motion abnormalities was not always related to the reduction of LVEF in DCM. However, all 13 patients with ICM having an aggravation of wall motion during exercise showed decrease in LVEF.

4. Follow-up study in DCM

During the follow-up period, eight patients died of intractable congestive heart failure. LVEF was $22\pm9\%$ in the group who died, and $24\pm7\%$ in the survivors. There was no significant difference between the groups. The wall motion score was 6.1 ± 2.2 in those who died and 6.4 ± 1.6 in the survivors, and again, there was no significant difference between them.

The duration of exercise was 6.4 ± 1.0 minutes in the deceased group and 7.5 ± 2.1 minutes in the survivors, with longer exercise duration in the survivors ($p<0.09$). LVEF of the deceased group decreased during exercise in five, increased in two and was unchanged in one patient. In the 18 survivors, LVEF decreased in four, was unchanged in three, and increased in 11 patients. By the chi-square test, there was a significant difference ($p<0.01$) in the incidence of a decrease in LVEF during exercise between the survivors and patients who died. However, since the observation periods were different, any correlation of decrease in LVEF and death during the follow-up period was analyzed using survival curves, as shown in **Fig. 3**. There was no significant difference in the Log-Rank test, although there was a gap between the two groups.

Discussion

DCM is a disorder of cardiac muscle of unknown etiology. Heredity, abnormal metabolism[6], poisoning and latent myocarditis[7] are the possible causes. Clinically, these etiological factors seem to combine to induce the condition. This disease has an extremely poor prognosis due to intractable arrhythmias or congestive heart failure. The most valuable treatment available in severe cases at present is heart transplantation[8]. To estimate the optimal timing for heart transplantation, intensive clinical research is needed to clarify the prognosis of the disease.

ICM is accompanied by fibrosis of a wide area of the left ventricle as a result of sclerotic coronary artery disease. It produces similar cardiac muscle dysfunction to DCM, thus, it is sometimes difficult to distinguish these two diseases

clinically.

1. Abnormalities of regional wall motion of the left ventricle

Myocardial involvement in DCM was previously considered to be diffuse[9], but is recently thought to be regional in terms of segmental wall motion and severity of myocardial involvement in individual cases. Indeed, left ventriculography[10] and radionuclide ventriculography[11] disclosed that impairment of the left ventricle, local fibrosis and myocardial degeneration in various degrees have been reported[12]. According to earlier reports[10,11,13~15], the incidence of abnormal regional wall motion in DCM varies from 6 to 67%. In the present study, segmental akinesis or dyskinesis was noted in 40%.

Concerning abnormality of the left ventricular wall motion, patients with ICM have more severe regional wall motion abnormality than those with DCM. This seems to indicate that the etiology of left ventricular impairment may be different than reported previously[14,16]. Although exercise-induced regional wall motion abnormality is a well-known fact in ischemic heart disease, it is interesting that this phenomenon was observed in 35% of patients with DCM. Among possible causes of this phenomenon, the first is an abnormality of the microcirculation[17] ; i.e., microcirculatory defects or a decrease of coronary flow reserve. However, whether the circulatory changes result in abnormal wall motion is debatable. In our previous investigation[18] using thallium myocardial scintigraphy during exercise, redistribution was observed in only three cases (15%) of 20 patients with DCM, and the concept of microcirculation seems to have been neglected. Secondly, the preload and afterload of the left ventricle increase during exercise which increases left ventricular wall stress[17], thereby aggravating the abnormality of wall motion. The third possibility is an abnormalitiy of metabolism[6] in the cardiac muscle. It is possible that abnormal energy production makes it impossible for the heart to withstand the load of exercise. To verify this hypothesis, more intensive investigation using positron CT or magnetic resonance spectroscopy should be performed. Clinically, recognizing the presence of abnormal exercise-induced regional wall motion is important for distinguishing DCM from ICM.

2. LVEF during exercise

The value of exercise testing for estimating prognosis[19~21] in advanced left ventricular disease is not known. In the present study, LVEF was unchanged in DCM, but significantly decreased in ICM. Left ventricular volume should be measured in discussing left ventricular systolic function during exercise, but this could not be done in all patients in the present study. Regarding LVEF and regional wall motion abnormalities during exercise in DCM, aggravation of left ventricular regional wall motion was unrelated to a decrease of the LVEF, and this shows that decrease of left ventricular function during exercise cannot be explained merely by regional wall motion abnormalities. By contrast, in the ICM, LVEF decreased in all patients with exercise-induced regional wall motion abnormalities, a major causative factor appeared to be myocardial ischemia.

There have been few reports of responses of LVEF to exercise in patients with advanced left ventricular dysfunction. Shen et al.[20] reported that it increased from $21\pm5\%$ to $26\pm7\%$ in congestive cardiomyopathy, but was unchanged ($22\pm4\%$ vs $22\pm6\%$) in ICM. Schoolmeester et al.[21] stated that it increased from $19.3\pm4.3\%$ to $24.6\pm6.4\%$ in congestive cardiomyopathy, and decreased from $22.3\pm6.1\%$ to $16.7\pm6.8\%$ in ICM. In our study, during exercise, LVEF was unchanged in DCM, but decreased in ICM. In the previous reports[20,21], LVEF increased in congestive cardiomyopathy during exercise. This may suggest that left ventricular function is reasonably well maintained, even in DCM. However, the prognosis is extremely poor in DCM, and it is hard to understand why the left ventricular function is preserved in many cases. In our study, some patients improved and some worsened, but most patients were unchanged. The causes of a decrease of LVEF during exercise in DCM

is still under investigation as mentioned earlier. Failure of the physiological response of the left ventricular muscles to exercise stress may suggest the loss of preservation of left ventricular function, and an ongoing to the terminal stage. It is very interesting that five out of eight patients with decreased LVEF during exercise died in this study. In addition, the exercise duration tended to be shorter in those in the group who eventually died. Radionuclide ventriculography can better clarify abnormalities of the ventricle in DCM during exercise test and may facilitate estimations of prognosis.

要　約

拡張型心筋症における運動負荷時左室反応：虚血性心筋症との対比

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左室駆出率 35% 以下の拡張型心筋症と虚血性心筋症において，エルゴメーター運動負荷に対する左室反応の差を radionuclide ventriculography (RNV) を用いて検討した．

拡張型心筋症(26 例)では，運動負荷により，左室駆出率は安静時 23±8% から運動負荷時 24±8% と，有意の変化を示さなかった．一方，虚血性心筋症(23 例)では，左室駆出率は安静時の 26±4% から運動負荷時に 22±5% と，有意に減少した．左室駆出率が同程度に障害されているにもかかわらず，左室局所壁運動障害の程度は拡張型心筋症の方で軽度であった．運動負荷による左室局所壁運動の増悪は拡張型心筋症では 9 例(35%)に，虚血性心筋症では 13 例 (57%) に認められ，運動負荷時，両群の鑑別上注意を要した．経過観察中死亡した 8 例の検討では，運動負荷時左室駆出率が低下した 8 例中 5 例は死亡し，一方，低下しなかった 18 例では 3 例が死亡しただけであった．運動負荷は拡張型心筋症の予後を推察する指標になり得ることが示唆された．

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