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Effect of Physical Exercise Training on Health-Related Quality of Life and Exercise Tolerance in Patients With Left Ventricular Dysfunction

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Abstract

Objectives. The improvement of exercise tolerance and quality of life (QOL) are essential in the treatment of patients with heart failure. The influence of physical exercise training on QOL was investigated in patients with left ventricular dysfunction.

Methods. Health-related QOL was evaluated using the Medical Outcomes Study Short-Form 36 Health Status Survey (SF-36) before and 3 months after individualized exercise training determined by cardiopulmonary exercise testing in 65 patients. The 44 patients who could carry out more than two-thirds of the prescribed exercise were classified into two groups: Group A (11 patients) with left ventricular ejection fraction < 40% and Group B (33 patients) with left ventricular ejection fraction ≥ 40%. The remaining 21 patients served as the control group.

Results. The mean value of SF-36 improved significantly with exercise training only in Group A (50.8 ± 25.3 to 62.1 ± 22.2, $p < 0.05$). Group A also had an increase in peak $\dot{V}O_2$ (18.9 ± 3.5 to 21.4 ± 3.6 m*l*/min/kg, $p < 0.005$) and a decrease in brain natriuretic peptide. The 24 patients (9 in Group A, 15 in Group B) with improved SF-36 values after the exercise training showed a negative correlation between the change of the mental component summary and the peak $\dot{V}O_2$ ($r = -0.606$, $p < 0.05$).

Conclusions. Exercise training improves both the QOL, especially the mental component, and the exercise tolerance in patients with left ventricular dysfunction.

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Key Words

■**Quality of life (health-related, SF-36)** ■**Exercise tests** ■**Heart failure**

INTRODUCTION

Cardiac rehabilitation has been developed primarily to reintegrate post-myocardial infarction patients into society. Recently, exercise training therapy has been indicated not only for ischemic heart disease but also for heart failure, and its efficacy has been widely established[1−6]. Patients with chronic heart failure have a deteriorating quality of life (QOL) as their condition worsens due to various factors, including poor exercise tolerance and anxiety[4,7]. QOL improvement is one of the important targets in the treatment of patients with heart failure. The correct amount of exercise training may allow such patients to resume an active life and may eliminate their anxiety about exercise loading. Consequently, exercise training can be expected to give patients improved exercise tolerance and

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QOL[3,4,8]. However, whether the exercise training improves QOL remains controversial. The differing views on the effect of exercise training on QOL may result from differences in the QOL assessment methods, and the variations in the duration and content of the exercise training in the studies investigating the relationship between exercise training and QOL, ranging from only physical training to more comprehensive programs, with and without supervision. For example, in the case of unsupervised exercise training, it is not easy to be certain that the subjects could or did carry out the prescribed exercise training adequately.

Recently, the Medical Outcomes Study Short-Form 36 Health Status Survey (SF-36)[9] has become widely recognized as a useful outcome measure that can objectively express a subjective health-related QOL. We examined and compared the changes in the health-related QOL occurring as a result of the exercise training using SF-36 (Japanese version 1.2)[10] in patients with and without left ventricular dysfunction and in patients that could not adequately carry out the exercise training.

SUBJECTS AND METHODS

Study population

The subjects consisted of 65 outpatients, 42 men and 23 women aged from 37 to 81 years (mean age 61.0 ± 11.0 years) who were given an exercise prescription based on cardiopulmonary exercise testing between May 2001 and April 2002. The patients had the following underlying diseases: 37 ischemic heart diseases; 17 dilated cardiomyopathy; 4 hypertrophic non-obstructive cardiomyopathy; 6 operated valvular heart diseases; and 1 arteriosclerosis obliterans. There were no patients whose cardiac condition had worsened or had been unstable within at least 1 month before starting the exercise training, and there were no patients who showed signs of myocardial ischemia during the cardiopulmonary exercise testing.

The subjects were divided into three groups based on a questionnaire that surveyed the degree of fulfillment of the prescribed exercise training 3 months from the start of the exercise program. The 44 patients who answered the questionnaire as 1) having carried out more than the prescribed exercise training, or 2) having carried out the prescribed exercise training, or 3) having carried out more than two-thirds of the prescribed exercise training, were classified as exercise achievement cases. These 44 patients were further divided into Groups A and B based on left ventricular ejection fraction (LVEF) values that were determined using echocardiography. Group A consisted of 11 patients with LVEF $<$ 40% and Group B consisted of 33 patients with LVEF $\geq$ 40%. The remaining 21 patients who answered the questionnaire as 4) having carried out half of the prescribed exercise, or 5) having carried out less than half of the prescribed exercise, or 6) not being able to carry out the prescribed exercise prescription, were used as controls. Five patients had LVEF $<$ 40%, and 16 patients had LVEF $\geq$ 40%. The patients in the control group were also asked the reasons why they could not carry out the prescribed exercise. We examined the health-related QOL using SF-36 before and 3 months after the exercise training, and compared the scores between the three groups. The patient characteristics of the three groups are shown in **Table 1**.

Medications for heart failure such as angiotensin-converting enzyme inhibitors, angiotensin-II receptor antagonists, β-blockers, diuretics and digitalis were not altered throughout the exercise training period.

Cardiopulmonary exercise testing

All patients underwent a symptom-limited bicycle ergometer exercise test immediately before starting the exercise training. A continuous ramp protocol at a constant rate of 50 rpm was used with a work rate that was increased by 15 W/min after a 2-minute rest period. Standard 12-lead electrocardiography was continuously monitored throughout the test. Their arterial blood pressure was measured by cuff sphygmomanometry at rest and subsequently every minute during the exercise and recovery phase. Breath-by-breath gas exchange measurements were performed with a computerized metabolic cart (JAEGER, Oxycon Alpha). Oxygen uptake ($\dot{V}O_2$), carbon dioxide production ($\dot{V}CO_2$), minute ventilation and the respiratory exchange ratio were measured. Peak $\dot{V}O_2$ was determined as the highest $\dot{V}O_2$ achieved during exercise. The anaerobic threshold was measured by the V-slope method. We regarded the values of peak $\dot{V}O_2$ as an index of exercise tolerance. Cardiopulmonary exercise testing and brain natriuretic peptide measurements were performed before and 3 months after starting the exercise training in 8 of the 11 patients in Group A.

Table 1 Baseline characteristics of the subjects

	Group A (n=11)	Group B (n=33)	Control (n=21)
Sex (male/female)	6/5	23/10	13/8
Age (yr)	61.8±10.5	62.8±11.2	58.3±10.9
Underlying heart disease			
Ischemic heart disease	5	22	10
Dilated cardiomyopathy	6	3	8
Hypertrophic cardiomyopathy	0	2	2
Valvular heart disease	0	5	1
Arteriosclerosis obliterance	0	1	0
NYHA classification			
I	1	14	9
II	3	15	8
III	7	4	4
IV	0	0	0
LVEF (%)	30.5±7.9	59.6±9.0*	54.1±16.9*
LVDD (mm)	64.8±5.9	50.3±6.4*	53.6±8.4*
AT $\dot{V}O_2$ (ml/kg/m^2)	12.7±3.1	15.1±3.6	14.3±4.0
Peak $\dot{V}O_2$ (ml/kg/m^2)	20.4±5.7	24.3±7.0	22.0±6.5

Continuous values are mean±SD. *$p<0.0001$ compared to the values in Group A.
Group A: exercise achievement cases, LVEF<40%. Group B: exercise achievement cases, LVEF≥40%. Control: exercise non-achievement cases.
NYHA=New York Heart Association; LVEF=left ventricular ejection fraction; LVDD=left ventricular diastolic diameter; AT $\dot{V}O_2$=oxygen consumption at anaerobic threshold level; Peak $\dot{V}O_2$=oxygen consumption at peak exercise level.

Exercise prescription

The exercise prescription was based on the results of cardiopulmonary exercise testing immediately before exercise training, with unsupervised walking on a level road for more than 30 min as the exercise method. The frequency of exercise training was once or twice a day, 3 to 5 days per week. Exercise intensity was designated with a target pulse rate and symptom level. The target pulse rate was set as the heart rate at the anaerobic threshold level measured by cardiopulmonary exercise testing. For patients with severe left ventricular dysfunction, the target heart rate was set based on the 1 min period before the anaerobic threshold level. We instructed the patients to do the exercise within the limit of their symptoms as denoted by the Borg index[11] 13, feeling "somewhat hard".

Health-related QOL (SF-36)

SF-36 (Japanese version 1.2)[10] is a self-administered questionnaire suitably translated into Japanese to evaluate the health-related QOL. The 36-item questionnaire is scored on a scale ranging from 0 to 100, with higher scores representing a higher QOL, and consists of the following eight sub-scales: 1) physical functioning (PF), 2) role-physical (RP), 3) body pain (BP), 4) general health (GH), 5) vitality (VT), 6) social functioning (SF), 7) role-emotional (RE), and 8) mental health (MH). Sub-scales of categories 1) to 4) were calculated as the physical component summary (PCS), and sub-scales of categories 5) to 8) were calculated as the mental component summary (MCS).

The study complied with the Declaration of Helsinki, the locally appointed ethics committee approved the research protocol, and informed consent was obtained from the subjects.

Statistical analysis

Data before and after the exercise training were compared using paired Student's t-tests. Comparisons of the patients' characteristics and SF-36 scores between three groups were made using the chi-square test or ANOVA. Linear regression analyses were performed using Fisher's exact test. Values of $p<0.05$ were considered to be statistically significant. Data were expressed as mean value ± standard deviation.

RESULTS

Change in SF-36 scores with exercise training

The mean scores of SF-36 values before and after the exercise training for the three groups are shown in **Fig. 1**. Before exercise training, the mean score in Group A was significantly lower than that in Group B (50.8 ± 25.3 vs 74.0 ± 17.5, p = 0.001). However, the mean scores significantly increased after exercise training only in Group A (Group A: from 50.8 ± 25.3 to 62.1 ± 22.2, p = 0.015, Group B: from 74.0 ± 17.5 to 75.7 ± 14.0, p = 0.510, control group: from 67.8 ± 20.3 to 64.1 ± 26.5, p = 0.250).

The scores of sub-scales PCS and MCS before and 3 months after exercise training in the three groups are shown in **Table 2**. All scores of each sub-scale before exercise training in Group A were low compared to those in the other two groups, but all increased after exercise training. The increase in RP (from 25.0 ± 38.7 to 50.0 ± 41.8, p = 0.041), PCS (from 49.1 ± 21.4 to 59.4 ± 23.5, p = 0.018), and MCS (from 52.5 ± 30.7 to 64.8 ± 22.8, p = 0.039) were statistically significant for Group A. In Group B, most scores before exercise training were relatively high, and did not change significantly after exercise training, although most scores increased slightly. In the control group, the scores after exercise training showed a slight decrease in

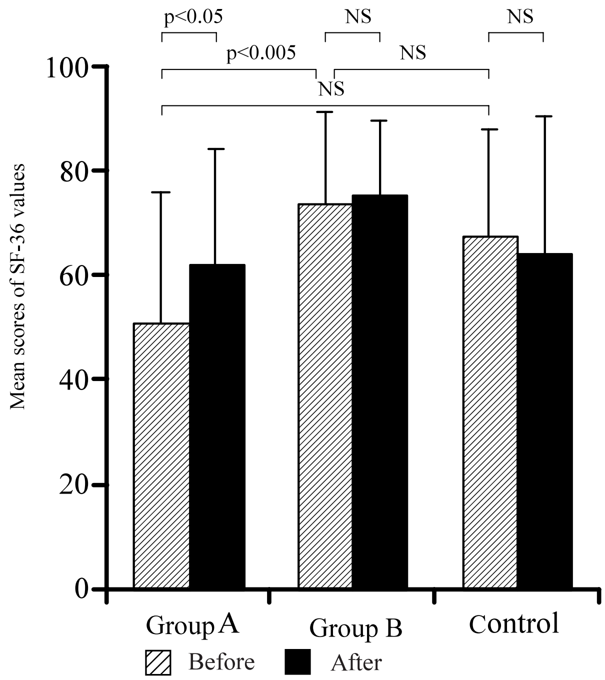

Fig. 1 Changes in mean SF-36 values before and 3 months after exercise training
The score in Group A was significantly lower compared to that in Group B at baseline, and increased significantly after exercise training. The score in Group B was relatively high at baseline and did not show a significant increase after exercise training. In the control group, the score after exercise training decreased slightly compared to baseline levels.
SF-36 = Medical Outcomes Study Short-Form 36 Health Status Survey.

Table 2 SF-36 scores before and after exercise training

	Group A (n=11)		Group B (n=33)		Control (n=21)	
	Before	After	Before	After	Before	After
PF	67.3±26.1	69.5±23.0	81.4±14.5	84.2±12.3	75.5±20.1	72.9±24.1
RP	25.0±38.7	50.0±41.8*	79.5±34.5	75.8±33.9	72.6±37.0	65.5±45.7
BP	58.1±31.7	68.3±25.9	67.7±28.7	73.8±24.0	72.4±22.6	73.5±27.4
GH	45.9±16.9	49.6±17.0	57.6±12.8	57.6±12.4	47.9±17.0	50.3±25.8
VT	48.6±29.5	62.7±24.5	65.8±16.0	68.0±19.2	59.0±24.1	51.0±27.0
SF	62.5±36.2	69.3±25.2	86.0±18.9	81.1±21.5	77..4±26.1	70.8±29.4
RE	39.4±49.0	57.6±49.6	79.8±37.2	88.9±28.5	68.3±42.8	66.7±42.2
MH	59.6±24.8	69.5±16.4	74.5±16.7	76.1±18.2	69.7±21.0	62.3±23.9*
PCS	49.1±21.4	59.4±23.5*	71.6±17.7	72.9±14.4	67.1±18.6	65.5±27.8
MCS	52.5±30.7	64.8±22.8*	76.5±18.2	78.5±16.0	68.6±23.8	62.7±27.5

Values are mean±SD. *p<0.05 compared to the values before exercise training.
PF = physical functioning; RP = role-physical; BP = body pain; GH = general health; VT = vitality; SF = social functioning; RE = role-emotional; MH = mental health; PCS = physical component summary; MCS = mental component summary. Other abbreviation as in Fig. 1.

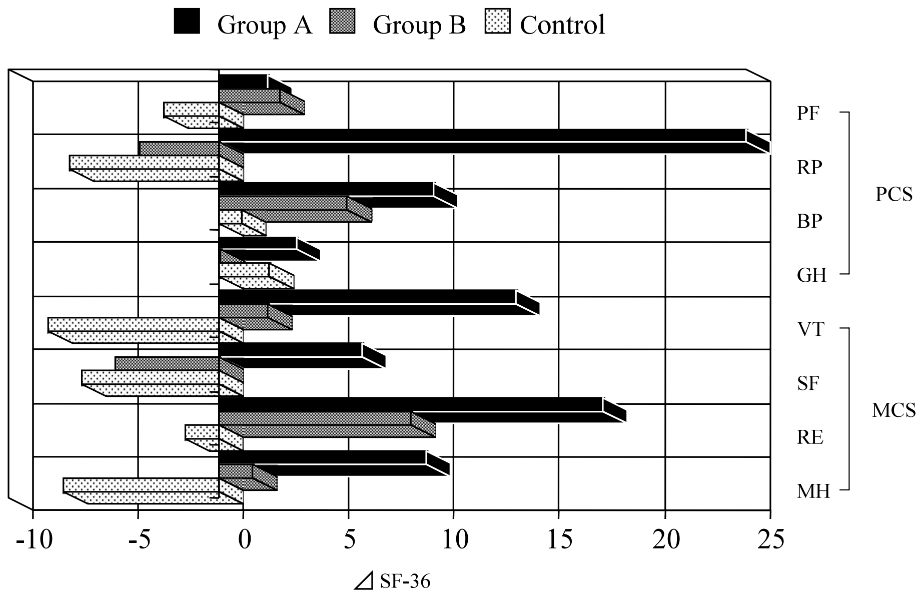

Fig. 2 Difference of SF-36 sub-scales before and 3 months after exercise training
The degree of improvement in Group A was high in most subscales, especially in RP, RE and VT. Many sub-scales showed slight improvement in Group B, and slight deterioration in the control group. Abbreviations as in Fig. 1, Table 2.

many items compared to the baseline levels, with the decrease in MH being statistically significant (from 69.7 ± 21.0 to 62.3 ± 23.9, $p = 0.029$).

Degree of change in SF-36 scores with exercise training

The differences in the SF-36 sub-scales before and after exercise training in the three groups are shown in **Fig. 2**. The positive values represent improvement of the health-related QOL. The degree of improvement in Group A was relatively high in most sub-scales, especially in RP, RE and VT, compared to those in the other groups. In Group B, there were many sub-scales that showed a slight improvement, whereas in the control group, many sub-scales showed a slight deterioration.

Exercise tolerance and SF-36 scores

The relationships of PCS and MCS to the peak $\dot{V}O_2$ measured before exercise training are shown in **Fig. 3**. There were significant positive correlations between both scores and the peak $\dot{V}O_2$. The correlation between PCS and peak $\dot{V}O_2$ was stronger than that between MCS and peak $\dot{V}O_2$ (PCS: $r = 0.581$, $p < 0.0001$, MCS: $r = 0.436$, $p < 0.0005$).

There were no significant correlations between the differences in both scales before and after exercise training and the peak $\dot{V}O_2$ measured before exercise training in all subjects (PCS: $r = 0.111$, $p = 0.382$, MCS: $r = 0.007$, $p = 0.955$). However, in the 24 patients (9 patients in Group A, 15 patients in Group B) whose mean SF-36 values increased after exercise training, there was a significant negative correlation between the degree of change in MCS and the peak $\dot{V}O_2$ (PCS: $r = -0.289$, $p = 0.173$, MCS: $r = -0.606$, $p = 0.001$; **Fig. 4**).

Change of brain natriuretic peptide and peak $\dot{V}O_2$ with exercise training

Fig. 5 shows the values of brain natriuretic peptide and the peak $\dot{V}O_2$ before and after exercise training in 8 of 11 patients in Group A. After exercise training, their brain natriuretic peptide showed a downward trend (from 279.4 ± 304.0 to 123.6 ± 111.5 pg/m*l*, $p = 0.117$) and the peak $\dot{V}O_2$ increased significantly (from 18.9 ± 3.5 to 21.4 ± 3.6 m*l*/min/kg, $p = 0.003$).

Reasons for non-achievement of the exercise prescription in the control group

The patients in the control group could not carry out the exercise prescription fully because of anxiety over the exercise training (eight patients), no time for exercise training (seven patients), no recognition of the necessity for exercise training

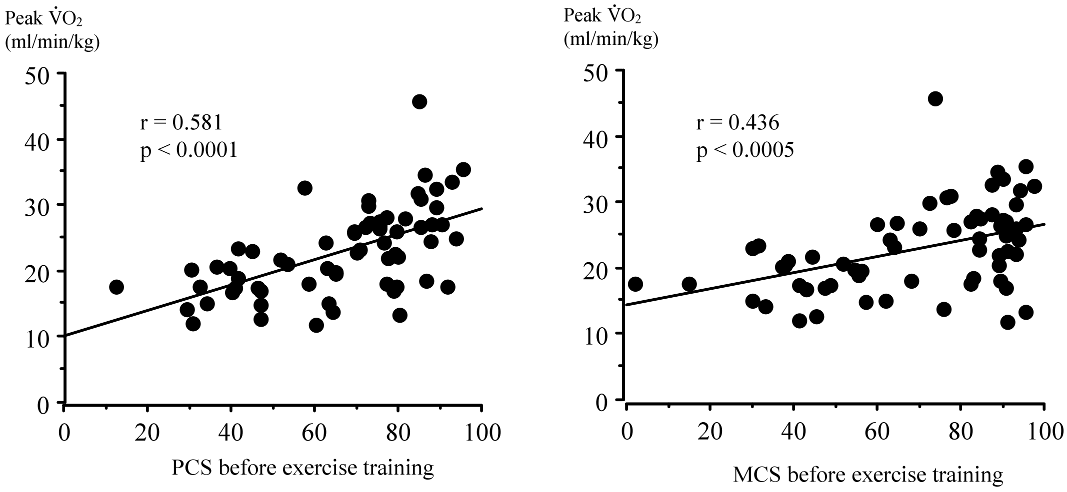

Fig. 3 Relationship of peak $\dot{V}O_2$ to PCS and MCS examined before exercise training
There were positive correlations between both scores and the peak $\dot{V}O_2$. The correlation of PCS and the peak $\dot{V}O_2$ was stronger than that between MCS and the peak $\dot{V}O_2$.
Abbreviations as in Tables 1, 2.

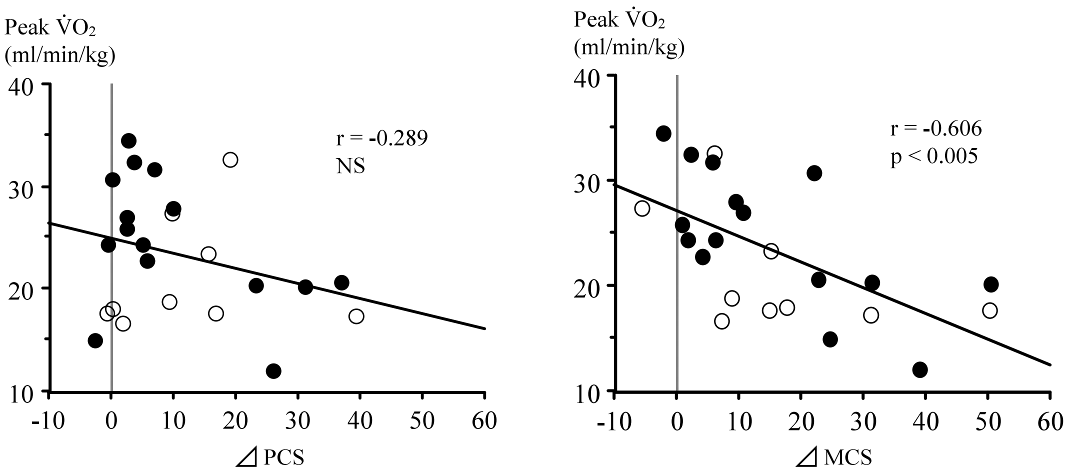

Fig. 4 Relationship of the degree of change in PCS and MCS to the peak $\dot{V}O_2$ in 24 patients with increased mean SF-36 values after the exercise training
There was a significant negative correlation between the degree of change in MCS and the peak $\dot{V}O_2$. Open circles show the patients in Group A. Closed circles show the patients in Group B.
Abbreviations as in Tables 1, 2, Fig. 1.

(four patients), body pain (one patient), mental fatigue (one patient), mental stress (one patient), and no place for walking (one patient).

DISCUSSION

In the present study, the mean SF-36 values, PCS and MCS, increased significantly after exercise training only in patients with left ventricular dysfunction who could adequately carry out exercise training (Group A). The degree of improvement in the SF-36 sub-scales (RP, RE and VT) was high in Group A. There were significant positive correlations between PCS, MCS and the peak $\dot{V}O_2$ measured before exercise training. In 8 of the 11 Group A patients, the peak $\dot{V}O_2$ increased significantly with exercise training. However, in the 24 patients whose mean SF-36 values increased after exercise training (9 in Group A, 15 in Group B), there was a significant negative correlation between the degree of change in MCS and the peak $\dot{V}O_2$.

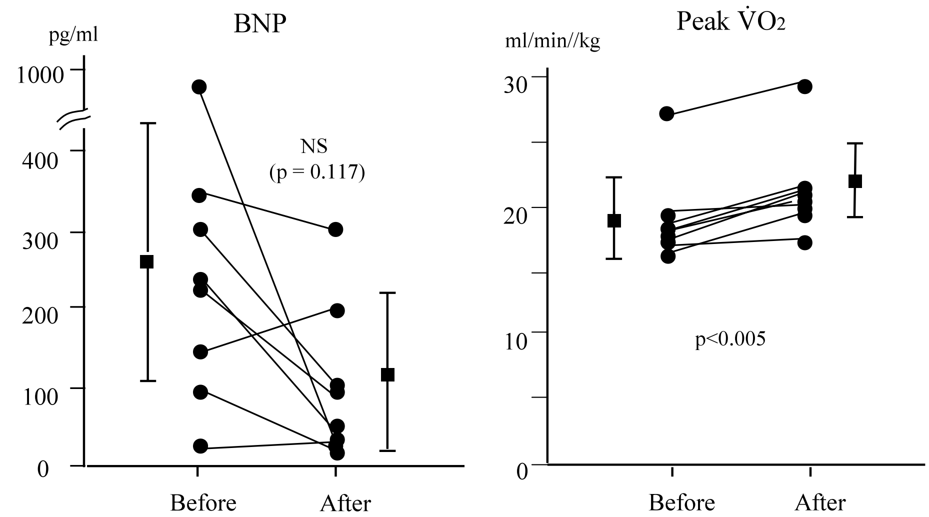

Fig. 5 Changes in brain natriuretic peptide and the peak $\dot{V}O_2$ with exercise training in 8 of 11 patients in Group A

The values of brain natriuretic peptide showed a downward trend and the peak $\dot{V}O_2$ increased significantly after the exercise training.

BNP = brain natriuretic peptide. Other abbreviations as in Table 1.

The efficacy of exercise training in patients with chronic heart failure has been proven by various large-scale trials[3,4,12]. Exercise training is generally agreed to improve exercise tolerance[1−4,13]. The mechanism of the improvement appears to be multifactorial, including improvements in cardiac function[2,6], respiratory function[1,3,13], and peripheral circulation including skeletal muscle[1,13−17]. Though the improvement of exercise tolerance and QOL is closely linked[3,4,8], it is not easy to assess QOL in patients with chronic heart failure, because QOL consists of, and thus reflects, various factors, including mental and physical stress, anxiety, depression, relationships with families and neighbors, physical activity, and occupational problems.

We used SF-36 (Japanese version 1.2) for the assessment of health-related QOL, as prepared for use with Japanese patients[10]. SF-36 has already been applied to other areas of cardiovascular disease, such as coronary heart disease and heart failure[7,18]. SF-36 scores in patients with chronic heart failure were lower, except for body pain, compared to the Japanese national norm[7]. In our study, all scores of the SF-36 sub-scales examined before the exercise training in patients with left ventricular dysfunction were low compared to those in patients without left ventricular dysfunction. Thus, we assume that SF-36 can comprehensively assess the health-related QOL in patients with left ventricular dysfunction.

Improvement of the health-related QOL by exercise training was found only in Group A. The cardiac condition of Group A patients did not deteriorate after exercise training, as shown by brain natriuretic peptide values. Moreover, their exercise tolerance improved after exercise training, as shown by the change in the peak $\dot{V}O_2$. These changes may result in improvement of both the physical and mental components of health-related QOL. Most Group A patients had been forced to remain at rest before the present study started, because they were anxious that their heart failure could deteriorate with exercise. Thus, it is likely that simply being able to do the exercise training for 3 months without any heart failure was chiefly responsible for producing the improvement in the mental component of the health-related QOL.

Positive correlations between PCS, MCS and the peak $\dot{V}O_2$ measured before exercise training were noted and likely mean that better exercise tolerance in patients was related to the better health-related QOL obtained. However, there was a significant negative correlation between the degree of improvement in MCS and the peak $\dot{V}O_2$, which can be interpreted to mean that the degree of improvement of mental QOL by the exercise training was stronger in patients with poor exercise tolerance than in those with good exercise tolerance.

Both home- and hospital-based cardiac rehabilitation are useful in older patients with old myocardial infarction to improve exercise tolerance and QOL[8]. With home-based unsupervised exercise training, it is essential to confirm the patients' fulfillment of the prescribed exercise program. In order to do this, we administered a questionnaire 3 months after the start of exercise training. We separately evaluated the patients who reported that they could not carry out more than two-thirds of the exercise prescription as the non-achievement group, which served as the control group. The SF-36 values in this control group decreased slightly after exercise training. Although the control group included five patients with LVEF values $<40\%$, their heart failure did not deteriorate during the observation period. The worsening of the health-related QOL in the control group may be due to the fact that they could not carry out the prescribed exercise. In view of the reasons given for non-achievement of the exercise training, we became keenly aware of the importance of adequately explaining the usefulness of exercise training to each patient and of providing an exercise prescription suited to each patient's lifestyle.

There are several limitations to our study. No control group not given exercise prescription was incorporated into the design of this study. Since the exercise training in this study was unsupervised, the confirmation of whether the exercise training was really performed depended on the veracity of patient responses. Furthermore, the pulse rate that was set as one measure of exercise intensity may not have been measured accurately, especially in patients with arrhythmia. However, to overcome this limitation in such patients, the exercise intensity was assessed by classifying their symptoms according to the Borg index.

CONCLUSIONS

Exercise training improves both QOL, especially the mental component, and exercise tolerance in patients with left ventricular dysfunction.

要　　約

左室機能低下症例の健康関連Quality of Lifeおよび運動耐容能に対する運動療法の効果

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目　的: 運動耐容能の低下は心不全患者のquality of life(QOL)を低下させる．そこで低左室機能を有する患者に運動療法を行い，運動耐容能およびSF-36を使用した健康関連QOLへの効果を検討した．

方　法: 対象は心肺運動負荷試験により運動処方を行い，非監視型運動療法を3ヵ月以上施行した65例(虚血性心疾患37例，拡張型心筋症17例，弁膜症その他11例)である．運動後のアンケートにより，運動処方の少なくとも2/3以上の運動療法を実行したと回答した44例中，心カテーテルあるいは心エコー図上で左室駆出率が40%未満であった11例をA群(男性6例，女性5例，平均年齢61.8±10.5歳)，40%以上であった33例をB群(男性23，女性10，平均年齢62.8±11.2歳)，運動処方の半分以下しか実行できなかった21例を対照群(男性13例，女性8例，平均年齢58.3±10.9歳)に分類し，運動療法前と3ヵ月後のSF-36の変化を比較検討した．

結　果: 運動前のSF-36の平均値はA群が最も低値であったが，運動療法後はA群のみ改善した(A群: 50.8±25.3→62.1±22.2，$p<0.05$，B群: 74.0±17.5→75.7±14.0，有意差なし)，対照群: 67.8±20.3→64.1±26.5，有意差なし)．A群の最大酸素摂取量は有意に上昇し(18.9±3.5→21.4±3.6 m*l*/min/kg，$p<0.005$)，脳性Na利尿ペプチドは低下傾向を示した．SF-36の平均点数が改善した24例(A群9例，B群15例)では精神的サマリースコアの変化と最大酸素摂取量との間に負の相関がみられた($r=-0.606$，$p<0.05$)．

結　論: 左室機能低下患者では適度の運動療法により運動耐容能が改善し，それによりとくに精神面でのQOLの改善がもたらされる．

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