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Case Report

Inspiratory muscle training for advanced heart failure with lamin-related muscular dystrophy

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ABSTRACT

Respiratory muscle weakness is often complicated in patients with heart failure. Its presence further worsens the clinical course of heart failure. However, the effect and appropriate method of inspiratory muscle training has not previously been elucidated.

A 55-year-old man with dilated cardiomyopathy was admitted for intractable heart failure. His heart failure was dependent on catecholamine infusion and the implantation of left ventricular assist device was planned. He also had suffered from some muscle weakness, which was later diagnosed as lamin dystrophy due to mutation of *LMNA* c.G97T E33X. Preoperatively we started aerobic rehabilitation with inspiratory muscle training. Before training, inspiratory and expiratory muscle strength was significantly reduced and exercise capacity was decreased. The load of inspiratory training could be gradually increased along the result of regular evaluation of respiratory muscle strength. During 8 weeks of training, there was no worsening of heart failure and no significant events related to arrhythmia. After training, respiratory muscle strength and exercise capacity were improved significantly.

<**Learning objective:** Inspiratory muscle training was effective and safe in a patient with intractable heart failure, which was complicated by skeletal muscle myopathy due to lamin-related muscular dystrophy.>

Background

Some cases of advanced heart failure with dilated cardiomyopathy (DCM) are complicated by neuromuscular diseases, such as muscular dystrophy. The prognosis in DCM with muscular dystrophy is worse than that of DCM alone [1]. Lamin mutations are associated with significant arrhythmia and cardiomyopathy burden, and mutation of the lamin A/C gene is associated with variable skeletal muscle involvement [2]. Therefore, the prognosis in a patient with DCM is worse if the patient also has a lamin gene mutation.

Respiratory muscle weakness is generally reported to be associated with heart failure. Inspiratory muscle strength may be related to cardiac function and may be one of the factors that determine exercise capacity in patients with heart failure. In addition, a decrease in maximal inspiratory muscle power was reported to be related to ventilation perfusion mismatch in patients with heart failure [3].

The presence of myopathy may exacerbate the negative effect of respiratory muscle weakness. In patients with DCM and muscular dystrophy, worsening of their condition is partly a result of the respiratory muscle dysfunction [4]. However, there has been no previous report about the effect of respiratory muscle rehabilitation on respiratory muscle dysfunction caused by lamin-related muscular dystrophy in patients with advanced heart failure. We present a case of respiratory muscle rehabilitation that was very successful in such a patient.

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Case report

A 55-year-old man was admitted to the hospital because he had had shortness of breath for several days. His electrocardiogram showed atrial fibrillation with complete atrial-ventricular block and resulting symptomatic bradycardia. Echocardiography revealed severe left ventricular systolic dysfunction with 21% of ejection fraction, in addition to mild mitral valve regurgitation. Coronary angiography revealed no organic lesion, and endomyocardial biopsy demonstrated mild myocardial fibrosis. DCM was diagnosed, and a cardiac resynchronization therapy device was implanted. In addition, optimal medical therapies, including beta blocker and enalapril, were prescribed to stabilize his heart failure status temporarily. However, his heart failure worsened soon again. He was transferred to our hospital for implantation of a left ventricular assist device (LVAD) and possible heart transplantation.

In addition to the cardiac dysfunction, he experienced muscle weakness of upper limbs. Neurological examination revealed weakness of the gluteus maximus. Computed tomography demonstrated fatty replacement of the paraspinal muscles and gluteus maximus. Respiratory function test revealed severe restriction (vital capacity, 2.35 L, estimated at 62.2% of normal), possibly as a result of the enlarged heart and respiratory muscle dysfunction. His percent forced expiratory volume in 1 s was 82.2% and diffusing capacity of the lung for carbon monoxide standardized by alveolar volume was 95.2%. Genetic testing revealed that he had an *LMNA* c.G97T E33X mutation, and lamin-related muscular dystrophy was diagnosed.

The patient underwent symptom-limited cardiopulmonary exercise testing on an electromagnetically braked upright cycle ergometer (Corival; Lode, Groningen, The Netherlands) with a metabolic gas analyzer (AE-300S; Minato Medical Science, Osaka, Japan). It revealed a severe decrease in peak maximal oxygen uptake, which suggested significant compromise of exercise tolerance (Table 1). We evaluated the respiratory muscles and measured maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP) before cardiopulmonary exercise testing in addition to grip muscle strength and knee extensor strength (Table 1). His MIP was significantly reduced to 45.0 cm H_2O (54.9%). These results suggested he suffered from severe respiratory muscle weakness in addition to medically intractable heart failure due to DCM.

After the hospitalization, he felt spasmodic severe respiratory distress and dobutamine infusion was started. After the start of dobutamine, the status of heart failure was stabilized and aerobic exercise training was started using ergometer [15–20 W (7–15 min)] × 1–2 sets, the work load and duration was gradually increased). Simultaneously we started inspiratory muscle training (IMT) in parallel with aerobic training with low intensity. First, we started IMT of 20% intensity of MIP using a variable flow-resistive loading device (POWERbreatheKH1; HaB Direct, Southam, UK), in two sets of 30 repetitions, and he trained 7 days per week and the intensity of IMT training was demonstrated in Fig. 1. The follow-up measurements of PI max were performed every week and used to calculate the training load to be implemented the following week. Rates of perceived inspiratory effort on Borg scale (4–6 of 10) was also used to support decisions on training load increments

After the start of training, we certificated that there was no increase in the value of brain natriuretic peptide (BNP) and the occurrence of respiratory distress lessened (Fig. 2). There was no occurrence of arrhythmia events during training.

After the IMT for 7 weeks, the re-evaluation of lung function test revealed a slight improvement in vital capacity and a significant improvement in inspiratory muscle strength (Table 1). In addition, cardiopulmonary exercise test demonstrated a significant improvement of peak VO2. Despite the remarkable improvement in exercise tolerance, LVAD implantation was considered to be appropriate in this case because of the low exercise capacity and the risk of worsening heart failure and it was successfully performed without significant perioperative complications.

Table 1 Patient characteristics.

	Pre-training	Post-training
Laboratory data		
Brain natriuretic peptide (pg/mL)	506.4	207.9
Total bilirubin (mg/dl)	1.6	1.1
Serum creatinine (mg/dl)	0.65	0.39
Body composition		
Body weight (kg)	59.8	56.4
Muscle strength		
Hand grip strength (kg)	29.8	29.2
Knee extensor strength (N)	164/154	223/185
Cardiopulmonary exercise test		
Peak systolic blood pressure (mmHg)	78	78
Peak diastolic blood pressure (mmHg)	36	40
Peak VO2 (ml/min/kg)	6.8	10.9
Peak load (watt)	19	40
VE/VCO2 slope		
([L/min VE] / [ml/min CO2]))	57.5	45.3
Oxygen uptake efficiency slope		
([ml/min O2])/ [L/min VE])	245.6	359.0
Pulmonary function test		
Vital capacity (L)	2.41 (69.3%)	2.51 (72.1%)
Inspiratory muscle strength (mmHg)	45.0 (54.9%)	83.4 (102.3%)
Expiratory muscle strength (mmHg)	57.5 (48.8%)	65.2 (62.7%)

Discussion

In general, respiratory muscle weakness is often observed in patients with heart failure. The presence of respiratory muscle weakness itself worsens the clinical course of heart failure. The specific strategy for recovery of respiratory muscle strength might also help the improvement of dyspnea derived from heart failure. Recently one review article demonstrated the effectiveness of IMT on the relief of the symptoms of dyspnea [5]. In addition, there was a report about effectiveness of IMT for patients with heart failure

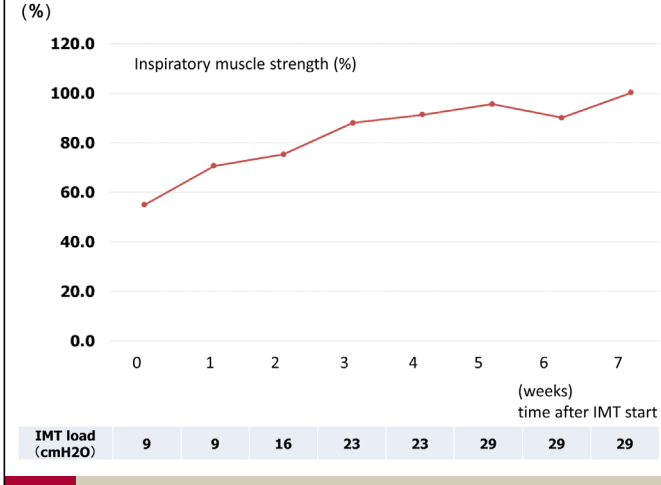

Fig. 1. The change in inspiratory muscle strength, which was presented as percentage of standard values and loads of inspiratory muscle training (IMT).

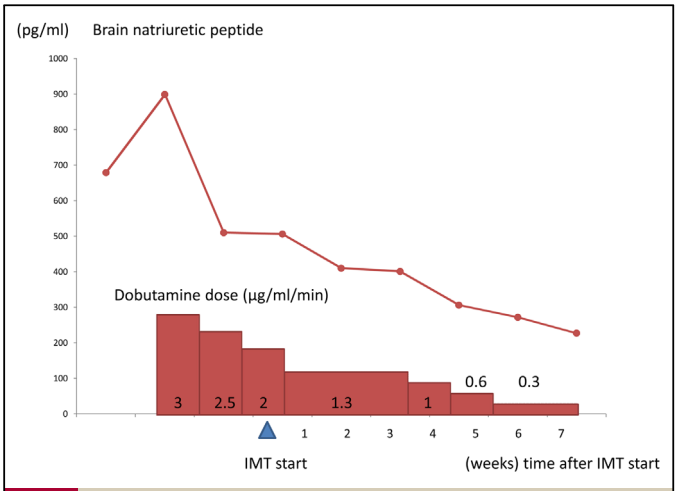

Fig. 2. The change in brain natriuretic peptide and dose of dobutamine infusion.
IMT, inspiratory muscle training.

[6]. IMT is one therapeutic strategy, however there has been insufficient evidence and methodology of it.

In the current study, IMT was comparatively challenging in two meanings. One was that it was a case with advanced heart failure exhibiting catecholamine dependency, which suggested significant decrease of exercise tolerance. The other was that the patients suffered from myopathy, in which exercise training should be performed with great caution.

LVAD implantation was planned so as to relieve heart failure; however, right-sided heart failure sometimes complicates the clinical course to a variable extent. In addition, the presence of right-sided heart failure can limit exercise tolerance [7]. Therefore, a rehabilitation program to improve exercise capacity would be needed even after LVAD implantation. In addition, preoperative preparation of the patient for LVAD implantation decreases the risk of peri-operative complications. Specifically, the reinforcement of respiratory muscle would contribute to decrease the number and degree of respiratory complications such as pneumonia or atelectasis.

On the other hand, fragile patients with advanced heart failure cannot tolerate even small exercise loads, and the risk of worsening heart failure would be significant. In our patient, however, levels of BNP did not increase during IMT, which suggests that these interventions can be performed safely even in patients at high risk for worsening heart failure.

Another challenging point in this case was the complication of muscular dystrophy, which somewhat complicated the effect of rehabilitation. The presence of muscle dystrophy might complicate the problem because the muscle training for patients with muscle dystrophy is controversial. Enforced exercise was reported to exacerbate the muscle pathophysiology in some muscle disease [8], whereas there had been some reports demonstrating the beneficial effect of exercise for muscle disease. With regard to rehabilitation for muscular dystrophy, IMT has been also reported to be beneficial in patients with neuromuscular diseases [9]. Wanke et al. [10] reported the effectiveness of IMT in patients with neuromuscular diseases such as Duchenne muscular dystrophy. Of 15 patients in their study, 10 demonstrated improvement in respiratory muscle function as early as 1 month after the initiation of training. However, there has been little study of the effectiveness of IMT in patients with advanced heart failure. Therefore, clinical investigations are warranted.

In limitation, the improvement in exercise tolerance was probably derived from the effect of aerobic exercise, in addition to the improvement in lung function derived from IMT. Therefore, we could not identify the exact effect of IMT on the improvement of peak VO_2. However, the improvement in respiratory muscle function appeared to be derived mainly from IMT because other types of training have little effect on respiratory muscles. The significant improvement in the strength of respiratory muscle would contribute somewhat to the improvement in exercise capacity.

Competing interests

The authors state that they have no competing interests

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