Pulmonary rehabilitation program including respiratory conditioning for chronic obstructive pulmonary disease (COPD): Improved hyperinflation and expiratory flow during tidal breathing

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ABSTRACT

Background: Pulmonary rehabilitation has generally relieved symptoms, strengthened exercise endurance and improved health-related quality of life (QOL) in patients with COPD, but recovery of pulmonary function remains questionable. This analysis of our innovative rehabilitation program is directed at documenting changes in patients' expiratory airflow limitation, pulmonary symptoms and QOL. This program is designed to provide "respiratory conditioning", a physical therapist-assisted intensive flexibility training that focuses on stretching and rib cage mobilization. **Methods:** Thirty-one patients with COPD who attended rehabilitation sessions at Juntendo University Hospital from

1999 to 2006 were analyzed. Pulmonary function, expiratory flow limitation during tidal breathing, six minute walk distance (6MWD), respiratory muscle strength, and St. George Respiratory Questionnaire (SGRQ) were measured before and after pulmonary rehabilitation.

Results: In participants ages 68 ± 7 years, the FEV₁% predicted was $39.3\pm15.7\%$. 6MWD, SGRQ and respiratory muscle strength were significantly improved after pulmonary rehabilitation. Although neither FEV₁% predicted nor FEV₁/FVC was affected to a significant extent, indicating little effect on airflow limitation, expiratory flow limitation in supine as well as seated during tidal breathing improved significantly. Moreover, rehabilitation significantly diminished TLC% predicted, FRC% predicted, RV% predicted and RV/TLC values, thus indicating a reduction of hyperinflation of the lungs at rest.

Conclusions: The present results suggest that our rehabilitation program with respiratory conditioning significantly lowered the hyperinflation of lungs at rest as well as the expiratory flow limitation during tidal breathing. In patients with COPD, overall pulmonary function improved, exercise endurance increased and health-related QOL was enhanced.

KEY WORDS Expiratory flow limitation; hyperinflation; negative expiratory pressure; pulmonary rehabilitation; respiratory conditioning

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Introduction

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ISSN: 2072-1439 © Pioneer Bioscience Publishing Company. All rights reserved. Chronic obstructive pulmonary disease (COPD) is a common disease in the elderly and its prevalence is increasing worldwide. The impact of COPD on public health is highlighted in the Global Initiative for Chronic Obstructive Lung Disease (GOLD) Workshop Report (1). A nation-wide epidemiological study indicated the great burden of COPD in Japan, eliciting an urgent need for promoting awareness of this disease in this country (2). Airflow limitation suggesting the existence of COPD was prevalent in 10.9% of individuals aged \geq 40 years and significantly more prevalent in older subjects (3.5% in 40-49 years old *vs.* 24.4% in those >70 years) (2).

Pulmonary rehabilitation is an important nonpharmacological treatment for COPD. Many studies have shown that such therapy reduces dyspnea on exertion, increases exercise capacity and improves health-related quality of life (QOL) (3-6). Progressive airflow limitation in COPD patients results in exercise de-conditioning, immobility and muscle wasting, relative social isolation, altered mood states, especially depression, and body weight loss over a prolonged period (1). These problems interact with each other resulting in a vicious cycle of deterioration. In this context, pulmonary rehabilitation is therefore considered beneficial and effective for COPD patients, since it mitigates each of these conditions and can interrupt deterioration process (1). However, whether pulmonary rehabilitation actually improves pulmonary function, including airflow limitation, remains controversial (4,7-9).

We designed to provide a "respiratory conditioning" segment in conjunction with exercise training and respiratory muscle training. Respiratory conditioning maneuvers involve the optimization of breathing patterns, physical therapist-assisted rib cage mobilization and improvement of body flexibility. We considered the physiotherapy working on thoracic cage would be a critical component for successful rehabilitation program since a static lung volume fraction and the level of functional residual capacity (FRC) is determined by the compliance of the lung as well as that of chest wall. We report here that our pulmonary rehabilitation program including a "respiratory conditioning" ameliorated pulmonary symptoms and upgraded exercise endurance as well as QOL in patients with COPD. Furthermore, we confirmed that both expiratory flow limitation (EFL) during tidal breathing as well as hyperinflation of the lungs at rest improved after completing the program.

Methods

Study population

We encouraged patients with stable COPD to participate in the pulmonary rehabilitation program, who were treated in the respiratory outpatient clinic of Juntendo University and expected to visit regularly 2 days per week for 6 weeks during the program. The study protocol was approved by the Ethics Committee of the Juntendo University Hospital. From 1999 to 2006, 37 patients with stable COPD participated in our pulmonary rehabilitation program. Each patient was diagnosed with COPD and treated with medicines according to GOLD guideline (1). They were treated with inhaled bronchodilators, and most of them were given either short- or long-acting anticholinergics. During pulmonary rehabilitation, all patients were allowed to continue their pharmacological therapy. Five patients were on supplemental oxygen therapy. Six patients were excluded from the analysis because their pulmonary function data after pulmonary rehabilitation were not obtainable after an exacerbation of COPD. Accordingly, 31 patients with COPD, including one patient with stage I (FEV₁≥80% predicted), 4 with stage II (50%≤FEV₁<80% predicted), 18 with stage III (30%≤FEV₁<50% predicted), and 8 with stage IV (FEV₁<30% predicted) according to the disease severity of GOLD criteria (1), were retrospectively analyzed. All the patients were males, exsmokers and 67 ± 7 (mean ± SD) years old.

Comprehensive multidisciplinary pulmonary rehabilitation program

All the patients participated in the pulmonary rehabilitation program on an outpatient basis. The comprehensive outpatient pulmonary rehabilitation program included 2 sessions per day (60 minutes per session), 2 days per week for 6 weeks and was provided by a multidisciplinary team that included various health care professionals (physician, nurse, physical and respiratory therapist, pulmonary function laboratory technician, pharmacist, dietitian, medical social worker, and a provider of long-term home oxygen therapy). Treatment groups consisted of a maximum of three patients. The program included physiotherapy, exercise, respiratory muscle training (12 sessions, one on one), self-management education (11 sessions, as a group) and nutritional consultation (1 session, one on one).

The physiotherapy respiratory conditioning involves the optimization of breathing patterns, therapist-assisted rib cage mobilization and improvement of body flexibility. For the rib cage mobilization of COPD patients, the physical therapist performed continuous manual compressions of the rib cage during exhalation (not shaking/vibrations) as well as manual stretching and relaxation of the intercostal and pectoral muscles, neck muscles and back muscles. Therapists also applied manual mobilization of the spine and correction of posture during exercise or breathing. Manual stretching of the abdominal muscles and hamstrings and manual mobilization of the pelvis were performed for therapist-assisted improvement of body flexibility. During the initial three sessions, most of each session was spent on respiratory conditioning. As the sessions proceeded, the time used for conditioning in each session gradually decreased, while the time used for exercise training increased. These exercises included low-intensity endurance and strength training of the upper and lower extremities and respiratory muscle training. Walking (hall walk) and stationary bike training (cycle ergometer 5 to 15 W) was extended (symptom-limited maximum) to promote endurance of the lower extremities. Upper and lower extremity strength training started with free weights, then hand and ankle light weights (0.5 to 2 kg) were used. The ThresholdTM inspiratory muscle trainer

	Before	After	P value
Body weight (kg)	54.4±10.2	54.9±9.9	< 0.05
Pulmonary function tests $(n=31)$			
FEV ₁ (L)	1.05±0.41	1.04±0.41	0.50
VC (L)	3.16±0.64	3.25±0.72	0.118
FEV, % predicted	40.3±15.8	39.9±15.8	0.502
DLco/VA % predicted	37.2±11.6	37.4±10.8	0.880
TLC % predicted	137.4±22.7	131.5±18.9	<0.01
RV % predicted	230.3±61.4	210.3±52.8	<0.0
FRC % predicted	148.4±31.8	140.0±26.8	<0.0
RV/TLC	58.4±7.4	56.3±8.0	< 0.05
6MWD	405±92.0	436±83.0	<0.0
Respiratory muscle strength $(n=27)^*$			
Pimax	-58.3±16.7	-69.3±18.4	<0.0
Pemax	149.4±40.0	162.1±36.5	<0.0
SGRQ (n=24) ⁺			
Total	42.4±12.5	31.7±14.5	<0.01
[*] Four patients were excluded for exacerbation acute lumbago (n=1), or a recent episode of p scheduled; [†] SGRQ was not evaluated in 7 patie	pneumothorax $(n=2)$ at the time v		

(HealthScan, Cedar Grove NJ, USA) was used for the inspiratory muscle training at 30% of PImax. The patients were encouraged to exercise (for example, stretching of the intercostal and pectoral muscles, low-intensity endurance and strength training of the upper and lower extremities) at home between sessions while they were on the program.

Initial assessment and outcome measures of pulmonary rehabilitation

When each patient's COPD was stable, ventilatory function was assessed by spirometry (Autospirometer system 9, Minato Inc., Japan), and lung volumes were evaluated by body plethysmography (Bodyplethysmograph BX-9, Minato Inc., Japan). The reference values obtained from the Japanese population were utilized to calculate the % predicted value (10). With patients in supine as well as sitting positions, EFL during tidal breathing was measured according to the negative expiratory pressure method of Koulouris et al. (11). EFL assessment included the two indices described by Eltayara et al. (12). One is a discrete variable, a score expressing the degree of flow limitation (FL): 0= none, 1= mild, 2= moderate, 3= severe and 4= very severe. The other is a continuous variable, the FL (%), a percentage of flow-limited volume to control expired tidal volume (VT). Respiratory muscle strength was determined by the measurement of PImax and PEmax (Pmax Mouth Pressure Monitor, PK Morgan, UK) according to the American Thoracic Society/European Respiratory Society statement (13). Six-minute walk distance (6MWD) was measured according to the American Thoracic Society statement (14). Health-related QOL was assessed by The St. George's Respiratory Questionnaire (SGRQ).

Statistical analysis

Data are presented as means±SD. Comparisons of the data before and after rehabilitation were evaluated by the paired *t*-test using the StatView[®] software program, and a value of P<0.05 was considered to be significant.

Results

The outcomes of the comprehensive multidisciplinary pulmonary rehabilitation

The baseline characteristics of the 31 COPD patients and results after pulmonary rehabilitation are summarized in Table 1. Attendance at the sessions was excellent with a mean percentage of 99.5%. The pulmonary rehabilitation's significantly improved outcomes were recorded as the following values: TLC% predicted (137.4 \pm 22.7 vs. 131.5 \pm 18.9, P<0.01), FRC% predicted (148.4 \pm 31.8 vs. 140.0 \pm 26.8, P<0.01), RV% predicted (230.3 \pm 61.4 vs. 210.3 \pm 52.8, P<0.01) and RV/TLC

	Before	After	P value
FL score(range 0-4)*	2.2±1.5	1.0±1.5	<0.01
FL (%) (seated)	20.9±28.1	10.4±20.8	< 0.05
FL (%) (supine)	49.9±32.9	20.7±29.2	<0.01

but not flow-limited seated of supine, T = now-limited < 50% tidal breating volume (v_T) supine but not flow-limited seated; 2 = flow-limited >50% V_T supine but not flow-limited seated; 3 = flow-limited <50% V_T seated but flow-limited supine; and 4 = flow-limited >50% VT seated but flow-limited supine.

(58.4 \pm 7.4 vs. 56.3 \pm 8.0, P<0.05), thus indicating the reduction of hyperinflation in the lungs at rest. Values not significantly improved were FEV₁, FEV₁% predicted, VC and DLco/ VA% predicted. Although obstructive ventilatory impairment during forced-expiratory maneuver did not lessen during our rehabilitation program, EFL during tidal breathing improved notably to a statistically significant extent. Both FL score and FL (%) (seated as well as supine) decreased after our pulmonary rehabilitation, although evaluation was limited to only 19 patients of the total study population (Table 2). The EFL while sitting completely disappeared in 3 of 8 COPD patients examined; even better, EFL vanished from 8 of 15 supine patients with COPD.

Overall, exercise endurance significantly improved after pulmonary rehabilitation, as indicated by an increase of 6MWD from 405±92 to 436±83 m, closely approximating that described by Puhan et al. (15) as an important advance. They reported that 6MWD should change by -35 m for patients with moderate to severe COPD in order to represent an important effect. In addition, respiratory muscle strength measured by PImax and PEmax significantly improved after pulmonary rehabilitation. The PImax increased from -58.3 ± 16.7 to -69.3 ± 18.4 cmH₂O, and the PEmax increased from 149.4±40.0 to 162.1±36.5 cmH₂O. Nutritional status also responded well to this pulmonary rehabilitation as indicated by the patients' increase of body weight from 54.4±10.2 to 54.9±9.9 (P<0.05, statistically significant although the magnitude of increment is small). Health-related QOL improved after rehabilitation as indicated by a decrease of the total score from 42.4 ± 12.5 to 31.0 ± 14.5 , which satisfied the minimal clinical importance of 4 points.

Discussion

Our comprehensive pulmonary rehabilitation program presented here significantly improved hyperinflation of the lungs at rest, EFL during tidal breathing, exercise endurance and healthrelated QOL for patients with COPD. Although pulmonary rehabilitation has typically benefited such patients (1,3-6,16,17), few improvements in pulmonary functions have been established (7-9). However, we have demonstrated for the first time that our pulmonary rehabilitation program including respiratory conditioning can significantly reduce EFL during tidal breathing, which should be interpreted as particularly relevant in this physiological setting.

The factor that most differentiated our rehabilitation program from others was the introduction of "respiratory conditioning," defined as a procedure for improving the flexibility of the chest with the correction of posture and the stretching and mobilization of the rib cage. We considered that respiratory conditioning would contribute to expanding expiratory flow and reducing hyperinflation of the lungs at rest. In fact, respiratory muscle stretch gymnastics have been proposed as an additional form of pulmonary rehabilitation for COPD patients. The objective is to decrease chest wall stiffness by stretching the respiratory muscles of the chest wall during breathing. Accordingly, Minoguchi et al. (7) and Yamada et al. (8) suggested that respiratory muscle stretching would decrease FRC while increasing chest wall expansion and exercise capacity. However, on their own, those patients were required to perform 5 patterns of muscle stretching gymnastics 3 times every day for 4 weeks to obtain any benefit. In contrast, our program incorporated physical therapist-assisted manual stretching of the respiratory muscles to reduce dyspnea before starting exercise training. Moreover, the effect of this technique on chest wall compliance did not depend on patients' skill but rather on the knowledge of trained therapists.

Similar to the results of other studies (4), our pulmonary rehabilitation program did not improve the airflow limitation as assessed by spirometry. For the FVC maneuver, a subject is requested to exhale with a maximal effort in order to assess pulmonary function. However, this maneuver is quite unusual and not experienced in daily living, hence not an actual physiological assessment of pulmonary function. In daily living, those patients utilize a much lower flow in tidal breathing, and parameters obtained with the FVC maneuver cannot reflect changes in the lower flow ranges. However, the negative expiratory pressure method claims validity in detecting small changes in expiratory flow during tidal breathing. EFL is as sensitive as FEV₁% predicted, but has a stronger correlation with the severity of dyspnea in COPD patients, therefore, is more appropriate for evaluating effects on airflow limitation relevant to the activities of daily life (12).

We theorized that the improvement of EFL would contribute to a reduction of hyperinflation in lungs at rest and other functions. However, the improvement of EFL did not correlate with a reduction of hyperinflation of lungs at rest, SGRQ or 6MWD (data not shown). Our study population may have been too small to produce such data; hence, a larger study is needed to prove the clinical implication of EFL regarding mechanistic and physiologic significance on an outcome measure of pulmonary rehabilitation in patients with COPD.

Hyperinflation of the lungs at rest and/or during exercise is an important physiological feature in COPD. The narrowing of the small airways, reduced elastic recoil pressure due to destruction of alveoli, blood gas abnormalities, and increased chest wall stiffness are possible mechanisms for their hyperinflation (16,18,19). In addition, the FRC increases with age mainly due to a decrease in chest wall compliance or an increase in chest wall stiffness, thus increasing the outward recoil force of chest wall and the lungs (20). An improvement of airflow limitation using a bronchodilator has been reported to reduce the hyperinflation of the lungs (decreased FRC) with an increase in IC (21). Albuquerque et al. (22) reported that not only the postbronchodilator FEV1 and IC but also IC/TLC values provide useful information for estimating a COPD patient's maximal exercise capacity, whether severely reduced or not. In the current study, no increase in the IC was observed, since the amount of reduction between TLC and FRC was about the same. In addition, IC/TLC did not increase significantly (P=0.103), although it tended increase after the pulmonary rehabilitation. Although it is unlikely that our pulmonary rehabilitation program directly affected the airways or lung parenchyma, the reduction of hyperinflation of lungs at rest at the baseline appeared to retard the progression of dynamic hyperinflation on effort, which would eventually raise the end-expiratory level to the dyspnea limit (23). In addition, by decreasing chest wall stiffness thereby increasing its flexibility, the reduced hyperinflation of lungs at rest may generate greater mobility of the diaphragm. Consequently, this effect may improve exercise capacity. In this context, we believe that respiratory conditioning in our pulmonary rehabilitation program can ameliorate symptoms, raise exercise capacity and improve QOL.

Our program resulted in the improvement in all domains of health-related QOL and a reduction of 10.6 in the SGRQ total score: that is, greater than the mean reduction of 6.11 in SGRQ total score obtained from the meta-analysis done by Lacasse *et al* (5). Good attendance and adherence to our rehabilitation program would have contributed for the participants to achieve its optimal benefits. Sabit R *et al.* reported that poor attendance at pulmonary rehabilitation programs was independently associated with being a current smoker, participating in a longer rehabilitation program, having more numerous hospital admissions, suffering a higher degree of breathlessness or enduring a long journey to the hospital (24). Factors contributing to our high attendance rate may be the non-smoking status (all were ex-smokers) and an appropriate duration of pulmonary rehabilitation programs (2 sessions per day, 2 days per week and 6 weeks duration) (17). Other factors we speculate that might have played a role include: (I) respiratory conditioning (physical therapist-assisted manual compression and relaxation of the thoracic cage) created a strong interaction between patient and physical therapist, thereby decreasing anxiety about exercise training and reducing breathlessness, (II) an early amelioration of exertional dyspnea during the program motivated COPD patients to complete the program, while also enhancing the efficacy of exercise training, and (III) the reduction of hyperinflation of the lungs at rest obtained by our rehabilitation program improved the function and mobility of diaphragm, which in turn decreased symptoms and increased exercise tolerance.

Our study has several limitations including (I) a retrospective analysis, (II) a small number of study subjects, and (III) participants were very heterogeneous regarding the severity of COPD. They therefore clearly impede us to draw a precise conclusion. However, the present study focused for the first time on the significance of respiratory conditioning during pulmonary rehabilitation and reported that its beneficial effect on chest wall kinematics are likely to improve EFL and reduce hyperinflation of the lungs for the many victims of COPD. Further study on the understanding of the role of respiratory conditioning during pulmonary rehabilitation seems to be warranted.

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References

- Global Initiative for Chronic Obstructive Lung Disease. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease (2006): NHLBI/WHO, Workshop Report, 2006.
- Fukuchi Y, Nishimura M, Ichinose M, Adachi M, Nagai A, Kuriyama T, et al. COPD in Japan: the Nippon COPD Epidemiology study. Respirology 2004;9:458-65.
- 3. Pulmonary rehabilitation: joint ACCP/AACVPR evidence-based guidelines. ACCP/AACVPR Pulmonary Rehabilitation Guidelines

Panel. American College of Chest Physicians. American Association of Cardiovascular and Pulmonary Rehabilitation. Chest 1997;112:1363-96.

- Goldstein RS, Gort EH, Stubbing D, Avendano MA, Guyatt GH. Randomised controlled trial of respiratory rehabilitation. Lancet 1994;344:1394-7.
- Lacasse Y, Martin S, Lasserson TJ, Goldstein RS. Meta-analysis of respiratory rehabilitation in chronic obstructive pulmonary disease. A Cochrane systematic review. Eura Medicophys 2007;43:475-85.
- Nici L, Donner C, Wouters E, Zuwallack R, Ambrosino N, Bourbeau J, et al. American Thoracic Society/European Respiratory Society statement on pulmonary rehabilitation. Am J Respir Crit Care Med 2006;173:1390-413.
- Minoguchi H, Shibuya M, Miyagawa T, Kokubu F, Yamada M, Tanaka H, et al. Cross-over comparison between respiratory muscle stretch gymnastics and inspiratory muscle training. Intern Med 2002;41:805-12.
- Yamada M, Kakizaki F, Sibuya M, Nakayama H, Tsuzura Y, Tanaka K, et al. [Clinical effects of four weeks of respiratory muscle stretch gymnastics in patients with chronic obstructive pulmonary disease]. Nihon Kyobu Shikkan Gakkai Zasshi 1996;34:646-52.
- Porszasz J, Emtner M, Goto S, Somfay A, Whipp BJ, Casaburi R. Exercise training decreases ventilatory requirements and exercise-induced hyperinflation at submaximal intensities in patients with COPD. Chest 2005;128:2025-34.
- Sharp DS. Reference values for lung function in the Japanese: recording of normal lung function from 14 institutes in Japan. Jpn J Thoracic Dis 1993;31:421-7.
- Koulouris NG, Valta P, Lavoie A, Corbeil C, Chassé M, Braidy J, et al. A simple method to detect expiratory flow limitation during spontaneous breathing. Eur Respir J 1995;8:306-13.
- Eltayara L, Becklake MR, Volta CA, Milic-Emili J. Relationship between chronic dyspnea and expiratory flow limitation in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med 1996;154:1726-34.
- 13. American Thoracic Society/European Respiratory Society. ATS/ERS



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- ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med 2002;166:111-7.
- Puhan MA, Mador MJ, Held U, Goldstein R, Guyatt GH, Schünemann HJ. Interpretation of treatment changes in 6-minute walk distance in patients with COPD. Eur Respir J 2008;32:637-43.
- Gibson GJ. Pulmonary hyperinflation a clinical overview. Eur Respir J 1996;9:2640-9.
- 17. Pulmonary rehabilitation-1999. American Thoracic Society. Am J Respir Crit Care Med 1999;159:1666-82.
- Garfinkel F, Fitzgerald RS. The effect of hyperoxia, hypoxia and hypercapnia on FRC and occlusion pressure in human subjects. Respir Physiol 1978;33:241-50.
- Krumholz RA, Albright CD. The compliance of the chest wall and thorax in emphysema. Am Rev Respir Dis 1968;97:827-31.
- Mittman C, Edelman NH, Norris AH, Shock NW. Relationship between chest wall and pulmonary compliance and age. J Appl Physiol 1965;20:1211-6.
- Celli B, ZuWallack R, Wang S, Kesten S. Improvement in resting inspiratory capacity and hyperinflation with tiotropium in COPD patients with increased static lung volumes. Chest 2003;124:1743-8.
- 22. Albuquerque AL, Nery LE, Villaça DS, Machado TY, Oliveira CC, Paes AT, et al. Inspiratory fraction and exercise impairment in COPD patients GOLD stages II-III. Eur Respir J 2006;28:939-44.
- 23. Cooper CB. The connection between chronic obstructive pulmonary disease symptoms and hyperinflation and its impact on exercise and function. Am J Med 2006;119:21-31.
- Sabit R, Griffiths TL, Watkins AJ, Evans W, Bolton CE, Shale DJ, et al. Predictors of poor attendance at an outpatient pulmonary rehabilitation programme. Respir Med 2008;102:819-24.