Benefits of Pulmonary Rehabilitation in Patients With COPD and Normal Exercise Capacity

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BACKGROUND: Pulmonary rehabilitation (PR) is beneficial for patients with COPD, with improvement in exercise capacity and health-related quality of life. Despite these overall benefits, the responses to PR vary significantly among different individuals. It is not clear if PR is beneficial for patients with COPD and normal exercise capacity. We aimed to investigate the effects of PR in patients with normal exercise capacity on health-related quality of life and exercise capacity. METHODS: Twenty-six subjects with COPD and normal exercise capacity were studied. All subjects participated in 12-week, 2 sessions per week, hospital-based, out-patient PR. Baseline and post-PR status were evaluated by spirometry, the St George's Respiratory Questionnaire, cardiopulmonary exercise test, respiratory muscle strength, and dyspnea scores. RESULTS: The mean FEV_1 in the subjects was 1.29 ± 0.47 L/min, 64.8 ± 23.0% of predicted. After PR there was significant improvement in maximal oxygen uptake and work rate. Improvements in St George's Respiratory Questionnaire scores of total, symptoms, activity, and impact were accompanied by improvements of exercise capacity, respiratory muscle strength, maximum oxygen pulse, and exertional dyspnea scores (all $P < .05$). There were no significant changes in pulmonary function test results (FEV_1, FVC, and FEV_1/FVC), minute ventilation, breathing frequency, or tidal volume at rest or exercise after PR. CONCLUSIONS: Exercise training can result in significant improvement in health-related quality of life, exercise capacity, respiratory muscle strength, and exertional dyspnea in subjects with COPD and normal exercise capacity. Exercise training is still indicated for patients with normal exercise capacity. *Key words: pulmonary rehabilitation; health-related quality of life; exercise training; COPD; exercise capacity.* [Respir Care 2013;58(9):1482–1488. © 2013 Daedalus Enterprises]

Introduction

There are many studies about the benefits of pulmonary rehabilitation (PR) in patients with COPD.[1-5] PR has been shown to lead to improvement in exercise capacity, health-related quality of life (HRQL), and work efficiency in patients with COPD.[1-3] Therefore, PR has been recommended as an integral part of management for these patients.[6,7] The American Thoracic Society recommends PR for patients with persistent exercise intolerance despite receiving optimal medical therapy.[7] According to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) consensus document on the management of COPD, PR should be considered in symptomatic patients with a FEV_1 below 80%.[8]

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The authors have disclosed no conflicts of interest.

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Despite these overall benefits, the responses to PR may vary significantly among individuals. Ngaage et al suggested that PR in end-stage COPD can improve exercise tolerance and physical activity.[4] Takigawa et al performed PR for subjects with different stages of COPD, and demonstrated that all subjects benefited from PR, regardless of disease severity.[9] Ergün et al also suggested that PR in the early stages (stages I and II) is as effective as in the late stages (stages III and IV) COPD.[5] Since PR is beneficial to patients with even mild COPD, it is reasonable to conclude that PR should also be beneficial to symptomatic patients with normal exercise capacity. However, previous studies have been on the different stages of COPD, and not on exercise capacity. There are no studies about PR in subjects with normal exercise capacity. Physicians may mistakenly consider that such subjects have limited improvement because they already have normal exercise capacity. Thus, the benefits of PR in subjects with normal exercise capacity should be investigated.

Since there are no previous studies on the benefits of PR in subjects with normal exercise capacity, the present study attempted to define these issues by investigating the effects of PR in subjects with normal exercise capacity on HRQL, exercise capacity, dyspnea, and respiratory muscle strength. A comprehensive understanding of these outcomes is important to optimize the management of patients with COPD.

QUICK LOOK

Current knowledge

Pulmonary rehabilitation benefits patients with COPD by improving exercise capacity and health-related quality of life (HRQL). However, it is not clear if pulmonary rehabilitation benefits patients with COPD and normal exercise capacity.

What this paper contributes to our knowledge

Exercise training improved HRQL, exercise capacity, respiratory muscle strength, and exertional dyspnea in patients with COPD and normal exercise capacity, suggesting that exercise training is indicated in these patients.

Methods

The research protocol was approved by the ethics committee of the Taipei Tzu Chi Hospital, the Buddhist Tzu Chi Medical Foundation. Signed informed consent was obtained from all subjects.

Subject Selection

Twenty-six subjects with COPD and normal exercise capacity were recruited from our out-patient clinic, from August 2009 to March 2011. They met the following inclusion criteria: a diagnosis of COPD based on the GOLD staging of the disease[10]; normal exercise capacity, with maximal oxygen uptake ($\dot{V}_{O_2}$) of 85% by incremental cardiopulmonary exercise test[11,12]; stable from exacerbations, with no worsening of respiratory symptoms (ie, dyspnea, chest tightness, and cough), no increase in the use of rescue medication, and no unscheduled visits due to COPD worsening for at least 3 months[13]; and ability to mobilize independently. The exclusion criteria were: use of oral corticosteroids; history of other lung diseases, including pneumoconiosis, bronchiectasis, pulmonary tuberculosis, primary pulmonary hypertension, pulmonary embolism, interstitial lung disease; and orthopedic, neurologic, or cardiovascular impairment that might render the subject incapable of completing the exercise training.

Measurements

Physiologic parameters were assessed by spirometry, respiratory muscle strength testing (maximal inspiratory pressure [P_{Imax}] and maximal expiratory pressure [P_{Emax}]), and cardiopulmonary exercise test before and after PR. The HRQL and dyspnea symptom were assessed by the St George's Respiratory Questionnaire (SGRQ)[14] and dyspnea scores.[15]

Pulmonary Function Test

Pulmonary function tests for measurement of $FEV_1$and FVC were made by spirometry (CPFS/D USB, Medical Graphics, St Paul, Minnesota), following the standards of the American Thoracic Society and European Respiratory Society.[16,17] The best flow-volume loop was used in the final data analysis. Reference equations for FEV_1 and FVC based on the normal populations were made available by Knudson et al.[18]

Respiratory Muscle Strength

The P_{Imax} and P_{Emax} were assessed using a standard mouthpiece and a direct dial pressure gauge (MicroRPM, Micro Medical/CareFusion, San Diego, California). P_{Imax} was measured at residual volume, and P_{Emax} at total lung capacity, according to procedures previously described.[19] The P_{Imax} and P_{Emax} were measured several times, and after 4 or 5 attempts, a plateau of values then showed relatively little variability (± 10% of reading).[20] The highest values for P_{Imax} and P_{Emax} were recorded.[19]

Cardiopulmonary Exercise Test

An incremental, symptom-limited exercise test was performed on an electronically braked cycle ergometer (906900, Lode Corival, Groningen, the Netherlands) before and after PR. The standard bicycle exercise ramp work load protocol was according to the method of Wasserman et al.[11] To stabilize gas measurement, subjects were asked to remain still for at least 3 min before beginning upright graded bicycle exercise testing. The subjects then performed unloaded pedaling for 3 min, followed by the ramp increase in work rate. The work rate increment (10–20 watts/min) was judged for each individual subject by considering age, sex, height, and weight, for obtaining an exercise phase of 8–12 min.[11] The subjects were asked to maintain a cycling cadence of 60 revolutions per minute, and were strongly encouraged to achieve their point of maximal exercise.

Expired air was continuously analyzed using a cardiopulmonary diagnostic system (Breeze 6.1, MGC Diagnostics, St Paul, Minnesota) to assess physiologic responses to exercise. $\dot{V}_{O_2}$, carbon dioxide output, minute ventilation, breathing frequency, tidal volume, S_{pO_2}, end-tidal P_{CO_2}, electrocardiogram, heart rate, and blood pressure were measured continuously during the exercise test. Peak $\dot{V}_{O_2}$ was expressed as the highest 30-second average value obtained during the last stage of the exercise test. Dyspnea scores were rated at rest and peak exercise. Anaerobic threshold was assessed using the V-slope method.[11] Maximal oxygen pulse was calculated by dividing maximal $\dot{V}_{O_2}$ by maximal heart rate.[11] The subject's data with maximal exercise was used if the following criteria were met: 85% of age-predicted heart rate; respiratory exchange ratio $\geq$ 1.09; and a plateau of $\dot{V}_{O_2}$.[11] Equations for peak $\dot{V}_{O_2}$ were according to previous references.[21,22]

Health-Related Quality of Life Assessment

HRQL of these subjects was assessed by the validated Chinese version of the SGRQ.[14] The SGRQ is a questionnaire designed to measure the influence of chest diseases on HRQL.[14,23,24] The 50 items can be aggregated into an overall score and 3 subscores, for symptoms (8 items), activity (16 items), and impact (26 items). Responses are weighted and scores are calculated by dividing the summed weights by the maximum possible weight, 0 being the best possible score, and 100 the worst.[14,23,24] The SGRQ has been reported to be valid and reliable in subjects with COPD, asthma, and bronchiectasis.[14,23,24]

Pulmonary Rehabilitation

All subjects participated in a 12-week, 2 sessions per week, out-patient-based PR program. In each session, formal education, including breathing retraining, proper use of medications, and self-management skills, was given individually. After the education, the exercise training with lower limb cycle ergometer exercise was given. Exercise sessions were 40 min, and exercise intensity targets were set at high intensity, with 75–100% of the maximal $\dot{V}_{O_2}$ observed in the pre-PR incremental exercise test. Sessions were closely monitored by a rehabilitation therapist. We monitored work rate, S_{pO_2}, heart rate, dyspnea scores, and leg fatigue during every exercise training session. During the period of PR, these subjects were not allowed to perform exercise by themselves at home.

Table 1. Baseline Characteristics of Patients With COPD and Normal Exercise Capacity

Age, y	71.0 ± 10.7
Body mass index, kg/m^2	23.8 ± 5.1
COPD stage, no. (%)	
I: mild	6 (23.1)
II: moderate	13 (50.0)
III: severe	7 (26.9)
IV: very severe	0 (0)
P_{Imax}, cm H_2O	68.1 ± 25.7
P_{Imax}, % of predicted	73.6 ± 25.6
P_{Emax}, cm H_2O	109.4 ± 30.5
P_{Emax}, % of predicted	65.2 ± 20.7
Major medications, no. (%)	
Theophylline	20 (76.9)
Inhaled long-acting muscarinic antagonists	14 (53.8)
Inhaled long-acting β agonist plus inhaled corticosteroid	12 (46.2)
Oral corticosteroid	0 (0)

± Values are mean ± SD.
P_{Imax} = maximum inspiratory pressure
P_{Emax} = maximum expiratory pressure

Statistical Analysis

Baseline measurements and results after PR are expressed as mean ± SD. Paired *t* tests were used to compare measurements before and after PR in these subjects. A *P* value < .05 was considered to be significant. Statistical analyses was with statistics software (SPSS 18.0, SPSS, Chicago, Illinois).

Results

Anthropometric and Spirometric Data

The clinical characteristics and lung function of these subjects with COPD are shown in Table 1. The mean FEV_1/FVC was 59.4 ± 14.1%, and the mean FEV_1 was 64.8 ± 23.0% of predicted. Most subjects had mild to moderate COPD. The P_{Imax} and P_{Emax} were normal. These

Table 2. Effects of Pulmonary Rehabilitation on Pulmonary Function Tests, Respiratory Muscle Strength, and Health-Related Quality of Life

	Before Pulmonary Rehabilitation	After Pulmonary Rehabilitation	Mean Difference	*P*
FEV_1/FVC, %	59.4 ± 14.1	61.5 ± 15.0	2.1	.34
FEV_1, L	1.29 ± 0.47	1.33 ± 0.46	0.04	.46
FEV_1, % predicted	64.8 ± 23.0	66.7 ± 22.3	2.0	.42
FVC, L	2.24 ± 0.79	2.21 ± 0.66	−0.03	.75
FVC, % predicted	88.3 ± 34.5	87.7 ± 32.0	−0.6	.87
P_{Imax}, cm H_2O	68.1 ± 25.7	75.9 ± 24.0	7.8	.02
P_{Imax}, % of predicted	73.6 ± 25.6	82.5 ± 22.2	8.9	.02
P_{Emax}, cm H_2O	109.4 ± 30.5	121.4 ± 37.3	12.0	.03
P_{Emax}, % of predicted	65.2 ± 20.7	71.5 ± 20.4	6.3	.04
SGRQ scores				
Total	39.8 ± 16.3	28.6 ± 16.0	−12.4	< .001
Symptoms	47.8 ± 23.9	35.5 ± 25.9	−7.8	.03
Activity	50.6 ± 18.7	42.8 ± 18.2	−12.5	< .001
Impact	31.2 ± 20.1	18.7 ± 15.3	−11.1	< .001

Values are mean ± SD.
P_{Imax} = maximum inspiratory pressure
P_{Emax} = maximum expiratory pressure
SGRQ = St George's Respiratory Questionnaire

subjects had no previous participation in home-based or hospital-based PR.

Changes in HRQL With Pulmonary Rehabilitation

Table 2 shows the SGRQ scores: total, symptoms, activity, and impact before and after PR. There were significant improvements in all domains of SGRQ (all $P < .001$). The mean changes of scores of all domains were more that 4 units, which was associated with clinical importance.[25]

Changes in Lung Function and Respiratory Muscle Strength With Pulmonary Rehabilitation

There were no significant changes in pulmonary function test results (FEV_1, FVC, and FEV_1/FVC) after 12 weeks of PR, as shown in Table 2. However, respiratory muscle strength (P_{Imax} and P_{Emax}) was significantly improved ($P < .05$).

Changes of Exercise Capacity, Cardiorespiratory Function and Dyspnea With Pulmonary Rehabilitation

The post-PR changes of exercise capacity, cardiorespiratory function, and dyspnea are shown in Table 3. All the subjects had normal maximal $\dot{V}_{O_2}$ and work rate before PR. After PR there were still significant improvements in maximal $\dot{V}_{O_2}$ (mean increase of 101.3 mL/min, $P = .001$) and work rate (mean increase of 8.2 watts, $P = .001$). Ventilation, heart rate, and mean blood pressure were unchanged following PR. The maximum oxygen pulse at maximum exercise was significantly increased with PR ($P = .02$). The S_{pO_2} and end-tidal P_{CO_2} at peak exercise did not significantly change after PR. Although dyspnea scores at rest were low and did not change significantly with PR, dyspnea at end-exercise was significantly improved after PR ($P = .01$).

Discussion

In this study our primary aim was to evaluate the effects of PR in subjects with COPD and normal exercise capacity. Clinicians may hesitate to recommend PR to these subjects, considering their already normal exercise capacity. However, we have shown that subjects with normal exercise capacity who participated in PR still had substantial improvements in HRQL, with decreased SGRQ total, symptom, activity, and impact scores. The exercise capacity and level of exertional dyspnea also showed significant improvement. Their respiratory muscle strength was normal at baseline and also improved after PR. The goals of PR in patients with COPD are to reduce symptoms, improve activity, and restore the highest level of independent function.[6,26] As such, PR still offers important benefits for patients with normal exercise capacity, and, conversely, patients with normal exercise capacity are still suitable for PR.

Impaired functional status and dyspnea are pivotal features of COPD.[27] In this study, subjects with normal exercise capacity (peak $\dot{V}_{O_2}$ 91.6%) still had an 8.4% improvement in peak $\dot{V}_{O_2}$ after PR. The degree of improve-

Table 3. Effect of Pulmonary Rehabilitation on Exercise Capacity, Cardiorespiratory Function, and Dyspnea

	Before Pulmonary Rehabilitation	After Pulmonary Rehabilitation	Mean Difference	P
Work rate, watts	82.1 ± 30.4	90.3 ± 32.7	8.2	.001
Work rate, % predicted	97.8 ± 15.9	108.6 ± 18.8	10.8	.003
$\dot{V}_{O_2}$, mL/min	1,232.6 ± 327.9	1,334.0 ± 359.3	101.3	.001
$\dot{V}_{O_2}$, % predicted	91.6 ± 8.2	100.0 ± 12.6	7.9	.001
$\dot{V}_E$, L/min	40.2 ± 13.2	39.3 ± 12.4	−0.9	.52
V_T, mL	1,152.8 ± 394.6	1,153.4 ± 406.7	0.6	.99
$\dot{V}_E/V_{CO_2}$	33.6 ± 7.5	32.3 ± 7.8	−1.4	.16
Heart rate, beats/min	134.5 ± 14.9	137.4 ± 19.9	3.0	.36
Mean blood pressure, mm Hg	109.6 ± 15.7	110.3 ± 15.1	0.7	.72
Oxygen pulse, mL/beat	9.2 ± 2.5	9.8 ± 2.7	0.6	.02
S_{pO_2}, %	93.9 ± 3.1	94.0 ± 2.9	0.1	.79
P_{ETCO_2}, mm Hg	39.8 ± 8.3	41.2 ± 6.8	1.4	.28
Exertional dyspnea score	5.7 ± 1.3	4.8 ± 2.0	−0.9	.01

Values are mean ± SD.
$\dot{V}_{O_2}$ = oxygen uptake
V_T = tidal volume
$\dot{V}_E$ = minute ventilation
$\dot{V}_{CO_2}$ = carbon dioxide clearance
P_{ETCO_2} = end-tidal P_{CO_2}

ment in exercise capacity is similar to previous studies of PR in different populations of COPD. Performing PR in underweight (FEV_1 52.8%, peak $\dot{V}_{O_2}$ 72.7%) and normal weight (FEV_1 51.5%, peak $\dot{V}_{O_2}$ 69.4%)[3] subjects, the improvements in peak $\dot{V}_{O_2}$ were 9.0% and 5.8%, respectively.[3] Pitta et al performed 3 months of PR in subjects with COPD (FEV_1 46%, peak $\dot{V}_{O_2}$ 63%) and showed a 7% increase in peak $\dot{V}_{O_2}$, with improved muscle force, HRQL, and functional status.[28] Bianchi et al performed 4 weeks of PR in subjects with COPD (FEV_1 52.7%, peak $\dot{V}_{O_2}$ 68.8%), and found that PR resulted in 4.5% improvement in peak $\dot{V}_{O_2}$. They posited that PR enabled subjects to tolerate a greater amount of restrictive dynamic ventilatory defect.[29] In the present study, subjects with COPD and normal exercise capacity benefitted from PR, with improving exercise capacity. Exercise capacity is important because peak $\dot{V}_{O_2}$ significantly correlates with mortality in subjects with COPD.[30] Previous studies also suggest that PR improves hospitalization and mortality in subjects with COPD.[31,32] However, the benefit of PR on disease progression and mortality in subjects with already normal exercise capacity remains unclear. Further studies about the benefit of PR on survival in subjects with normal exercise capacity are warranted.

Aside from improving exercise capacity, PR also improved the level of exertional dyspnea. The dyspnea scores at end-exercise were 5.7 points before PR and 4.8 points after PR. After PR the level of exertional dyspnea in these subjects was near that of healthy subjects.[33,34]

The subjects with COPD in the current study had a normal exercise capacity before PR and they were able to perform high intensity exercise training. An important factor influencing the benefits of PR is training intensity.[2,6,7] In a previous study, only high intensity exercise training resulted in a significant increase in maximal $\dot{V}_{O_2}$.[2] Casaburi et al also showed that only high intensity exercise training can improve cardiovascular and peripheral muscle function.[35] Therefore, high intensity exercise training can result in a greater physiological benefit. We suspect that the high intensity exercise training contributed to the benefits observed in the subjects with normal exercise capacity.

The mechanisms of benefits of PR should be addressed. In previous studies the combination of improved mechanical efficiency, improved respiratory and skeletal muscle strength,[36] adaptations in breathing pattern,[37] desensitization to dyspnea,[37] and consequently reduced dynamic hyperinflation,[38] all contributed to the benefits of PR. It is not clear if the mechanisms of benefit for subjects with normal exercise capacity are the same as in previous studies. In the current study, improvement of respiratory muscle strength after PR was found, and this is one possible mechanism for benefits of PR in these patients. Further studies about PR on dynamic hyperinflation, peripheral muscle strength, adaptations in breathing pattern, and desensitization to dyspnea should be conducted in subjects with normal exercise capacity.

In this study respiratory muscle strength was normal, and we did not perform specific respiratory muscle training. However, general exercise training improved subjects' respiratory muscle strength. Previous study suggests that respiratory muscle training in subjects with P_{Imax} below

60 cm H_2O can allow optimal benefits.[39] However, according to the current study, subjects with normal respiratory muscle strength still benefit from PR. One previous study on normal subjects without respiratory muscle weakness also revealed the same result.[40] Improvement of respiratory muscle strength is important in that it associates with the reduction in dyspnea.[41-43] Mechanisms about improvement of respiratory muscle strength after general exercise training are not quite clear. Since exercise increases ventilation by more than 12-fold, it is expected that exercise training will constitute a training load to the respiratory muscle.[41]

Limitations of the Study

The present study has some limitations. First, the study defined normal exercise capacity based on maximal $\dot{V}_{O_2}$ by cardiopulmonary exercise test. The comprehensive assessments of exercise capacity include peripheral muscle function, functional exercise capacity (6-min walk test), and the level of physical activity in daily life.[43] However, none of these parameters was measured in this study. Second, lung volume changes were also not measured before and after PR. Thus, lung volume changes like dynamic hyper-inflation remain unknown.

Conclusions

We analyzed the benefits of PR for subjects with COPD and normal exercise capacity. PR did result in significant improvements in HRQL, exercise capacity, exertional dyspnea, and respiratory muscle strength. Our study suggests that PR may still be indicated for patients with COPD and normal exercise capacity. PR should be part of the clinical management of patients with COPD, even for those with normal exercise capacity. However, benefits on disease progression, hospitalization, and survival for these patients remain unknown.

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