

Differences in Response to Pulmonary Rehabilitation in Idiopathic Pulmonary Fibrosis and Chronic Obstructive Pulmonary Disease

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Abstract

Background: The benefits of pulmonary rehabilitation in COPD are well recognized. However, whether individuals with idiopathic pulmonary fibrosis (IPF) benefit is less clear.

Objectives: To evaluate the effects of pulmonary rehabilitation in subjects with IPF and compare their responses with a group of COPD subjects who underwent an identical program.

Methods: Forty-five subjects with IPF and 45 age and Medical Research Council (MRC) grade-matched COPD subjects were recruited. Subjects completed an 8-week outpatient pulmonary rehabilitation program. Dyspnea, peripheral muscle force, exercise capacity (6-minute walk distance, 6MWD), activities of daily living (ADL), and health status (36-item short-form survey, SF-36) were assessed at baseline, immediately following and at 6 months following completion of the program.

Results: Adherence to the program was similar in both groups. Significant improvements in dyspnea, muscle force, exercise capacity and ADL occurred in both groups (all $p < 0.05$), however the magnitude of improvement in all outcomes was less in the IPF group (mean [95% CI] improvement in 6MWD, IPF 16.2m [7.4 to 25.1]; COPD 53.1m [45.2 to 61]). All domains of SF-36, with the exception of social function improved (all $p < 0.05$) in the COPD group; however there were no changes in SF-36 scores in the IPF group. The benefits were well maintained in the COPD group at 6 months, but, with the exception of the ADL score, the benefits were no longer present in the IPF group.

Conclusions: Pulmonary rehabilitation in IPF produces only modest short-term gains in dyspnea, exercise capacity and ADL, but does not improve health status.

Introduction

Idiopathic pulmonary fibrosis (IPF) is the most common and clinically important interstitial lung disease (ILD), and is a chronic progressive disorder with a poor prognosis [1]. Progressive dyspnea, frequently accompanied by a non-productive cough, is the hallmark symptom and causes exercise limitation. Exertional dyspnea and exercise limitation lead to difficulties in performing daily activities and are the major contributors to the impairments in health related quality of life (HRQoL) [2]. Treatment options are limited and conventional pharmacotherapy for IPF has not been shown convincingly to improve morbidity, physiological or radiological markers of disease severity, HRQoL, or survival [1].

The presence of exercise limitation and significant disability suggests that individuals with IPF are likely to be appropriate candidates for pulmonary rehabilitation [3]. Although the benefits of rehabilitation have been extensively reported in subjects with chronic obstructive pulmonary disease (COPD) [4], data to support rehabilitation in subjects with IPF are scant. Studies in subjects with non-COPD that have included IPF subjects, report improvements in dyspnea, exercise capacity and HRQoL following rehabilitation [5-9]. Recently, a study of a large subject cohort (n=113) with ILD reported similar findings [10]. One randomized controlled trial in subjects with IPF demonstrated benefit from pulmonary rehabilitation however the subjects had relatively mild disease [11]. To date, the effects of pulmonary rehabilitation in subjects with IPF and associated moderate to severe disability are unknown.

The guidelines for exercise training in subjects with chronic lung disease are largely based on studies in COPD cohorts [12] with the assumption that the recommendations are applicable to subjects with other lung diseases. The pathophysiology and exercise limitation in IPF differs from COPD [13]. In COPD, ventilatory limitation and skeletal muscle dysfunction are the predominant factors contributing to exercise limitation [14], whereas impaired pulmonary gas exchange [15, 16] and circulatory factors [17] may be the primary limitations to exercise in IPF. Exercise programs, especially high-intensity endurance training, improve muscle function, and

decrease lactic acidosis at a given level of sub-maximal exercise resulting in a decreased ventilatory demand and dyspnea in COPD [18]. It is unclear whether this mechanism similarly contributes to the benefits following exercise training in individuals with IPF. We hypothesized that a pulmonary rehabilitation program based on the guidelines developed for COPD would produce benefits of a smaller magnitude in IPF subjects than in a cohort with COPD.

The aims of the present study were to: (i) evaluate the effects of pulmonary rehabilitation on dyspnea, exercise capacity and health status in subjects with IPF who have functional limitation and, (ii) compare the responses in subjects with IPF with the changes seen in a control group of COPD subjects who underwent an identical pulmonary rehabilitation program.

Material and Methods

Study Design

We performed a prospective nonrandomized open trial in which two subject cohorts (IPF and COPD) underwent an 8-week out-patient pulmonary rehabilitation program. Measures were made at baseline, immediately following the 8-week program and at 6 months following completion of the program.

Subjects

Subjects were eligible to participate if they reported dyspnea on exertion leading to a limitation in daily activities (Medical Research Council [MRC] grade > 1) [19] and were on stable medical treatment. The diagnosis of IPF was based on published criteria [1]. Individuals with collagen vascular disease, occupational lung disease, sarcoidosis, hypersensitivity pneumonitis and other idiopathic interstitial pneumonias were excluded. Other exclusions were MRC grade 5, severe orthopedic or neurological disorders limiting exercise performance, unstable cardiac disease, inability to understand or complete questionnaires and previous participation in a pulmonary rehabilitation program.

The control group comprised age and MRC grade-matched COPD subjects. Since the pathophysiology and exercise limitation in IPF significantly differs from that seen in COPD, we matched subjects based on their level of their functional limitation due to dyspnea. The diagnosis of COPD was made according published guidelines [20]. Exclusion criteria were identical to those for the IPF group.

Prior to recruitment, subjects in both groups were required to be clinically stable for at least 4 weeks. All patients were under the care of a respiratory physician. Medical treatment, including dose of oral corticosteroids and immunosuppressives was not changed during the rehabilitation program.

This study was approved by the Human Ethics Review Committee of Nagasaki University

Graduate School of Biomedical Sciences and subjects gave written informed consent prior to participation.

Baseline Assessments

Baseline measurements comprised age, gender, body mass index, time since diagnosis, use of long term oxygen therapy (LTOT) and oral corticosteroids, symptoms of cough, transthoracic echocardiographic data (right ventricular systolic pressure) and pulmonary function. The outcome measures in this study were dyspnea and functional status, peripheral muscle force, functional exercise capacity, limitation in daily activities and health status. These measures were made at baseline and repeated immediately following and at 6 months after completion of the 8-week program.

Spirometry, static lung volumes and diffusing capacity of the lung for carbon monoxide (D_{LCO}) were measured in accordance with a standard protocol [21, 22]. Arterial blood gas tensions were measured at rest, and were undertaken with oxygen supplementation for subjects who were receiving LTOT.

Dyspnea and functional status were evaluated using the MRC dyspnea grade [19] and the baseline dyspnea index (BDI)/transition dyspnea index (TDI) respectively [23].

Quadriceps force (QF) was measured as the peak force (kg) developed during a maximal isometric knee extension maneuver with the hip and knee in 90 degrees flexion using a hand-held dynamometer with fixing-belt (μ Tas F-1; Anima Corporation; Tokyo, Japan). The highest value from three attempts on the dominant side was recorded and expressed in kg and as a percentage of body weight. This protocol has good test retest reliability with an intraclass correlation coefficient of 0.94 [24]. Handgrip force (HF) was assessed with a hydraulic hand dynamometer (Smedley's Dynamometer; TTM; Tokyo, Japan). Peak force (kg) was measured on the dominant hand and the highest value of three attempts was used in the analyses.

The 6-minute walk test (6MWT) was performed according to published guidelines along a

30m corridor [25]. The test was performed twice on consecutive days and the greatest distance (6-minute walk distance [6MWD]) was used in the analysis. Oxygen saturation (SpO_2) was monitored continuously throughout the test and the test was terminated if SpO_2 fell to below 80%. Pre-exercise and the lowest SpO_2 recorded during the test was recorded. Heart rate was monitored continuously throughout the test (Polar, Polar Electro, Oy, Finland).

Subjects performed a symptom-limited incremental cycle ergometry test (ICET) on an electrically braked cycle ergometer (Rehcor version 2.21; Lode BV; Groningen, the Netherlands) to volitional exhaustion. After a period of rest followed by 2 minutes of unloaded pedaling, work load was increased by 5 W/min for subjects with MRC grade 4 and 10 W/min for those with grades 2 and 3. Test termination was determined by the subject or by the tester if oxygen saturation fell below 80%. At the end of each minute, symptom scores for dyspnea [26] and leg fatigue [26] were recorded. Peak work-rate (PWR) was recorded as the maximum work-rate (Watts) maintained for at least 30 seconds. Dyspnea ratings obtained from this test were used as a target for subjects to regulate and monitor the intensity of exercise during the initial stages of the rehabilitation program. This test was only performed at the baseline assessment.

During the 6MWT and ICET, subjects receiving LTOT used the same flow rate of supplemental oxygen as prescribed for their normal daily activities. All follow-up exercise tests were performed with subjects using the same flow rate of supplemental oxygen as used during the baseline exercise tests.

Limitations in activities of daily living (ADL) were assessed using a standard scoring system [27]. This system evaluates six fundamental daily activities (i.e., feeding, transfer, dressing, bathing, shopping, and transportation) and assigns a score of 1 (independent) or 0 (dependent) for each activity. The total score was used in the analysis.

Health status was measured using the self-administered Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36, Version 2) adapted and psychometrically validated for the

Japanese population [28].

Pulmonary Rehabilitation Program

Subjects attended an 8-week outpatient program comprising two classes each week, (90 minutes duration), that included exercise training, breathing retraining, and education. The same training protocol was used for the IPF and COPD cohorts, During each class, subjects performed 40 to 50 minutes of exercise supervised by a physiotherapist. Subjects also were instructed to undertake daily exercise at home and were encouraged to continue their home-based program at the end of the 8 weeks. Adherence with the home program was assessed using a diary card.

Exercise training included stretches and endurance and strength training. Lower limb endurance training was performed using a cycle ergometer with the initial workload prescribed at 50% of the PWR achieved on the baseline cycle ergometer test. In the early stages of the program, cycling was limited to 5 to 10 minutes and progressively increased, within symptom tolerance, to 20 minutes of continuous cycling. Once subjects had achieved 20 minutes cycling, the workload was increased. Upper limb endurance training comprised repetitive bilateral shoulder flexion and abduction using a light weight and synchronized with expiration for 2 minutes. Strength training was accomplished using free weights or the subject's own body weight. One set of 10 repetitions was initially prescribed increasing to 3 sets when the subject could perform the exercises without any difficulty. Arterial oxygen saturation was monitored during each session, and supplemental oxygen was given as necessary, to maintain arterial oxygen saturation above 85%. We recorded the duration of cycle-based exercise (in minutes) and workload (in Watts) of all subjects for each of the exercise sessions.

Breathing retraining consisted of relaxation with breathing control, pursed-lip breathing and pacing during exercise training and ADL. The rationale for pursed-lip breathing in the IPF cohort was to assist subjects to control their breathing by reducing respiratory frequency. All subjects received the same instructions.

The education component was provided by a physiotherapist at each class and consisted of the benefits and importance of daily exercise, pacing and energy conservation techniques to manage ADL and self-management strategies for coping with an exacerbation.

Subjects were considered to have completed the program if they attended at least 12 (75%) of the 16 supervised sessions. At the end of the 8 week program, all subjects were encouraged to continue with their home exercise program however no formal maintenance program was provided.

Statistical Analysis

The Kolmogorov-Smirnov test was used to examine the distribution of the data. Data that did not conform to a normal distribution were transformed or were analyzed using non-parametric tests. Differences between groups at baseline were assessed using unpaired t tests, Mann-Whitney U test and Chi-square test. Within group and between group changes following rehabilitation were evaluated using paired t tests, Wilcoxon signed-rank and Mann-Whitney U tests respectively. Total work done (in kJ) between groups for each exercise session were compared using a two-way repeated measures analysis of variance to account for group and time interaction. Pearson product moment correlation or Spearman rank correlation were used to examine relationships between the changes in 6MWD and QF in both groups, and mean daily dose of corticosteroids and change in QF in subjects with IPF. Data are expressed as means \pm SD or 95% confidence intervals (95% CI). All analyses were performed using SPSS software Version 16 (SPSS Inc, Chicago, Illinois, USA).

Results

One hundred and twelve consecutive subjects were screened of whom 90 were recruited to the study (Figure 1). Surgical lung biopsies were performed in 9 subjects with IPF. Baseline characteristics of the 90 subjects are shown in Table 1. A higher proportion of the IPF cohort reported cough as a major symptom (67% vs. 9%, $p<0.001$), and were prescribed LTOT (58% vs. 22%, $p<0.001$). The use of oral corticosteroids was higher ($p=0.001$) and QF (% body weight) lower in the IPF group ($p=0.031$). 6MWD was similar in the two groups however the magnitude of desaturation during the 6MWT was greater in the IPF group (Table 1). There were no significant differences between the groups in SF-36 scores (Table 1).

Adherence with the Rehabilitation Program

Adherence with the program was similar in the two groups. The mean number of supervised sessions attended was 13.3 ± 3.8 and 14.1 ± 2.7 for the IPF and COPD groups respectively ($p=0.24$). No adverse events were recorded during the program. Subjects completed an average of 3.9 ± 1.9 (IPF group) and 4.1 ± 1.6 (COPD group) sessions of home-based exercise each week ($p=0.59$).

Data for cycle ergometry training are displayed in Figure 2 as total work done (kJ) and the intensity of training expressed as a percentage of the PWR achieved on the baseline ICET. There was a significant interaction between group and time for total work ($p<0.001$). The IPF subjects were unable to progress the intensity of exercise as rapidly as the COPD subjects due to dyspnea and/or cough and profound desaturation. At the end of the program, training intensity was 33.6 ± 22.1 W and 44.3 ± 21.7 W (69 ± 15 % baseline PWR and 89 ± 8 % baseline PWR) in the IPF and COPD groups, respectively ($p=0.037$, $p<0.001$). Total work performed was significantly lower in the IPF group compared to the COPD group (445 ± 333 kJ vs. 594 ± 341 kJ, $p=0.013$).

Effects of the Rehabilitation Program

Seventy-six subjects (IPF n=36, COPD n=40) completed the 8-week program. Attrition was 20% in IPF group and 11% in COPD group (p=0.24, Figure 1). Sixty-seven subjects (IPF n=30, COPD n=37, p=0.09) completed the 6 month follow-up assessments. There were four deaths in the IPF group, with all occurring during the follow-up period.

The 9 subjects with IPF who did not complete the program had lower ADL scores (2.3 ± 1.0 , p=0.004) and the physical functioning (p=0.047), vitality (p=0.002) and role emotional (p=0.002) domains of the SF-36 compared to those who completed. In the COPD group, the 5 subjects who did not complete had a lower QF (14.3 ± 9.9 kg, p=0.042).

Significant improvements in dyspnea, muscle force, 6MWD and ADL occurred in both groups following the program (Table 2). These benefits were maintained at the 6-month follow-up in the COPD group. In contrast, with the exception of the ADL score none of the improvements were maintained in the IPF group (Table 2).

All subscales of the SF-36, with the exception of social function improved (all p<0.05) in the COPD group following the program (Table 2). In contrast no significant changes were seen in the IPF group. At the 6 month follow-up, the improvement in physical functioning and mental health were maintained in the COPD group (Table 2).

The magnitude of improvement in all outcomes was less in the IPF group than in the COPD group. At the 6 month follow-up, there was a deterioration in the TDI score, 6MWD, and all subscales of the SF-36 in the IPF group when compared to baseline (Table 3).

The change in 6MWD was positively correlated with the change in QF in both groups (IPF; r=0.43, p=0.013 vs. COPD; r=0.35, p=0.023). In the IPF group, there was an inverse relationship between the mean daily dose of oral corticosteroids and change in QF (r= -0.62, p=0.04). Further, the improvement in QF was less in subjects taking oral corticosteroids than those not receiving corticosteroids (IPF; -0.2 ± 1.0 kg vs. 3.3 ± 3.5 kg, p=0.002: COPD; 2.0 ± 2.8 kg vs. 5.8 ± 2.8 kg, p=0.016, respectively).

In both subject groups, all indices of pulmonary function had significantly declined at the 6 month follow-up when compared to baseline measures. The only exceptions were the FEV₁ and FVC in the COPD cohort (Table 4).

Discussion

The present study is the first prospective controlled trial to evaluate the effects of pulmonary rehabilitation in subjects with IPF who have functional limitation, and to compare the responses to rehabilitation to those seen in a cohort with COPD. Because the mechanisms of exercise limitation are different in the two disease cohorts, we matched subjects for age and MRC grade. At the baseline assessment the groups were similar in terms of exercise capacity (6MWD, PWR), functional status (ADL score) and health status (SF-36 scores). Thus, we consider that a comparison of response to rehabilitation in these two distinct disease cohorts is valid. Although the rehabilitation program significantly improved dyspnea, muscle force, exercise capacity and ADL in both groups, health status did not change in the IPF group. Further, the magnitude of improvement was significantly less in the IPF group despite both groups presenting with a similar level of disability at baseline assessment. Moreover, at 6 months after completion of the program, the improvements were no longer evident in the IPF group although were well maintained in the subjects with COPD. Thus, this study demonstrates that a pulmonary rehabilitation program based on guidelines for subjects with COPD has limited efficacy when applied to individuals with advanced IPF.

Recently, two randomized controlled trials in subjects with IPF [11] and ILD [7] provide support for the benefits of pulmonary rehabilitation. In both trials exercise prescription was based on recommendations for individuals with COPD [12]. Nishiyama and colleagues [11] reported significant improvements in 6MWD and St George's Respiratory Questionnaire in subjects with IPF who had mild impairment. Holland et al [7] found significant improvements following rehabilitation in 6MWD, dyspnea, and the Chronic Respiratory Disease Questionnaire in a randomized controlled trial of 57 subjects with ILD (34 with IPF). However, none of the benefits were maintained at 6 months. The systematic review of exercise training in ILD also provides support for the short-term benefits of this intervention in patients with IPF [29].

Our data are consistent with the findings of Holland et al who reported only a modest

improvement in 6MWD and a significant decline in 6MWD in the IPF cohort at 6 month follow-up. These authors recently reported that the threshold for a clinically significant change in 6MWD for subjects with IPF to be in the range 29-34 m [30]. Our program achieved a smaller increase in 6MWD (16m) and suggests that the magnitude of improvement following pulmonary rehabilitation is modest in subjects with IPF and is not well maintained after cessation of the program.

The relatively small improvements in dyspnea and exercise capacity may have contributed to the lack of a change in health status in the IPF cohort. In COPD, exercise capacity and dyspnea are the main determinants of HRQoL [31]. Other studies in ILD and IPF cohorts have shown a relationship between improvements in dyspnea and exercise capacity [7, 11]. Differences between the outcomes in the COPD and IPF subjects in our study may in part be due to the characteristic symptom of frequent cough and severe hypoxemia, and the use of oral corticosteroids in the IPF group.

Factors Limiting Improvement Following Pulmonary Rehabilitation

Our findings of limited short-term improvement following pulmonary rehabilitation in IPF may be explained by disease heterogeneity, the intensity of the endurance exercise achieved and the nature of the lower limb muscle weakness. Disease progression in IPF is variable [1]. Thus, the effects of pulmonary rehabilitation depend on the rate of disease progression. In our study, the majority of the IPF group had severely impaired pulmonary function and we speculate that their disease was comparatively well advanced. This may have limited the potential for subjects to gain improvements from rehabilitation.

Although we attempted to progress training intensity, severe oxygen desaturation, and paroxysms of cough and severe dyspnea, limited the ability of the IPF group to increase intensity. Thus it is likely that the intensity of exercise in this group was insufficient to achieve a physiologic training effect. Arterial hypoxemia during exercise may cause early onset of lactic

acidosis in peripheral muscles and increased central drive during low-intensity exercise. Moreover these factors contribute to the increased ventilatory demand and dyspnea.

Muscle weakness in COPD is mainly considered to be related to disuse or physical deconditioning [32], with the improvements in exercise capacity after exercise training occurring as a result of peripheral muscle adaptation [33]. Quadriceps force was significantly lower in the IPF group at baseline and the magnitude of improvement in QF and exercise capacity was lower in this cohort. This finding suggests that the ability to achieve peripheral muscle adaptation following training may be limited in IPF.

Previous research demonstrated that QF is reduced in IPF subjects with only mild-to-moderate pulmonary impairment, and is related to exercise capacity [34], suggesting possible mechanisms responsible for this finding might include deconditioning, the inflammatory disease process of IPF and decreased levels of anabolic hormones and myopathy specific to IPF [34]. However, as yet the pathophysiology underlying QF weakness in IPF is unclear. We speculate that skeletal muscle weakness and the poor response to exercise training in subjects with IPF may be related to corticosteroid treatment. In addition, deconditioning or atrophy of skeletal muscles further contribute to the myopathy .

The lack of a sustained benefit following rehabilitation in the IPF group is consistent with a previous report [7]. Although we encouraged subjects to continue with their home-based exercise program after cessation of supervised classes, we did not provide a formal maintenance program. Several trials of pulmonary rehabilitation in COPD suggest that the benefits decline towards baseline after 6 to 12 months following cessation of the intervention [12]. The rapid decline in our IPF subjects could be explained by their disease progression. Attrition tended to be higher in the IPF group and may also have influenced these findings. The finding that the ADL score was preserved at follow-up may be explained by the patient education component that aimed at improving the ability of subjects to undertake ADL.

Limitations

We utilized COPD subjects as a control group and did not include a control group of IPF subjects who received only usual medical care thus limiting our ability to evaluate the longer-term effects of pulmonary rehabilitation in IPF. Because IPF is a heterogeneous disease and our sample was relatively small we were unable to examine the effects of disease severity on responses to pulmonary rehabilitation. Although there are several disease specific health status or HRQoL instruments for COPD, there is no such scale for IPF. We therefore used the SF-36, because its validity and reliability have been established in both COPD [35] and IPF [36]. However this may have limited responsiveness. Further, we did not utilize interval training in an attempt to increase the training intensity tolerated by the IPF group. Pulmonary hypertension is frequently seen in subjects with IPF [37] and adversely affects exercise capacity [38]. We are unable to comment on the significance of pulmonary hypertension in our subjects, or the effects of exercise training on pulmonary hemodynamics, because most subjects did not undergo right heart catheterization.

Clinical Implications

Exercise training prescribed using guidelines for individuals with COPD appears to be less effective in IPF subjects hence a unique approach to training for IPF subjects is required. This should include provision of supplementary oxygen [39], specific occupational therapy interventions [40], and energy conservation strategies may be useful to control dyspnea and exercise induced hypoxemia. Further, the optimal timing for rehabilitation in the disease trajectory requires consideration.

Conclusions

Pulmonary rehabilitation in subjects with IPF achieves only modest improvements in dyspnea, exercise capacity and ADL, but does not appear to improve health status. Further, the benefits are not maintained once training ceases. These findings contrast to the larger and longer-lasting improvements following rehabilitation seen in COPD and suggest that future research should focus on developing a pulmonary rehabilitation program specifically tailored to the needs of IPF subjects in an attempt to optimize the benefits of rehabilitation.

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Figure legends

Figure 1. Participant flow diagram.

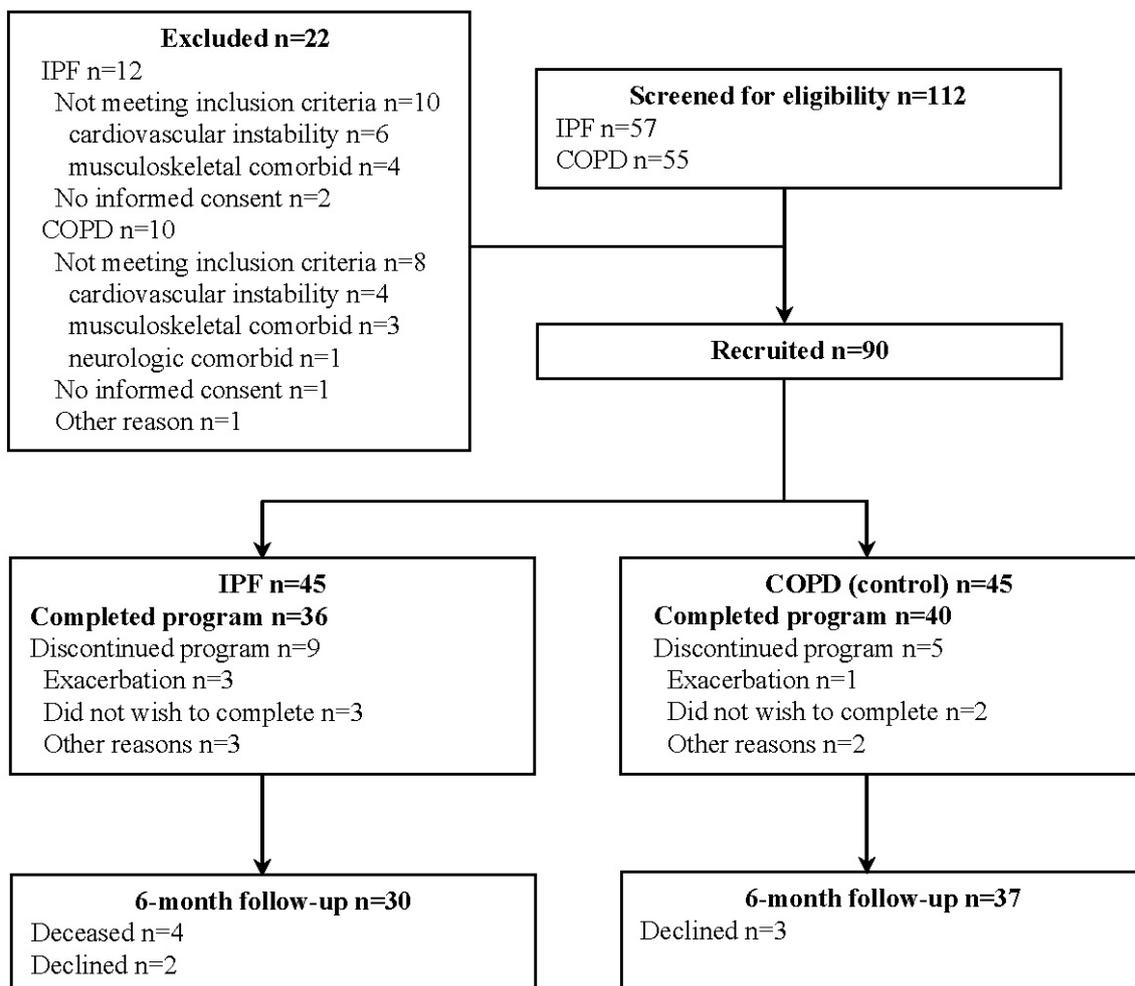
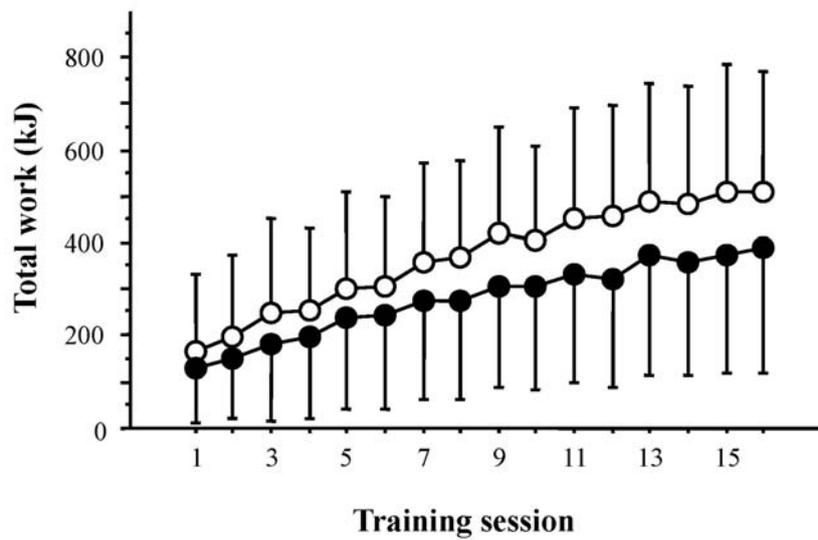


Figure 2. (a) Total work performed (kJ) during each training session and (b) training intensity expressed as %baseline PWR averaged for each week of training. Data are mean \pm SD for each group. Closed circles denote IPF groups, open circles represent COPD groups. (kJ = kilojoules; PWR = peak work-rate.)

(a)



(b)

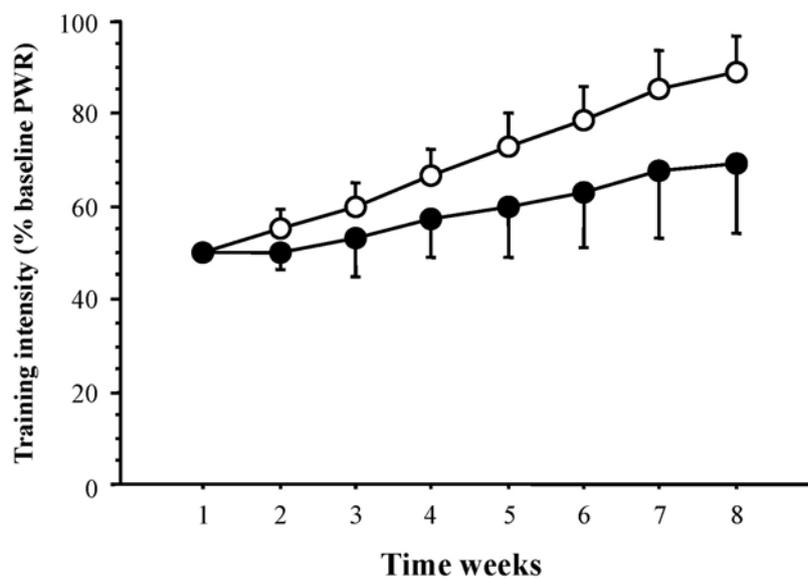


Table 1. Baseline characteristics of the subjects*

Characteristics	IPF group (n=45)	COPD group (n=45)	p Value
Age, yr	67.5 ± 7.8	67.3 ± 5.1	0.85
Gender, M/F	37/8	38/7	0.78
BMI, kg/m ²	21.2 ± 3.3	20.8 ± 2.2	0.75
Time since diagnosis, years	1.8 ± 1.8	1.7 ± 1.7	0.95
LTOT	26 (58%)	10 (22%)	0.001
Oral corticosteroids	20 (44%)	6 (13%)	0.001
mean dose, mg/day	22.6 ± 7.8	11.7 ± 4.1	0.001
Cough	30 (67%)	4 (9%)	0.001
RVSP, mm Hg	47 ± 21	30 ± 11	0.001
Blood gas data			
PaO ₂ at rest, mmHg †	72.8 ± 9.6	73.3 ± 8.0	0.78
PaCO ₂ at rest, mmHg †	40.8 ± 5.0	40.6 ± 4.4	0.89
PaO ₂ at rest, mmHg ‡	69.3 ± 8.8	70.2 ± 6.2	0.76
PaCO ₂ at rest, mmHg ‡	42.1 ± 4.8	42.5 ± 4.4	0.81
Pulmonary function			
FEV ₁ , L	1.7 ± 0.5	1.1 ± 0.5	0.001
FEV ₁ , %pred	80.1 ± 17.3	45.0 ± 11.8	0.001
FVC, L	2.0 ± 0.6	2.5 ± 0.7	0.001
FVC, %pred	68.6 ± 16	81.3 ± 23.4	0.011
FRC, L	1.6 ± 0.5	4.2 ± 1.0	0.001
FRC, %pred	65.4 ± 17.8	147 ± 22.7	0.001
TLC, L	3.0 ± 0.8	5.6 ± 1.0	0.001
TLC, %pred	63.8 ± 13.7	109.9 ± 14.5	0.001
D _{LCO} , mL/min/mmHg	6.0 ± 2.5	12.9 ± 6.1	0.001
D _{LCO} , %pred	38.8 ± 20	58.9 ± 24.1	0.001
Dyspnea and functional status			
MRC grade	3.0 ± 0.8	3.0 ± 0.8	
2	14 (31%)	14 (31%)	
3	15 (33%)	15 (33%)	
4	16 (36%)	16 (36%)	
BDI focal score	5.1 ± 3	5.2 ± 2.7	0.91
Muscle force			
HF, kg	23.2 ± 9.1	24.1 ± 8.3	0.62
QF, kg	19.1 ± 10.1	22.1 ± 9	0.155
QF, % body wt	35.4 ± 15.2	42.3 ± 14.5	0.031
Exercise capacity			
6MWT			
6MWD, m	308 ± 111	318 ± 109	0.69
Pre-exercise SpO ₂ , %	95 ± 2	96 ± 1	0.001
Lowest SpO ₂ during test, %	82 ± 8	91 ± 5	0.001
Desaturation, %	13 ± 8	6 ± 4	0.001
Pre-exercise heart rate, bpm	89 ± 10	85 ± 10	0.052
Peak heart rate during test, bpm	121 ± 14	115 ± 11	0.04
Pre-exercise dyspnea	0.2 ± 0.5	0.2 ± 0.3	0.95
Peak-exercise dyspnea	4.9 ± 1.3	4.4 ± 0.2	0.03
ICET			
Peak work-rate, W	42.2 ± 21.3	48.8 ± 23.3	0.16
ADL			

ADL score	3.4 ± 1.3	3.5 ± 1.4	0.81
Health status			
SF-36			
Physical functioning	35.7 ± 18.7	38.8 ± 22.4	0.58
Role physical	33.9 ± 21.7	32.2 ± 21	0.77
Bodily pain	62.4 ± 30.3	61.2 ± 29.3	0.81
General health	34.7 ± 19.9	33.3 ± 17.5	0.66
Vitality	38.3 ± 21.3	37.1 ± 18.5	0.71
Social function	48.3 ± 23.7	50.0 ± 17.7	0.75
Role emotional	36.5 ± 30.1	38.5 ± 26.9	0.84
Mental health	50.0 ± 18.7	49.9 ± 18.2	0.97

* Values are mean ± SD or numbers (%) of subjects. ADL = activities of daily living; BDI = baseline dyspnea index; BMI = body mass index; D_{LCO} = diffusing capacity of the lung for carbon monoxide; FEV_1 = forced expiratory volume in one second; FRC = functional residual capacity; FVC = forced vital capacity; HF = handgrip force; ICET = incremental cycle ergometry test; LTOT = long term oxygen therapy; MRC = Medical Research Council; $PaCO_2$ = arterial carbon dioxide tension; PaO_2 = arterial oxygen tension; %pred = percent predicted; QF = quadriceps force; RVSP = right ventricular systolic pressure; SF-36 = 36-item short-form survey; 6MWD = 6-minute walk distance; 6MWT = 6-minute walk test; SpO_2 = percutaneous oxygen saturation; TLC = total lung capacity; RVSP data IPF n=40, COPD n=36; blood gas data tensions shown for all 45 subjects in each group[†] and for the 19 subjects with IPF[‡] and 35 subjects with COPD who were not receiving LTOT[‡].

Table 2. Outcome measures of the subjects who completed program at baseline, and at 8 weeks and 6 months following pulmonary rehabilitation *

Outcome measures	IPF group			COPD group		
	Baseline (n=36)	8 weeks (n=36)	6 months (n=30)	Baseline (n=40)	8 weeks (n=40)	6 months (n=37)
Dyspnea and functional status						
MRC grade	3.0 ± 0.8	2.5 ± 1.1 ‡	2.9 ± 1	3.0 ± 0.8	2.3 ± 0.9 ‡	2.4 ± 0.9 ‡
TDI focal score		0.8 ± 1.7	-0.9 ± 0.9		1.8 ± 1.7	0.9 ± 1.4
Muscle force						
HF, kg	24 ± 9.2	24.8 ± 9.7 †	24.4 ± 9.7	24.7 ± 8.1	26.1 ± 8.4 ‡	25.3 ± 8 ‡
QF, kg	20.4 ± 10.5	22.4 ± 11.6 ‡	20.9 ± 11.7	23.0 ± 8.6	28.4 ± 10.3 ‡	27.0 ± 10.5 ‡
QF, % body wt	36.8 ± 15.8	41.1 ± 18.9 ‡	36.9 ± 18.1	43.8 ± 13.4	54 ± 15.7 ‡	51.8 ± 16.2 ‡
Exercise capacity						
6MWD, m	323 ± 109	340 ± 122 ‡	320 ± 106	325 ± 107	378 ± 99 ‡	367 ± 95 ‡
ADL						
ADL score	3.7 ± 1.2	4.8 ± 1.1 ‡	4.3 ± 1.2 ‡	3.6 ± 1.3	5.1 ± 0.9 ‡	5.1 ± 0.9 ‡
SF-36 Scale						
Physical functioning	38.6 ± 19	40.6 ± 22.6	37.8 ± 23	40.1 ± 21.4	47.1 ± 19.5 †	45.1 ± 20 †
Role physical	34.9 ± 21.5	35.9 ± 20.7	30.4 ± 23.7	32.8 ± 20.9	42.7 ± 22.7 ‡	39.7 ± 22.8
Bodily pain	66.1 ± 30	63.4 ± 28.1	62.5 ± 30.3 †	61.0 ± 28.5	63.5 ± 27.3 †	63.1 ± 25.4
General health	37.1 ± 20	36.9 ± 21.1	34.4 ± 21.5 †	34.7 ± 17.5	40.7 ± 18.1 †	38.0 ± 14.1
Vitality	43.1 ± 20	43.9 ± 21	42.1 ± 23.6	37.1 ± 19.2	45.2 ± 22.4 ‡	41.9 ± 19.7
Social function	51.0 ± 23.8	50.3 ± 25.3	45.8 ± 26.9 †	49.1 ± 17.1	54.1 ± 22.5	51.7 ± 22.3
Role emotional	39.6 ± 30.7	38.7 ± 31.3	35.8 ± 29.8	39.4 ± 25.8	46.7 ± 27.1 †	45.9 ± 28.8
Mental health	50.7 ± 18.7	52.6 ± 20.5	47.5 ± 21.8	49.3 ± 18.9	55.4 ± 17.4 ‡	54.5 ± 19.2 †

* Values are mean ± SD. MRC = Medical Research Council; TDI = transition dyspnea index; HF = handgrip force; QF = maximal quadriceps force; 6MWD = 6-minute walk distance; ADL = activities of daily living; SF-36 = 36-item short-form survey.

† p<0.05, ‡ p<0.01 compared with baseline in each group.

Table 3. Comparison of changes in the IPF and COPD groups after pulmonary rehabilitation*

Outcome measures	After 8 weeks			After 6 months		
	IPF group (n=36)	COPD group (n=40)	p Value	IPF group (n=30)	COPD group (n=37)	p Value
Dyspnea and functional status						
MRC grade	-0.4 (-0.6 – -0.3)	-0.8 (-0.9 – -0.6)	0.011	-0.1 (-0.3 – 0.2)	-0.6 (-0.8 – -0.4)	0.001
TDI score	0.8 (0.2 – 1.4)	1.8 (1.4 – 2.2)	0.04	-0.9 (-1.2 – -0.6)	0.9 (0.45 – 1.35)	0.001
Muscle force						
HF, kg	0.8 (0.2 – 1.5)	1.4 (1.1 – 1.6)	0.006	0.1 (-0.8 – 1)	0.9 (0.6 – 1.2)	0.007
QF, kg	2.0 (0.9 – 3.1)	5.4 (4.4 – 6.4)	0.001	0.01 (-1.2 – 1.2)	4.1 (3.0 – 5.2)	0.001
QF, % body wt	4.3 (1.8 – 6.7)	10.2 (8.5 – 11.8)	0.001	0.2 (-2 – 2.4)	7.7 (5.8 – 9.6)	0.001
Exercise capacity						
6MWD, m	16.2 (7.1 – 25.4)	53.1 (44.9 – 61.2)	0.001	-21.7 (-30 – -13.4)	49.2 (38.9 – 59.4)	0.001
ADL						
ADL score	1.1 (0.8 – 1.3)	1.5 (1.2 – 1.7)	0.04	0.5 (0.2 – 0.8)	1.5 (1.2 – 1.9)	0.001
SF-36 Scale						
Physical functioning	1.9 (-1.1 – 5)	7.0 (2 – 12)	0.163	-2.0 (-5.4 – 1.4)	5.5 (0.7 – 10.4)	0.007
Role physical	1.0 (-1.6 – 3.6)	9.9 (3.8 – 15.9)	0.002	-5.0 (-10.3 – 0.3)	6.4 (-0.9 – 13.7)	0.009
Bodily pain	-2.7 (-8.2 – 2.7)	2.6 (0.5 – 4.6)	0.03	-3.9 (-8.3 – 0.4)	-0.3 (-3 – 2.4)	0.251
General health	-0.2 (-2.8 – 2.4)	6.0 (0.1 – 11.8)	0.012	-4.2 (-8.4 – -0.1)	3.9 (-1.5 – 9.2)	0.035
Vitality	0.9 (-1.9 – 3.6)	8.1 (4.3 – 11.9)	0.014	-0.8 (-4.5 – 2.9)	3.9 (-0.5 – 8.2)	0.221
Social function	-0.7 (-3.2 – 1.8)	5.0 (-0.3 – 10.3)	0.055	-5.0 (-9.2 – -0.8)	2.4 (-4.2 – 8.9)	0.086
Role emotional	-0.9 (-5.4 – 3.6)	7.3 (1.4 – 13.1)	0.006	-3.9 (-8.8 – 1)	5.6 (-1.5 – 12.7)	0.014
Mental health	1.9 (-1.1 – 5)	6.1 (3.5 – 8.8)	0.019	-1.0 (-3.9 – 1.9)	4.1 (0.01 – 8.1)	0.043

* Values given as mean difference (95% CI) between baseline and 8 weeks, and baseline and 6 months after the program. A positive score indicates improvement except for MRC grade. MRC = Medical Research Council; TDI = transition dyspnea index; HF = handgrip force; QF = maximal quadriceps force; 6MWD = 6-minute walk distance; ADL = activities of daily living; SF-36 = 36-item short-form survey.

Table 4. Pulmonary function data of the subjects who completed program at baseline and at 6 months following pulmonary rehabilitation*

Variables	IPF group			COPD group		
	Baseline (n=36)	6 months (n=30)	p Value	Baseline (n=40)	6 months (n=37)	p Value
FEV ₁ , L	1.7 ± 0.5	1.6 ± 0.5	0.0001	1.1 ± 0.5	1.1 ± 0.5	0.265
FVC, L	2.0 ± 0.6	1.9 ± 0.7	0.0001	2.5 ± 0.7	2.4 ± 0.7	0.103
FRC, L	1.7 ± 0.5	1.6 ± 0.5	0.0001	4.2 ± 1.0	4.3 ± 1.0	0.006
TLC, L	3.0 ± 0.8	2.9 ± 0.9	0.0001	5.6 ± 1.0	5.7 ± 1.1	0.001
D _{LCO} , mL/min/mmHg	6.2 ± 2.3	5.2 ± 2.6	0.0001	12.5 ± 5.9	12.3 ± 5.6	0.001

*Values are mean ± SD. D_{LCO} = diffusing capacity of the lung for carbon monoxide; FEV₁ = forced expiratory volume in one second; FRC = functional residual capacity; FVC = forced vital capacity; %pred = percent predicted; TLC = total lung capacity.