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Pulmonary rehabilitation improves distance-saturation product in IPF: Greater benefits in patients with exercise-induced desaturation

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Abstract. *Background and aim:* Exercise-induced dyspnea and desaturation are hallmark features of idiopathic pulmonary fibrosis (IPF) and are linked to disease severity and poor outcomes. The distance-saturation product (DSP), calculated by multiplying the walking distance by oxygen saturation, has been proposed as a mortality predictor. This study aimed to investigate the effects of a pulmonary rehabilitation (PR) program on clinical outcomes and DSP in two IPF patient groups: those with and without desaturation during the six-minute walk test (6MWT). *Methods:* IPF patients who completed a standardized PR program were included. Assessments before and after PR included spirometry, arterial blood gas analysis, Medical Research Council (MRC) dyspnea scale, 6MWT, St. George's Respiratory Questionnaire (SGRQ), 36-Item Short Form Survey (SF-36), and Hospital Anxiety and Depression Scale (HADS). DSP was calculated at the end of the 6MWT. Patients with oxygen saturation ≤88% during baseline 6MWT were assigned to the desaturated group; others were assigned to the non-desaturated group. *Results:* Fifty patients were enrolled (20 desaturated, 30 non-desaturated). Following PR, only the desaturated group showed significant improvements in forced vital capacity (FVC), oxygen saturation, and SF-36 domains. In both groups, PaO_2, 6MWT distance, and DSP increased significantly, while MRC, SGRQ, and HADS scores decreased. However, the gains in 6MWT distance and DSP were significantly greater in the desaturated group. *Conclusion:* PR improved functional, psychological, and quality-of-life outcomes in both groups, with more pronounced benefits in desaturated patients. Referral to PR is especially recommended for this subgroup.

Key words: idiopathic pulmonary fibrosis, pulmonary rehabilitation, desaturation, saturation-distance product

Introduction

Idiopathic pulmonary fibrosis (IPF) is a difficult-to-treat disease with poor prognosis characterized by chronic, irreversible progression of fibrosis (1,2). Untreated patients have a median survival of 3-5 years from diagnosis with a progressive decline in respiratory and physical function (3). The normal course of IPF includes dry cough, exertional dyspnea, exercise intolerance, decreased physical activity, and deterioration in quality of life (2,4). It is aggressive in most patients, with a steady decline in lung function and highly fatal exacerbations (4). In many lung diseases, dynamic assessments of exercise performance reflect survival with greater accuracy than static measures of lung function (5). Decreased six-minute walking distance (6MWD) and oxygen desaturation measured during the six minute walk test (6MWT) are predictors of mortality (6). With the 6MWT, indices that integrate both the

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distance walked and oxygen desaturation, such as the distance–saturation product (DSP) and the ΔSpO_2/distance ratio, have been proposed to provide prognostic information. The DSP has been suggested to independently predict disease severity in COPD (7) and mortality in IPF with greater accuracy (5). Patients with IPF need multifaceted and long-term recovery, but an optimal treatment modality to meet these needs is unknown (2). Lung transplantation is the only intervention that has been reliably shown to improve outcomes, but this is only possible for a limited number of eligible patients (5). Although pharmacologic treatments slow the decline in lung function and improve survival in patients with IPF, their effects on symptom burden and quality of life are moderate (3,6,8). Improving dyspnea, exercise capacity, and daily physical activity are important goals in IPF management as they are associated with health-related quality of life and longevity (8). Pulmonary rehabilitation (PR), a multidisciplinary, personalized exercise and training program initially developed and validated for patients with chronic obstructive pulmonary disease (COPD), improves exercise capacity, dyspnea, and quality of life in patients with IPF. Moreover, it has been increasingly recognized as a valuable component in the overall management of IPF (3). Based on evidence from COPD populations, patients with more severe disease characterized by greater physiological impairment, reduced exercise capacity, and poorer health status, tend to achieve larger functional gains following PR (9-11). In the context of IPF, exercise-induced desaturation is a marker of advanced disease severity often associated with lower FVC and shorter walking distance (6, 12). Therefore, we hypothesized that desaturators may demonstrate greater improvements after PR compared to non-desaturators. Although numerous studies have examined the effects of PR in patients with IPF, none have specifically evaluated its impact on the distance–saturation product. Notably, no prior studies have compared the effects of PR between IPF patients who experience desaturation during exercise and those who do not. This study addresses this gap by investigating the effects of a structured PR program on the distance–saturation product and other health outcomes in two distinct IPF subgroups: those with and without oxygen desaturation during the 6MWT.

Methods

Study design and participants

This retrospective cohort study was conducted between January 2013 and October 2019 at Dr. Suat Seren Chest Diseases and Surgery Training and Research Hospital and was approved by the institutional ethics committee (Approval number:2025/05-07). Patients diagnosed with IPF by the hospital's interstitial lung disease council, initiated on antifibrotic therapy, and who successfully completed the PR program were included in the analysis. According to the hospital's standard outpatient PR program protocol, symptomatic IPF patients with reduced daily functioning and frequent hospital admissions were referred to the program. Patients who were deemed unfit for participation based on cardiology consultation, those with psychiatric disorders, severe joint diseases, or unwillingness to participate were not enrolled in the PR program. Furthermore, for the purposes of this retrospective study, patients who voluntarily discontinued the program, were hospitalized due to acute exacerbation, developed new medical conditions requiring withdrawal, or discontinued participation due to financial or transportation issues were excluded from the final analysis.

Assessments

Physical and demographic data, disease duration, smoking history, number of emergency admissions, and hospitalizations in the last year were recorded. Respiratory and cardiac system examinations and pulmonary function tests were performed in all cases. Lung radiograms and arterial blood gases were evaluated.

- **Respiratory functions:** Body plethysmograph (Zan 500, Germany) and carbon monoxide diffusion capacity (TLCO) (Zan 300, Germany) were measured.
- **Dyspnea assessment:** Modified Medical Research Council (mMRC) dyspnea scale, consisting of five items, was used to determine the severity of dyspnea. In 5-scoring, '0' indicates the best level and '5' indicates the worst level (13). Modified Borg Scale with a scoring system from 0 to 10 was used to evaluate dyspnea during the effort and walking test. '0'

indicates that there is no dyspnea, and '10' indicates that dyspnea is very severe (14).

Exercise capacity: A 6MWT measuring the distance walked at the patients' own stride rate was conducted. Heart rate and oxygen saturation were recorded before and after the test. Patients walked on a flat surface with encouraging words for each minute. Oxygen saturation was continuously measured by pulse oximetry during the test (15). Patients unable to maintain a resting SpO_2≥ 88% on room air were excluded from the study. Patients able to maintain a resting, room air SpO_2≥ 88% were instructed to walk at his/her own pace for a maximum of 6 minute. In patients whose oxygen saturation fell below 80 %, the test was terminated, and the test was repeated with supplemental oxygen. Total distance walked during the 6MWT was measured. DSP was defined as the product of the last walking distance in meters and the nadir room-air SpO_2 value recorded before initiation of supplemental oxygen (5).

Psychological symptoms: Hospital Anxiety and Depression (HAD) scale, consisting of 14 questions, was used to determine the psychological status of the patients. Anxiety and depression score of 0-7 indicates normal, 8-11 indicates borderline, and>11 indicates anxiety or depression (16).

Quality of life: The St. George Respiratory Questionnaire was used to determine disease-specific quality of life. Higher scores indicate worsening of the disease and an increase in symptoms. A change of four units for the total score and each subsection was considered significant (17). The 36- Item Short Form Survey, which assesses eight major health domains, was used to measure overall quality of life. An increase in scores was evaluated as an increase in quality of life (18).

PR program

All patients included in this retrospective study had previously completed a standardized outpatient PR and physiotherapy program at our institution prior to data collection. The program consisted of supervised sessions lasting approximately two hours, conducted twice weekly over a period of eight weeks. The exercise regimen included breathing exercises, relaxation and stretching exercises, peripheral muscle strengthening, and endurance training. Respiratory physiotherapy comprised pursed-lip breathing, diaphragmatic breathing, and thoracic expansion exercises. In addition, patients were instructed in bronchial hygiene techniques and dyspnea-relieving positions. Endurance training was performed for a total of 30 minutes per session. The endurance training component consisted of either treadmill walking or stationary cycling. The initial walking speed was set at 80% of the peak speed (km/h) achieved during the 6MWT. For stationary cycling, the starting workload was established at 70% of the maximum work rate, estimated from the 6MWT. Exercise intensity was progressively adjusted based on dyspnea severity (rated 4–6 on the Modified Borg Scale). The strength training program comprised upper and lower extremity exercises, including shoulder flexion/abduction, elbow flexion/extension, hip flexion/extension/abduction, and knee flexion/extension, performed with free weights. Resistance was adjusted according to individual patient tolerance, aiming for a perceived fatigue level of 4–6 on the Modified Borg Scale. Training began with 8 repetitions, progressing to 10. When the patient could perform 1–2 additional repetitions beyond the target, the load was increased by 2–10%. Rest intervals were set at 2 minutes between sets and 1 day between sessions. Patients with significant dyspnea or exercise-induced desaturation underwent intermittent exercise sessions with supplemental oxygen. All participants were also instructed on how to continue the exercises at home (19, 20). At the end of the eight-week program, patients were reassessed using all relevant parameters. For the purposes of this study, patients whose oxygen saturation dropped below 88% during the 6MWT were categorized into the desaturated group, while those who maintained saturation above this threshold were classified as non-desaturated (1). All outcome measures were compared between these two groups.

Statistical analysis

Statistical analyses were conducted using SPSS version 22.0 (IBM, Armonk, NY, USA). The Shapiro–Wilk test was applied to assess the normality of the data distribution. Descriptive statistics are presented as mean (standard deviation), median (interquartile range), or percentage, as appropriate. Changes (Δ) from baseline to post-intervention were calculated for all variables. Between-group comparisons of baseline characteristics and Δ values were performed using the Mann–Whitney U test, while categorical variables were analyzed with the Chi-square test. Within-group pre- and post-treatment differences were assessed using the Wilcoxon signed-rank test. A two-tailed p-value of < .05 was considered statistically significant.

Results

A total of 50 patients were included in the study: 20 in the desaturated group and 30 in the non-desaturated group. The two groups were comparable in terms of age, body mass index, comorbidities, number of emergency admissions, and hospitalizations (p>0.05). Cigarette consumption was significantly higher in the desaturated group (p=0.002). Among the participants, 39 were male and 11 were female; the proportion of male patients was significantly higher in the desaturated group (p=0.033) (Table 1). Regarding pulmonary function, forced vital capacity (FVC) and TLCO values were significantly lower in the desaturated group (p=0.042 and p=0.022, respectively). Partial arterial oxygen pressure (PaO_2) was also significantly lower in this group (p=0.001), whereas partial arterial carbondioxide pressure ($PaCO_2$) and resting oxygen saturation were similar between groups (p>0.05). The 6MWD and DSP were both significantly reduced in the desaturated group (p<0.001 for both). Additionally, changes in oxygen saturation and dyspnea before and after the walking test were significantly greater in the desaturated group (p<0.001 and p=0.009, respectively). In terms of health-related quality of life, no significant differences were found between the two groups across the SGRQ parameters. However, within the SF-36, the physical role functioning score was significantly lower in the desaturated group (p=0.015), while the remaining domains showed no significant differences. Anxiety and depression scores were comparable in both groups. The MRC dyspnea scale score was significantly higher in the desaturated group (p=0.03) (Table 2). Following the PR program, FVC showed a significant increase in the desaturated group (p=0.046), with no significant changes observed in other pulmonary function measures in either group. PaO_2 improved significantly in both groups (p=0.047 and p=0.021, respectively), while oxygen saturation increased significantly only in the desaturated group (p = 0.049). $PaCO_2$ remained unchanged. Both groups demonstrated significant improvements in 6MWD and DSP after PR (p<0.001 for both), with a greater increase observed in the desaturated group (p=0.002 and p=0.001, respectively). The difference in oxygen saturation pre- and post-walk test did not change significantly, whereas dyspnea difference improved significantly in both groups (p=0.017 and p=0.047, respectively) (Table 3). Significant improvements were observed in all SGRQ parameters in both groups following the intervention (p<0.05). Within the SF-36, social functioning, physical role functioning, pain, and vitality scores improved significantly in the desaturated group (p=0.019, p=0.002, p=0.008, and p=0.038, respectively), with no significant changes in other domains for either group. Anxiety and depression scores significantly decreased in both groups (desaturated: p=0.002 and p=0.008; non-desaturated: p<0.001 and p=0.015, respectively). Additionally, MRC dyspnea scores improved significantly in both groups (p<0.001) (Table 3).

Discussion

This study examined the effects of PR in patients with IPF, stratified by the presence or absence of exercise-induced desaturation. Overall, both groups showed significant improvements in functional capacity, dyspnea severity, psychological well-being, and quality of life following PR. Notably, patients in the desaturated group appeared to have greater gains in walking distance and distance–saturation product, as well as unique improvements in FVC, oxygen saturation, and several SF-36 domains. These findings suggest that patients with desaturation, despite having more impaired baseline function, may derive greater benefit from comprehensive PR programs. In line with previous studies, the predominance of male patients in our cohort was consistent with the literature (21). Consistent with Suadyna et al., who reported a negative correlation between smoking amount and oxygen saturation (22), our desaturated group appeared to have significantly higher cigarette consumption. Additionally, significantly lower FVC and TLCO values observed in the desaturated group are in agreement with findings that highlight the

Table 1. Socio-demographic and clinical characteristics of the groups

Variable	All patients (n=50)	Desaturated Patients (n=20)	Non-Desaturated Patients (n=30)	p
Age (year)	62.94 ± 8.78	65.20 ± 7.33	61.43 ± 9.44	0.139
Body mass index (kg/m^2)	27.04 ± 3.74	26.35 ± 3.97	27.52 ± 3.57	0.239
Smoking Consumption (p*years)	23 (5/32)	30 (20/60)	15(4/28)	**0.002**
Emergency admission (n/last year)	0(0/1)	0(0/1)	0(0/0)	0.344
Hospitalization (n/last year)	0(0/0)	0(0/0)	0(0/1)	0.315
	n(%)			
Gender Male Female	 39 (78.0) 11 (22.0)	 19 (95.0) 1(5.0)	 20(66.7) 10(33.3)	 **0.033**
Comorbidity Available None	32 (64.0) 18 (36.0)	12 (60) 8 (40)	20 (66.7) 10 (33.3)	0.765
Comorbidity Hypertension Coronary artery disease Type 2 diabetes Goiter	 13 (26.0) 11 (22.0) 12 (24.0) 2 (4.0)	 5 (25.0) 4 (20.0) 5 (25.0) -	 8 (26.6) 7 (23.3) 7 (23.3) 2 (6.6)	 0.895 0.780 0.892 -

Data are presented as mean ± standard deviation, median (interquartile range 25/75) or n(%). Bold indicates significant values. p: Independent Sample t Test, Mann Whitney-U Test or Chi Square Test.

Table 2. Comparison of pre-PR values of the groups

Variable	Desaturated Patients	Non-Desaturated Patients	p
FEV1 (%)	72.3 ± 14.9	77.7 ± 17.4	0.260
FVC (%)	63.1 ± 15.3	72.8 ± 16.2	**0.042**
FEV/FVC	90.2 ± 4.68	88.5 ± 10.5	0.512
TLCO (%)	34.4 ± 14.7	46.3 ± 16.7	**0.022**
PaO_2 (mmHg)	67.0 ± 10.6	79.6 ± 12.2	**0.001**
$PaCO_2$ (mmHg)	37.4 ± 5.6	38.4 ± 2.8	0.423
$SatO_2$ (%)	88.5 ± 20.1	87.7 ± 24.9	0.912
6-MWT (meter)	318.7 ± 100.9	405.3 ± 78.2	**<0.001**
Distance/Saturation	265.7 ± 86.4	378.9 ± 76.1	**<0.001**
ΔSpO_2 (%)	9.3 ± 4.4	3.0 ± 1.9	**<0.001**
ΔDyspnea (MB)	2.5 ± 1.43	1.42 ± 1.2	**0.009**
SGRQ Symptom	50.7 ± 19.1	44.3 ± 22.7	0.319
SGRQ Activity	64.1 ± 15.9	56.1 ± 22.1	0.187
SGRQ Impact	39.4 ± 19.2	37.1 ± 20.8	0.690
SGRQ Total	49.8 ± 15.6	44.1 ± 19.1	0.274
SF36 Physical Function	47.4 ± 25.1	57.6 ± 30.5	0.242
SF36 Social Function	62.8 ± 28.1	67.4 ± 29.2	0.597
SF36 Physical Role	22.6 ± 20.9	53.1 ± 45.1	**0.015**

Table 2 (*Continued*)

Variable	Desaturated Patients	Non-Desaturated Patients	p
SF36 Emotional Role	45.8 ± 41.6	47.7 ± 45.1	0.885
SF36 General Health	43.7 ± 20.1	41.6 ± 25.4	0.767
SF36 Mental	63.7 ± 22.1	62.0 ± 23.1	0.801
SF36 Pain	61.2 ± 31.3	60.1 ± 23.1	0.902
SF36 Vitality	52.4 ± 19.1	51.1 ± 25.8	0.853
HAD Anxiety	6.3 ± 3.2	7.10 ± 4.2	0.467
HAD Depression	5.8 ± 3.2	6.5 ± 5.2	0.629
mMRC	3.3 ± 1.2	2.5 ± 1.2	**0.030**

Data are presented as mean ± standard deviation, Bold indicates significant values.
p: Independent Sample t Test. Δ: Difference before and after the 6-MWT, FEV_1: Forced expiratory volume in the first second. *Abbreviations:* FVC: Forced vital capacity, TLCO: Carbon monoxide diffusion capacity, PaO_2: Partial arterial oxygen pressure, $PaCO_2$: Partial arterial carbon dioxide pressure, $SatO_2$: Oxygen saturation, 6-MWT: Six minute walk test, SGRQ: St. George Respiratory Questionnaire, SF-36: 36 Item Short Form Survey, HAD: Hospital Anxiety and Depression Scale, mMRC: Modified Medical Research Dyspnea Scale, MB: Modified Borg Scale.

prognostic significance of exercise-induced desaturation in IPF patients (15). IPF is characterized by progressive pulmonary restriction, ventilatory failure, impaired gas exchange, and hypoxemia, which collectively contribute to reduced exercise capacity (23). Echoing previous research demonstrating correlations between walking distance and oxygen saturation in dyspneic patients (24), we observed that patients with desaturation had shorter 6MWD, lower distance–saturation products, and greater dyspnea severity. While physical role functioning as measured by the SF-36 was poorer in the desaturated group, other quality of life parameters did not differ significantly between groups. Notably, the literature lacks studies directly examining the relationship between oxygen desaturation and quality of life in this patient population. Recent studies have demonstrated that PR is a safe and effective intervention to improve exercise capacity, dyspnea, and quality of life in patients with IPF (23). Our findings, which showed a significant increase in FVC after PR but no notable changes in other pulmonary function parameters, are consistent with previous reports (25–27). The observed increase in FVC following PR in the desaturated group may be physiologically plausible. Improvements in ventilatory muscle strength, thoracic mobility, and breathing efficiency resulting from structured exercise and respiratory physiotherapy could contribute to enhanced lung volumes (19, 28). Additionally, PR may reduce dynamic hyperinflation and improve inspiratory capacity through better coordination of breathing patterns (25). Although IPF is characterized by irreversible fibrosis, short-term gains in FVC might reflect optimization of pulmonary mechanics and increased patient effort during testing rather than true structural change. Similar short-term improvements in lung volumes after PR have been reported in previous studies involving patients with interstitial lung disease, highlighting the reproducibility of these effects across different patient cohorts (29, 30). Several studies have documented significant improvements in six-minute walk distance and PaO_2 following PR in IPF patients (2, 25–27, 31). In our study, both desaturated and non-desaturated groups showed comparable significant gains in 6MWD and PaO_2, reinforcing that these improvements are not unique to our cohort but are consistent with findings from other clinical settings. Similarly, in our study, both desaturated and non-desaturated groups showed significant gains in 6MWD and PaO_2 values. A longitudinal study investigating a 12-week outpatient PR program followed by 40 weeks of home-based rehabilitation in patients treated with nintedanib found that the PR group experienced a smaller decline in walking distance and greater endurance at week 52 compared to controls (2). Although some studies suggest that the response to PR may be attenuated in IPF patients compared to those with COPD—due to the rapid disease progression and higher incidence of exercise-induced desaturation (32, 33)—other research reports comparable improvements in dyspnea, walking distance, and quality of life between IPF and COPD populations after PR (3). These consistent findings across different studies support the generalizability of our results to other IPF populations undergoing similar rehabilitation protocols.

Contrary to findings proposing that PR is most effective in early disease stages (31), our

Table 3. Comparison of Pre-PR and Post-PR Values of Groups

Variable (n=50)	Desaturated Patients (n=20)			Non-Desaturated Patients (n=30)			p^b
	Before	After	p^a	Before	After	p^a	
FEV1 (%)	72.3 ± 14.9	73.7 ± 15.3	0.290	77.7 ± 17.4	78.4 ± 18.1	0.533	0.677
FVC (%)	63.1 ± 15.3	65.5 ± 14.4	**0.046**	72.8 ± 16.2	73.4 ± 17.1	0.551	0.267
FEV/FVC	90.2 ± 4.68	91.1 ± 11.1	0.725	88.5 ± 10.5	90.3 ± 1.9	0.479	0.804
TLCO (%)	34.4 ± 14.7	35.5 ± 15.8	0.400	46.3 ± 16.7	47.8 ± 18.1	0.352	0.824
PaO2 (mmHg)	67.0 ± 10.6	70.3 ± 10.6	**0.047**	79.6 ± 12.2	83.2 ± 11.3	**0.021**	0.960
PaCO2 (mmHg)	37.4 ± 5.6	37.8 ± 4.3	0.209	38.4 ± 2.8	38.7 ± 3.99	0.771	0.334
SatO2 (%)	88.5 ± 20.1	94.2 ± 4.3	0.266	87.7 ± 24.9	92.1 ± 18.5	0.256	0.852
6 DYM (meter)	318.7 ± 100.9	394.0 ± 79.7	**<0.001**	405.3 ± 78.2	446.6 ± 80.1	**<0.001**	**0.002**
Distance/Sat	265.7 ± 86.4	338.0 ±74.3	**<0.001**	378.9 ± 76.1	416.3 ± 72.1	**<0.001**	**0.001**
ΔSpO2	9.3 ± 4.4	9.7 ± 5.9	0.669	3.0 ± 1.9	3.33 ± 2.23	0.491	0.944
ΔDyspnea (MB)	2.5 ± 1.43	1.68 ±1.1	**0.017**	1.42 ± 1.2	0.95 ±1.12	**0.047**	0.346
SGRQ Symptom	50.7 ± 19.1	37.1 ± 15.1	**<0.001**	44.3 ± 22.7	33.9 ± 21.4	**0.001**	0.427
SGRQ Activity	64.1 ± 15.9	57.4 ± 14.9	**0.049**	56.1 ± 22.1	43.1 ± 25.1	**<0.001**	0.158
SGRQ Impact	39.4 ± 19.2	27.3 ± 13.5	**0.007**	37.1 ± 20.8	28.1 ± 17.1	**0.007**	0.519
SGRQTotal	49.8 ± 15.6	38.1 ± 12.6	**<0.001**	44.1 ± 19.1	33.7 ± 17.5	**<0.001**	0.686
SF36 Physical Function	47.4 ± 25.1	55.1 ± 22.9	0.129	57.6 ± 30.5	62.2 ± 22.9	0.062	0.532
SF36 Social Function	62.8 ± 28.1	75.3 ± 29.5	**0.019**	67.4 ± 29.2	69.1 ± 25.5	0.761	0.166
SF36 Physical Role	22.6 ± 20.9	55.5 ± 37.3	**0.002**	53.1 ± 45.1	58.1 ± 44.2	0.589	0.036
SF36 Emotional Role	45.8 ± 41.6	61.6 ± 36.8	0.082	47.7 ± 45.1	54.1 ± 40.8	0.451	0.438
SF36 General Health	43.7 ± 20.1	50.3 ± 20.1	0.194	41.6 ± 25.4	46.5 ± 23.1	0.108	0.740
SF36 Mental	63.7 ± 22.1	65.8 ± 23.1	0.467	62.0 ± 23.1	65.1 ± 22.6	0.310	0.809
SF36 Pain	61.2 ± 31.3	76.9 ± 25.4	**0.008**	60.1 ± 23.1	69.9 ± 25.7	0.061	0.425
SF36 Vitality	52.4 ± 19.1	59.6 ± 20.7	**0.038**	51.1 ± 25.8	55.1 ± 24.8	0.180	0.449
HAD Anxiety	6.3 ± 3.2	4.4 ± 3.4	**0.002**	7.10 ± 4.2	4.6 ± 3.7	**<0.001**	0.396
HAD Depression	5.8 ± 3.2	4.2 ± 3.1	**0.008**	6.5 ± 5.2	5.1 ± 4.5	**0.015**	0.800
MRC	3.3 ± 1.2	2.5 ± 0.9	**<0.001**	2.5 ± 1.2	1.57 ± 1.1	**<0.001**	0.259

Data are presented as mean ± standard deviation, Bold indicates significant values.
p^a: Paired Sample t Test. p^b: Mann Whitney-U Test. Δ: Difference before and after the 6-MWT, *Abbreviations:* FEV1: Forced expiratory volume in the first second. FVC: Forced vital capacity, TLCO: Carbon monoxide diffusion capacity, PaO2: Partial arterial oxygen pressure, PaCO2: Partial arterial carbon dioxide pressure, SatO2: Oxygen saturation, 6-MWT: Six minute walk test, SGRQ: St. George Respiratory Questionnaire, SF-36: 36 Item Short Form Survey. HAD: Hospital Anxiety and Depression Scale, mMRC: Modified Medical Research Dyspnea Scale, MB: Modified Borg Scale.

results suggest that oxygen saturation and FVC improved significantly only in the desaturated group, which also appeared to show greater increases in walking distance. This is in line with studies in COPD patients where those with more severe disease (lower FEV1%, reduced exercise capacity, poorer health status, and GOLD stage 3–4) tended to exhibit larger gains in exercise capacity following PR (9, 10). In IPF, exercise-induced desaturation is a marker of advanced disease severity, often reflecting reduced pulmonary reserve and lower baseline exercise capacity, which may provide a larger potential margin for measurable improvement (6,12). Although no previous studies have specifically evaluated the effects of PR on the DSP in IPF patients, our study found a significant increase in DSP in both desaturated and non-desaturated groups. Notably, the desaturated group appeared to have a greater improvement in both walking distance and DSP. Previous research has shown that IPF patients who respond positively to PR tend to have higher survival rates compared to those who do not respond or fail to complete the program (3). Furthermore, a study reporting higher survival rates in IPF patients with elevated DSP values (5) suggests that the observed increase in DSP following PR may potentially contribute to improved mortality outcomes. In addition to DSP, other composite indices such as the ΔSpO_2/distance ratio currently demonstrated in COPD populations (7) might also hold potential as complementary outcome measures in IPF. Future studies are warranted to investigate its prognostic and clinical utility in this patient group. A strength of our study is its comprehensive and novel approach in evaluating the effects of PR in IPF patients. By specifically comparing desaturated and non-desaturated patients, we provide insights into how exercise-induced desaturation may influence rehabilitation outcomes. Additionally, the use of the DSP adds a clinically relevant, integrative parameter that has been scarcely studied in IPF. Inclusion of patients receiving antifibrotic therapy enhances the real-world applicability of our findings, and the assessment of multiple outcomes including FVC, walking distance, DSP, oxygen saturation, dyspnea, quality of life, and psychological symptoms offers a holistic evaluation of PR benefits. However, the study has several limitations. First, it was conducted at a single center and retrospectively, which may limit generalizability. Second, analyses included only patients who completed the PR program, potentially introducing selection bias, as patients who discontinued may have had lower motivation or greater disease severity. Third, DSP calculations used the nadir SpO_2 measured before the initiation of supplemental oxygen, which might not fully capture exercise-induced desaturation in patients requiring oxygen during the 6MWT. Finally, long-term outcomes and exercise endurance beyond the program were not assessed, representing an avenue for future research. Following completion of the PR program, both desaturated and non-desaturated groups showed improvements in oxygenation, walking distance, DSP, dyspnea perception, quality of life, and psychological symptoms. Notably, FVC and oxygen saturation increased significantly only in the desaturated group. Moreover, the desaturated group appeared to have greater gains in walking distance and DSP, suggesting that IPF patients who experience exercise-induced desaturation may derive substantial benefits from PR.

Conclusion

Based on these findings, desaturation during the 6MWT may be considered as a priority criterion for PR referral in this patient population. Given the persistent under-utilization of PR in IPF, expanding access through innovative models—such as home-based or tele-rehabilitation programmes—could help bridge this gap and ensure that patients most likely to benefit receive timely intervention. These results suggest the importance of targeted referral strategies and warrant further investigation in larger, prospective studies.

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