Pulmonary rehabilitation in hypersensitivity pneumonitis: A retrospective case series

Nazire Nur Yıldız[1], Beyza Nur Öymez[2], Nilgün Yılmaz Demirci[3], Meral Boşnak Güçlü[4]

ORCID:
Nazire Nur Yıldız: 0000-0001-5838-4869
Beyza Nur Öymez: 0000-0002-7836-9014
Nilgün Yılmaz Demirci: 0000-0001-6160-3778
Meral Boşnak Güçlü: 0000-0002-3861-9912

[1]Department of Cardiopulmonary Physiotherapy, Niğde Ömer Halisdemir University Faculty of Bor Health Sciences, Niğde, Türkiye, [2]Department of Physiotherapy and Rehabilitation, Gazi University Institute of Health Sciences, Ankara, Türkiye, [3]Department of Pulmonology, Gazi University Faculty of Medicine, Ankara, Türkiye, [4]Department of Cardiopulmonary Physiotherapy and Rehabilitation, Gazi University Faculty of Health Sciences, Ankara, Türkiye

Address for correspondence:
P.T., Ph.D. Nazire Nur Yıldız, Department of Cardiopulmonary Physiotherapy, Niğde Ömer Halisdemir University Faculty of Bor Health Sciences, Niğde, Türkiye.
E-mail: nazirenuryildiz@ohu.edu.tr

Abstract:

Hypersensitivity pneumonitis is a rare disease that affects the pulmonary, cardiovascular, and musculoskeletal systems. Severe desaturation and hypoxemia reduce exercise capacity and exacerbate symptoms. Rehabilitation is essential for these patients to prevent symptom progression and manage the adverse effects of hypoxemia. This study aimed to present the pre- and post-rehabilitation outcomes of three patients with hypersensitivity pneumonitis who completed individualized rehabilitation programs in our unit. The programs included aerobic exercise training, inspiratory muscle training, resistance exercises, and neuromuscular electrical stimulation, delivered two-three times per week over six-eight weeks. Functional exercise capacity was assessed using the six-minute walk test; upper-extremity functional capacity with the six-minute pegboard and ring test; respiratory muscle strength with a mouth pressure device; peripheral muscle strength with a hand-held dynamometer; dyspnea using the Modified Medical Research Council scale; and physical activity level with a metabolic holter and the International Physical Activity Questionnaire – Short Form. Forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC) values increased in two cases. FEV_1/FVC improved in one case and remained unchanged in another. Forced expiratory flow at 25% to 75% of the pulmonary volume ($FEF_{25-75\%}$) and diffusing capacity of the lung for carbon monoxide (DLCO) increased in one case and decreased in another, while peak expiratory flow (PEF) increased in both. Respiratory muscle strength significantly improved in all cases. Inspiratory muscle endurance improved in two cases. Upper- and lower-extremity exercise capacity and peripheral muscle strength increased in all cases. Dyspnea and physical activity levels also improved across the board. This study indicates that a well-structured, individualized pulmonary rehabilitation (PR) program, tailored to the patient's needs, can improve dyspnea, physical activity, muscle strength, and pulmonary function in individuals with hypersensitivity pneumonitis.

Keywords:
Exercise, hypersensitivity pneumonitis, rare diseases, pulmonary rehabilitation

Introduction

Hypersensitivity pneumonitis (HP) is a rare pulmonary disease caused by an abnormal immune response to inhaled environmental triggers. Diagnosing HP is challenging and requires a detailed medical history, high-resolution computed tomography (HRCT), and a combination of diagnostic tests, as no single method can definitively confirm the disease.[1] The prognosis depends on both the type and level of exposure, and the disease is typically classified as acute, subacute, or chronic.[2]

Common symptoms include dyspnea, cough, and fatigue.[1] HP negatively affects exercise capacity, muscle strength, pulmonary function, diffusing capacity of the lung for carbon monoxide (DLCO), and oxygen saturation (SpO_2). These impairments are often debilitating, making early intervention essential.[3]

Although no studies have specifically focused on pulmonary rehabilitation (PR) in HP, some evidence supports its use in broader interstitial lung diseases (ILD).[4] This study presents outcomes from three HP cases who underwent individualized PR programs.

Case Reports

This retrospective study includes patients referred to our unit for outpatient rehabilitation. Informed consent was obtained from each participant. Table 1 summarizes the components of the PR programs provided to each case.

Case I

A 49-year-old female (Body Mass Index [BMI]: 30.9 kg/m²) diagnosed with fibrotic HP five years ago had a history of working in a bread factory and owning a budgerigar. She quit smoking following her diagnosis and was treated with cortisone for one year. Her symptoms worsened three years ago, requiring another 10-month course of cortisone. Two years ago, she was hospitalized for 11 days due to an exacerbation and began long-term oxygen therapy (LTOT). She reported dyspnea, fatigue, and chronic cough. No exacerbations occurred in the past year.

Pulmonary rehabilitation for case I

The patient underwent 30–40 minutes of moderate-intensity interval training (MIIT) on both an arm ergometer and treadmill with oxygen support. Each session included a five-minute warm-up, three-minute high-intensity intervals (60%–80% heart rate reserve, 150–160 bpm), four-minute low-intensity intervals (50%–60% heart rate reserve, 145–150 bpm), and a five-minute cool-down. This program was conducted three days per week for eight weeks. During the first two weeks, the workload was fixed, then increased by 5 watts per week based on patient tolerance. She was also prescribed a home inspiratory muscle training (IMT) program using a PowerBreathe Wellness® device. Strength training was set at 50% of her maximum inspiratory pressure (MIP) (48.5 cmH_2O), with sessions consisting of 10 breaths per cycle, lasting 15 minutes in total. Endurance training was set at 30% of MIP (29.1 cmH_2O), with sessions lasting 15 minutes (15 breaths per cycle). Both training types were performed once daily, seven days a week, for eight weeks.

The patient performed lower-extremity exercises using free weights and upper-extremity exercises with elastic bands, completing 10 repetitions for two sets, three days per week. Bilateral knee extensions began at 3.5 kg and were gradually increased to approximately 7 kg (50% of maximum strength).

Russian current at 40–50 mA was applied to the patient's bilateral quadriceps femoris (QF) muscles for 20 minutes, three days per week. The intensity was adjusted to the patient's maximum tolerance to elicit visible muscle contractions.

Additionally, posture exercises, including scapular adduction, bilateral shoulder elevation, and shoulder external rotation, were performed three days a week, in two sets of 15 repetitions.

Case II

A 60-year-old male (BMI: 33.03 kg/m²) with a 24-pack-year smoking history, which he ceased five years ago, presented to a pulmonologist with complaints of cough, dyspnea, and fatigue. Fibrotic HP was diagnosed via lung biopsy, five years after his initial diagnosis of ILD. He had been treated with corticosteroids for over three years and had lived for five-six years in a home with a pigeon loft on the balcony. He began LTOT two years ago.

Pulmonary rehabilitation for case II

The patient completed 40–50 minutes of high-intensity interval station-based aerobic exercise in three-minute intervals, including 20–25 minutes on an arm ergometer and

Table 1: Summary of pulmonary rehabilitation program components

PR component	Case I	Case II	Case III
AET			
Type	MIIT	HIIT, station-based AET	UE-MIIT
Ergometer	Treadmill + arm ergometer	Arm ergometer and treadmill	Arm ergometer
Duration	30–40 min	40–50 min	20–40 min
Intensity	TP workload:	TP workload:	TP workload:
	60%–80% HRR, 150–160 bpm	80%–95% HRmax, 128–152 bpm	60%–80% HRmax*
	ARP workload:	ARP workload:	ARP workload:
	50%–60% reserve, 145–150 bpm	60%–80% HRmax, 96–128 bpm	40%–60% HRmax*
Frequency	3 days/week, 8 weeks	2 days/week, 8 weeks	2 days/week, 6 weeks
Load adjustment	Fixed for first 2 weeks, then +5 W/week (based on tolerance)	+5–10 W/week	Fixed for first 2 weeks, then +5 W/week
O_2 support	O_2 via nasal cannula	O_2 via nasal cannula	O_2 via nasal cannula (week 1), CPAP (from week 2)
IMT			
Device & type	PowerBreathe Wellness® Strength and endurance	PowerBreathe Wellness® Endurance	PowerBreathe Wellness® Strength
Intensity	50% MIP (48.5 cmH$_2$O) 30% MIP (29.1 cmH$_2$O)	30% MIP (35.7 cmH$_2$O)	30%–50% MIP (27.3–45.5 cmH$_2$O)
Duration	15 min, 10 breaths/cycle 15 min, 15 breaths/cycle	15 min, 10 breaths/cycle	15 min, 8–10 breaths/cycle
Frequency	Once daily, 7 days/week, 8 weeks	Once daily, 7 days/week, 8 weeks	Twice daily, 7 days/week, 6 weeks
RT			
Muscle group	UE & LE muscles	–	QF and UE muscles
Type	UE: Elastic bands LE: Free weights	–	QF: Free weights UE: Elastic bands, PNF
Intensity	Dyspnea: 3–4 (MBS) Fatigue: 5–6 (MBS)		Dyspnea: 3–4 (MBS) Fatigue: 5–6 (MBS)
Repetitions	2×10 reps	–	2×10 reps
Load adjustment	UE: Progressive elastic resistance based on tolerance LE: 3.5–7 kg, progressively increased (50% max)	–	UE: Progressive elastic resistance based on tolerance LE: 1.5 kg, progressively increased
Frequency	3 days/week, 8 weeks	–	2 days/week, 6 weeks
NMES			
Current type	Russian current	HVGS	Russian current
Muscle group	QF muscles	QF muscles	QF muscles
Intensity	40–50 mA, adjusted to tolerance to achieve visible contraction	Adjusted to tolerance to achieve visible contraction	10–20 mA, adjusted to tolerance to achieve visible contraction
Duration	20 min	10 min	10 min
Frequency	3 days/week	2 days/week	2 days/week
Posture exercises			
Type	Scapular adduction, bilateral shoulder elevation, and shoulder external rotation	–	–
Frequency	2×15 reps, 3 days/week	–	–

*: For Case III, maximum heart rate (HRmax) was calculated before each session using the Karvonen formula due to a resting heart rate (HR) >100 bpm. PR: Pulmonary rehabilitation, AET: Aerobic exercise training, MIIT: Moderate-intensity interval training, HIIT: High-intensity interval training, UE-MIIT: Upper-extremity moderate-intensity interval training, min: Minute, TP: Training phase, ARP: Active recovery phase, bpm: Beats per minute, HRR: Heart rate reserve, HRmax: Maximum heart rate, %: Percent, W: Watts, IMT: Inspiratory muscle training, MIP: Maximal inspiratory pressure, cmH$_2$O: Centimeters of water, RT: Resistance training, LE: Lower extremity, UE: Upper extremity, PNF: Proprioceptive neuromuscular facilitation, MBS: Modified Borg scale, reps: Repetitions, kg: Kilogram, NMES: Neuromuscular electrical stimulation, mA: Milliampere, HVGS: High-voltage galvanic stimulation, QF: Quadriceps femoris

20–25 minutes on a treadmill, all with oxygen support. The active-recovery workload was constant, with weekly increases of 5–10 watts during high-intensity intervals based on patient tolerance. Each session began with a warm-up on the arm ergometer and concluded with a cool-down on the treadmill. This program was conducted two days per week for eight weeks. The patient was also prescribed home IMT using a PowerBreathe Wellness®

Table 2: Pulmonary function test results before and after the rehabilitation program

Parameter	Patients					
	Case I		Case II		Case III	
	Pre	Post	Pre	Post	Pre	Post
FVC (%)	65	95	75	76	61.66	–
FEV$_1$ (%)	68	99	82	84	68.45	–
FEV$_1$/FVC	111	108	113	113	110.38	–
PEF (%)	89	145	85	100	130.22	–
FEF$_{25-75\%}$ (%)	78	101	101	99	102.54	–
DLCO (%)	40	70	61	56	–	–

FVC: Forced vital capacity, FEV$_1$: Forced expiratory volume in one second, FEV$_1$/FVC: Ratio of forced expiratory volume in one second to forced vital capacity, PEF: Peak expiratory flow, FEF$_{25-75\%}$: Forced expiratory flow at 25–75% of the pulmonary volume, DLCO: Diffusing capacity of the lung for carbon monoxide, %: Percentage, Pre: Before the rehabilitation program, Post: After the rehabilitation program

device. Training was set at 30% of his MIP (35.70 cmH$_2$O), with sessions lasting 15 minutes (10 breaths per cycle), performed once daily, seven days a week, for eight weeks.

High-voltage galvanic stimulation was applied to the patient's bilateral QF for 10 minutes, two days per week. The intensity was adjusted to the patient's maximum personal tolerance, sufficient to produce visible muscle contraction.

Case III

A 67-year-old female patient (BMI: 31.63 kg/m^2) was diagnosed with HP four months ago. A bronchoscopy performed 3.5 months ago, prompted by lower zone fibrosis on HRCT, revealed no abnormalities. Her medical history included long-term steroid use and asthma treatment. She was hospitalized for 32 days due to pneumonitis and hypoxemia and was subsequently referred for rehabilitation with complaints of severe desaturation, dyspnea, and fatigue. She was also receiving LTOT.

Pulmonary rehabilitation for case III

Upper-extremity MIIT at 60–80% of maximal heart rate (HR) was supervised by a physiotherapist twice weekly for six weeks. Each session included a five-minute warm-up and cool-down, with four minutes of moderate exercise followed by four minutes of active recovery at 10 revolutions per minute. Oxygen support using a continuous positive airway pressure device was introduced in the second week, along with continuous monitoring of vital signs. Resistance training targeted the QF in an upright seated position, using free weights and bilateral Russian current. Upper-extremity training included elastic bands and proprioceptive neuromuscular facilitation patterns with gradually increasing resistance. The

program also included IMT at 30–50% of MIP to reduce fatigue and improve respiratory muscle strength (RMS). IMT was conducted as a home-based program with regular follow-ups at the rehabilitation unit.

The patient was scheduled for a post-program evaluation after six weeks but was hospitalized due to a sudden exacerbation linked to underlying psychological issues. Tragically, she contracted Coronavirus Disease 2019 (COVID-19) while in intensive care and passed away from respiratory complications. Despite completing only four rehabilitation sessions, the patient reported reduced dyspnea and fatigue during exercise. Previously non-ambulatory and reliant on a wheelchair, she was able to walk to the rehabilitation unit, suggesting improved functional exercise capacity (FEC) and a likely significant increase in her 6-minute walk distance (6MWD).

In addition, after identifying barriers to physical activity, the patient received physical activity counseling. Energy conservation techniques and breathing control strategies were also taught.

Results

Three cases diagnosed with HP, aged 49, 60, and 67, presented with dyspnea, fatigue, and dry cough. All were receiving LTOT. The first two cases had smoking histories of 7.5 and 24 pack-years, respectively. All patients had body mass indexes over 30 kg/m^2, classifying them as Class I obese (BMI>30 kg/m^2).

Pulmonary function test results are presented in Table 2. Both forced expiratory volume in one second (FEV$_1$) and forced vital capacity (FVC) increased after rehabili-

Table 3: Respiratory muscle strength before and after the rehabilitation program

	Patients					
	Case I		Case II		Case III	
Parameter	Pre	Post	Pre	Post	Pre	Post
MIP (cmH$_2$O)	97	116	119	132	91	115
MIP (% predicted)	121	145	113.1	125.4	131.8	166.5
MEP (cmH$_s$O)	133	165	141	134	84	102
MEP (% predicted)	89	111	65.4	62.2	62.9	76.4

MIP: Maximal inspiratory pressure, MEP: Maximal expiratory pressure, cmH$_2$O: Centimeters of water, %: Percentage, Pre: Before the rehabilitation program, Post: After the rehabilitation program

Table 4: Inspiratory muscle endurance before and after the rehabilitation program

	Patients					
	Case I		Case II		Case III	
Parameter	Pre	Post	Pre	Post	Pre	Post
Endurance MIP (cmH$_2$O)	29.10	34.80	83.30	92.40	–	–
Endurance time (sec)	37	300	541	573	–	–
Endurance value (cmH$_2$O×sec)	1,076.70	13,224	45,065.3	52,945.2	–	–
Δ Dyspnea (MBS, 0–10)	+2.5	+1	+4	+1	–	–
Δ SpO$_2$ (%)	-6	+3	+1	-4	–	–

MIP: Maximal inspiratory pressure, MEP: Maximal expiratory pressure, cmH$_2$O: Centimeters of water, sec: Seconds, %: Percentage, Pre: Before the rehabilitation program, Post: After the rehabilitation program, Pre-test: Before the test, Post-test: After the test, MBS: Modified Borg scale

tation in Cases I and II. In contrast, the FEV$_1$/FVC ratio decreased in Case I (by 3%) and remained unchanged in Case II. In Case I, peak expiratory flow (PEF), forced mid-expiratory flow (FEF$_{25–75\%}$), and DLCO all improved. In Case II, these values decreased slightly, except for PEF, which increased by 2% and 5%, respectively. Final post-rehabilitation measurements for Case III could not be obtained, as the patient was hospitalized and later passed away before the six-week evaluation. However, significant functional and symptomatic improvements were observed by the sixth week of participation.

Table 3 presents RMS data. In Case I, both MIP and maximum expiratory pressure (MEP) increased following the rehabilitation program (by 19 and 32 cmH$_2$O, respectively). In Case II, MIP improved by 13 cmH$_2$O, while MEP decreased slightly (by 7 cmH$_2$O), possibly due to increased chest wall stiffness from stronger inspiratory muscles and the use of gentler exhalation techniques. This minimal decline may also be an expected consequence of the progressive nature of ILDs. The final measurements for Case III, which were scheduled to be taken after six weeks of rehabilitation, could not be obtained due to exacerbation and hospitalization. However, both MIP and MEP values—measured regularly during the rehabilitation process—showed a clinically significant

increase compared to pre-rehabilitation (minimal clinically important difference [MCID]>13 cmH$_2$O, with increases of +24 and +39.1 cmH$_2$O, respectively).[5]

Table 4 presents the inspiratory muscle endurance (IME) values of the cases. Currently, there are no established reference values for IME in adults. IME values in the first two cases increased compared to pre-rehabilitation levels. In Case III, IME could not be measured before rehabilitation due to severe dyspnea, dry cough, and desaturation. The patient demonstrated low IME at baseline. With rehabilitation, her dyspnea and dry cough improved, and desaturation episodes became less frequent.

Table 5 shows the results of the six-minute walk test (6MWT) before and after rehabilitation. Case I exhibited a clinically significant improvement in six-minute walk distance (6MWD) compared to pre-rehabilitation (Δ6MWD: +186.6 m, MCID>25m, >80% of predicted).[6] The patient experienced less desaturation and had a higher resting SpO$_2$ post-rehabilitation. She was tachycardic at rest both before and after rehabilitation (>100 beats/min), and the maximum HR reached during the test was 9 beats/min higher after rehabilitation. She was able to complete the post-rehabilitation test without stopping, unlike during the pre-rehabilitation test. In Case II, there was a non-clin-

Table 5: Six-minute walk test and six-minute pegboard and ring test results before and after the rehabilitation program

	Patients					
	Case I		Case II		Case III	
	Pre	Post	Pre	Post	Pre	Post
Six-minute walk test parameters						
6MWT distance (m)	275.4	462	553.8	559.2	238.2	–
6MWT (% of predicted)	51	86	104	105	55.04	–
HR (beats/min, before test)	122	105	76	91	106	–
HR (beats/min, after test)	132	141	126	140	151	–
ΔHR (beats/min)	10	36	50	49	45	–
SpO$_2$ (%, before test)	94	98	96	95	95	
SpO$_2$ (%, after test)	72	71	84	79	70	–
ΔSpO$_2$ (%)	22	27	12	16	25	–
BF (breaths/min, before test)	24	24	24	24	36	–
BF (breaths/min, after test)	36	32	28	32	60	–
ΔBF (breaths/min)	11	8	4	8	24	–
Dyspnea (MBS, 0–10, before test)	0	0	0	0	0	–
Dyspnea (MBS, 0–10, after test)	2	4	1	0.5	7	–
ΔDyspnea (MBS, 0–10)	2	4	1	0.5	7	–
General fatigue (MBS, 0–10, before test)	2	0	0	0	0.5	–
General fatigue (MBS, 0–10, after test)	4	4	1	1	5	–
ΔGeneral fatigue (MBS, 0–10)	2	4	1	1	4.5	–
Leg fatigue (MBS, 0–10, before test)	0	0	0	0	0	–
Leg fatigue (MBS, 0–10, after test)	0	3	2	1	5	–
ΔLeg fatigue (MBS, 0–10)	0	3	2	1	5	–
Six-minute pegboard and ring test parameters						
6PBRT (n)	351	396	314	347	154	–
6PBRT (% of predicted)	74	84	74	82	39.2	–
HR (beats/min, before test)	104	100	86	93	123	–
HR (beats/min, after test)	112	110	87	100	123	–
ΔHR (beats/min)	8	10	1	7	0	–
SpO$_2$ (%, before test)	96	96	93	96	94	
SpO$_2$ (%, after test)	96	96	95	94	92*	–
ΔSpO$_2$ (%)	0	0	+2	2	2*	–
BF (breaths/min, before test)	24	24	24	24	28	–
BF (breaths/min, after test)	32	32	24	28	32	–
ΔBF (breaths/min)	8	8	0	4	4	–
Dyspnea (MBS, 0–10, before test)	2	0.5	0	0	2	–
Dyspnea (MBS, 0–10, after test)	3	1	0	0	3	–
ΔDyspnea (MBS, 0–10)	1	0.5	0	0	1	–
General fatigue (MBS, 0–10, before test)	0	0	0	0	2	–
General fatigue (MBS, 0–10, after test)	3	2	0.5	0	4	–
ΔGeneral fatigue (MBS, 0–10)	3	2	0.5	0	2	–
Leg fatigue (MBS, 0–10, before test)	0	0	0	0	0	–
Leg fatigue (MBS, 0–10, after test)	4	4	1	0.5	5	–
ΔLeg fatigue (MBS, 0–10)	4	4	1	0.5	5	–

*: Indicates measurement taken with 5L oxygen support. 6MWT: Six-minute walk test, m: Meter, %: Percentage, HR: Heart rate, min: Minute, Δ: Difference between post-test and pre-test values, BF: Breathing frequency, SpO$_2$: Oxygen saturation, MBS: Modified Borg scale, Pre: Before the rehabilitation program, Post: After the rehabilitation program, 6PBRT: Six-minute pegboard and ring test

ically significant increase in 6MWD after rehabilitation (Δ6MWD: +5.4 m; MCID>25 m). However, the maximum HR reached during the test was 14 beats/min higher after rehabilitation, and the test was considered maximal. The patient experienced more desaturation compared to before rehabilitation (ΔSpO$_2$: 12% pre vs. 16% post). Prior to rehabilitation, the case III arrived at the unit in a wheelchair due to severe desaturation and fatigue. The six-minute walk test was performed with oxygen support, and she was able to walk 55.04% of the predicted

Table 6: Peripheral muscle strength before and after the rehabilitation program

Parameter	Case I				Case II				Case III		
	Pre		Post		Pre		Post		Pre		Post
	R	L	R	L	R	L	R	L	R	L	–
QF strength (N)	223	272	242	294	422	426	474	460	246	178	–
%QF strength (%)	56	67	70	73	207.8	200.7	233.4	216.7	85.9	63.3	–
Shoulder abduction (N)	129	178	180	136	365	325	389	326	134	101	–
%Shoulder abduction (%)	88	117	124	88	290.6	248.9	309.8	249.7	99.8	80.2	–
Handgrip strength (N)	240	280	320	300	–	–	–	–	–	–	–
%Handgrip strength (%)	64	75	85	81	–	–	–	–	–	–	–

QF: Quadriceps femoris, N: Newton, %: Percentage, Pre: Before the rehabilitation program, Post: After the rehabilitation program, R: Right, L: Left

Table 7: Physical activity levels before and after the rehabilitation program

Parameter	Case I		Case II		Case III	
	Pre	Post	Pre	Post	Pre	Post
Total energy expenditure (J/day)	9,423	12,202	11,113	10,356	9,018	–
Active energy expenditure (J/day)	636	968	1,017	285	643	–
Physical activity duration (min/day)	30	70	39	11	33	–
Average MET (MET/day)	1.2	2.5	1.1	1	1.2	–
Steps (steps/day)	4,339	5,111	3,267	1,959	1,523	–
Lying down duration (min/day)	533	337	434	513	10.13	–
Sleep duration (min/day)	434	434	404	395	352	

MET: Metabolic equivalent task, min: Minute, Pre: Before the rehabilitation program, Post: After the rehabilitation program, J: Joules.

distance. After completing rehabilitation, she arrived at the unit on foot with an SpO$_2$ above 90%. The 6MWD of case III couldn't be measured after rehabilitation.

Table 5 presents the results of the six-minute pegboard and ring test (6PBRT) before and after rehabilitation. In Case I, the number of rings placed during the 6PBRT increased by 45 after rehabilitation, exceeding 80% of the predicted value. In Case II, the number of rings increased by 33 after rehabilitation and also reached 80% of the expected value. Other parameters were relatively consistent between the pre- and post-tests for both cases. The number of rings in the 6PBRT of Case III could not be measured after rehabilitation, but it was estimated to have exceeded the predicted value based on pre-rehabilitation performance.

Table 6 shows the peripheral muscle strength (PMS) values before and after rehabilitation. Following rehabilitation in Case I, bilateral grip and shoulder abductor muscle strengths exceeded 80% of the predicted level. Although bilateral QF strength remained below 80% of the expected level post-rehabilitation, it improved com-

pared to pre-rehabilitation values, with increases of 19 N and 22 N, respectively. Overall, PMS showed general improvement after rehabilitation. In Case II, both pre- and post-rehabilitation measurements for bilateral QF and shoulder abductor muscle strengths were above 80% of the predicted values. Furthermore, strength increased in both muscle groups compared to pre-rehabilitation, with gains of 52 N and 34 N for QF, and 24 and 1 N for shoulder abductors, respectively. The PMS of Case III could not be measured after rehabilitation. However, it was estimated to have improved beyond predicted pre-rehabilitation levels, as the patient was able to walk to the unit post-rehabilitation and tolerate increased training workloads (initial workload: 10 watts with oxygen support of 4.5–5 L, progressively increased to 20–25 watts and oxygen support reduced to 2.5–3 L in subsequent sessions.

Table 7 presents the physical activity levels (PAL) of the cases before and after rehabilitation. In Case I, after rehabilitation, total energy expenditure increased by 2,779 joules/day, active energy expenditure increased by 332 joules/day, activity duration increased by 40 minutes/day, and the average number of steps increased by 772

Table 8: Questionnaire and scale results before and after the rehabilitation program

Assessment tool	Patients					
	Case I		Case II		Case III	
	Pre	Post	Pre	Post	Pre	Post
mMRC dyspnea scale (0–4)	2	1	2	1	4	3
HADS						
HADS-A	8	12	–	–	19	–
HADS-D	8	7	–	–	18	–
IPAQ-SF (MET-min/week)	190	770	297	964	0*	–

*: This patient was completely immobile and wheelchair-dependent before rehabilitation. mMRC: Modified medical research council dyspnea scale, HADS: Hospital anxiety and depression scale, HADS-A: Hospital anxiety and depression scale – anxiety subscale, HADS-D: Hospital anxiety and depression scale – depression subscale, IPAQ-SF: International physical activity questionnaire – short form, Pre: Before the rehabilitation program, Post: After the rehabilitation program

steps/day. The increase in steps was clinically significant (MCID>600 steps/day). However, the patient remained less active than the average daily step and metabolic equivalent of task (MET) cutoff points (5,000–7,499 steps/day; 1.6–2.9 METs/day). Post-rehabilitation, PAL declined in Case II, as the patient perceived the rehabilitation sessions to be sufficient and subsequently reduced daily activity, despite an increase in International Physical Activity Questionnaire – Short Form (IPAQ-SF) scores. Only the lying-down duration increased. The PAL of Case III could not be measured after rehabilitation. However, it was estimated to have improved compared to pre-rehabilitation, as the patient (previously wheelchair-dependent) was able to walk to the unit following the program.

Table 8 presents the Modified Medical Research Council (mMRC) dyspnea scores, Hospital Anxiety and Depression Scale (HADS) results, and IPAQ-SF scores for the cases before and after rehabilitation. The mMRC scores for Cases I and II each decreased by one point after rehabilitation, which is considered clinically significant (MCID≥1 point).[7] The final mMRC score for Case III was obtained during follow-up and also showed a clinically significant change (MCID≥1 point). In Case I, the anxiety score increased by 4 points after rehabilitation, reaching 12, indicating clinically significant anxiety (score >10). However, the patient did not meet the threshold for depression (score <8). The total PAL of both Cases I and II increased after rehabilitation, according to the IPAQ-SF.

The mMRC score of Case III could not be formally assessed after rehabilitation but was estimated to be lower than the pre-rehabilitation score, based on her reports of reduced dyspnea during aerobic exercise and IMT. The patient also began walking without desaturation

and with fewer symptoms. Her anxiety and depression levels could not be evaluated post-rehabilitation due to ongoing psychiatric medication, but she reported feeling better as the rehabilitation progressed. Although PAL could not be measured after rehabilitation, the patient, who had previously been wheelchair-dependent and unable to walk, began walking without desaturation after the rehabilitation program.

Discussion

The present study demonstrates clinical improvements resulting from an appropriately designed PR program, including gains in pulmonary function, IME, functional capacity (6MWT: 186.6 m and 5.4 m), upper-extremity exercise capacity (6PBRT: 45 rings and 33 rings), PMS, dyspnea, and PAL. No adverse effects were observed during the rehabilitation sessions. Our previous experience with individuals diagnosed with ILD motivated us to report the clinical outcomes of patients undergoing PR in our unit.[8]

Respiratory abnormalities in HP resemble those seen in other ILDs, typically presenting as restrictive defects and reduced DLCO.[3] In our cases, both restrictive defects and diffusion impairments were observed. Chronic forms of HP may also exhibit obstructive features due to emphysematous changes.[3] Although the literature on HP predominantly focuses on pharmacological treatments and surgical interventions,[2] few studies emphasize PR, and none explicitly detail PR protocols tailored to HP.[9] However, studies on ILD populations suggest that IMT improves RMS, quality of life, and exercise capacity.[8,10] In our cases, RMS values were within normal limits (>80% predicted), yet IMT was included as a precautionary measure, given its potential to decline with disease pro-

gression.[10] IMT resulted in improvements in both muscle strength and symptoms. Consistent with findings from previous IMT studies, our patients also showed improvements in PMS, likely due to the activation of the muscle metaboreflex, which redistributes blood flow from the respiratory to the peripheral muscles and helps reduce fatigue.[11] These findings suggest that PMS improvements may result from a combination of training modalities. However, some ILD studies suggest that the muscle metaboreflex may not fully explain the observed muscle weakness and exercise intolerance in ILD patients.[12]

Patients with HP generally exhibit reduced exercise capacity.[1] In our cases, FEC was impaired in Case I and Case III (275.4 m and 238.2 m, corresponding to 51% and 55.04% of predicted values, respectively), while Case II had normal capacity (553.8 m, 104% of predicted). Case I showed a clinically significant improvement in 6MWD after rehabilitation (Δ6MWD: +186.6 m; MCID>25m; from 51% to 86%).[6] Case II had a minor, non-clinically significant increase (Δ6MWD: 5.4 m, MCID>25 m). Case III, initially wheelchair-bound, walked 55.04% of the predicted distance before rehabilitation and was later able to walk with SpO_2 above 90%.

The change in dyspnea reported by our patients following PR was clinically significant (ΔmMRC≥1 point).[7] Patients with HP often exhibit elevated HR at rest and during exercise, possibly as a compensatory response to reduced SpO_2, similar to patterns seen in chronic obstructive pulmonary disease.[13] Both Case I and Case III presented with resting tachycardia. The literature also suggests that ambulatory oxygen therapy can reduce HR during walking in patients with ILD.[14] In this context, providing oxygen support during training is essential not only for oxygenation but also from a cardiac safety perspective.

In addition to dyspnea, patients with HP frequently experience anxiety and depression.[15] One patient, who was unable to complete post-rehabilitation assessments due to death, had reported feeling less anxious about LTOT before passing. Despite the physical benefits of PR, psychological vulnerability may increase due to factors such as LTOT dependence, disease progression, and emotional burden. The sudden decline of Case III may reflect the combined effects of these factors. In Case I, anxiety scores increased, while depression scores showed a potentially clinically meaningful reduction (ΔHADS-D ≈

−1.5 points).[16] Despite the improvement in depressive symptoms, anxiety may have increased due to LTOT and heightened self-awareness resulting from participation in PR. These findings suggest that patients may experience psychological decline despite physical gains from PR, underscoring the importance of integrated psychological and motivational support.

As reported in previous studies on ILDs,[17,18] our cases had low PAL prior to rehabilitation. Following PR, PAL improved based on both metabolic holter data and IPAQ-SF scores. However, ILD studies using various assessment methods (e.g., metabolic holter monitoring and surveys) report inconsistent effects of PR on PAL. For example, one study on patients with Interstitial Pulmonary Fibrosis reported increased physical activity after a 12-week PR program,[19] while another six-month out-of-hospital program found no change.[20] In our study, one of the two patients with recorded data showed improvement in metabolic holter parameters, while both demonstrated increased IPAQ-SF scores.

This study demonstrates that PR, which includes individually tailored IMT and exercise programs for patients with HP, can improve FEC, along with various subjective and objective clinical outcomes. No adverse effects were observed during the intervention. Furthermore, oxygen support is critical for these patients to safely participate in training, as they are at risk for severe desaturation and hypoxemia. Therefore, continuous monitoring of vital signs and the provision of supplemental oxygen when necessary are strongly recommended during exercise.

Limitations and Future Directions

This study is a case series with a limited number of participants. A standardized PR program was not used; instead, individualized programs were applied based on each patient's clinical needs. Some evaluations could not be completed due to the death of one patient during clinical follow-up. The findings rely primarily on the researchers' clinical experience and judgment, and the hypotheses presented remain to be formally tested. To date, no studies have specifically investigated the role of PR programs in patients with HP. Given the unique pathophysiology and prognosis of each ILD, randomized controlled trials with larger sample sizes are needed to evaluate standardized PR approaches for HP. We hope that this report will serve as a foundation and inspire future prospective studies with broader participant groups.

Ethics Committee Approval

This is a case series, and therefore ethics committee approval was not required in accordance with institutional policies.

Informed Consent

Informed consent was obtained from each participant.

Conflict of Interest

The authors have no conflicts of interest to declare.

Funding

The authors declared that this study received no financial support.

Use of AI for Writing Assistance

During the revision of this manuscript, the authors used Grammarly artificial intelligence writing assistance to improve language and readability. Following the use of this tool, all authors reviewed and edited the manuscript as necessary and accepted full responsibility for the content of the publication.

Author Contributions

Concept – N.N.Y., B.N.Ö., M.B.G.; Design – N.N.Y., B.N.Ö., M.B.G.; Supervision – N.Y.D., M.B.G.; Resource – M.B.G.; Materials – N.Y.D.; Data Collection and/or Processing – N.N.Y., B.N.Ö.; Analysis and/or Interpretation – N.N.Y., B.N.Ö., N.Y.D., M.B.G.; Literature Review – N.N.Y., B.N.Ö.; Writing – N.N.Y., B.N.Ö.; Critical Review – N.N.Y., B.N.Ö., N.Y.D., M.B.G.

Peer-review

Externally peer-reviewed.

References

1. Sakamoto S, Masuoka M, Usui Y, Shimizu H, Sekiya M, Miyoshi S, et al. ATS/JRS/ALAT Hypersensitivity Pneumonitis Guidelines for Diagnosis of humidifier lung and summer-type hypersensitivity pneumonitis. Respir Investig 2023;61(5):660–7. [CrossRef]

2. Vasakova M, Morell F, Walsh S, Leslie K, Raghu G. Hypersensitivity Pneumonitis: Perspectives in Diagnosis and Management. Am J Respir Crit Care Med 2017;196(6):680–9. [CrossRef]

3. Anwar J, Kong WT, Balakrishnan B. Updates in Hypersensitivity Pneumonitis: A Narrative Review. Curr Pulmonol Rep 2022;11(4):106–15. [CrossRef]

4. Dowman L, Hill CJ, May A, Holland AE. Pulmonary rehabilitation for interstitial lung disease. Cochrane Database Syst Rev 2021;2(2):CD006322. [CrossRef]

5. Gosselink R, De Vos J, van den Heuvel SP, Segers J, Decramer M, Kwakkel G. Impact of inspiratory muscle training in patients with COPD: what is the evidence? Eur Respir J 2011;37(2):416–25. [CrossRef]

6. Holland AE, Hill CJ, Rasekaba T, Lee A, Naughton MT, McDonald CF. Updating the minimal important difference for six-minute walk distance in patients with chronic obstructive pulmonary disease. Arch Phys Med Rehabil 2010;91(2):221–5. [CrossRef]

7. de Torres JP, Pinto-Plata V, Ingenito E, Bagley P, Gray A, Berger R, et al. Power of outcome measurements to detect clinically significant changes in pulmonary rehabilitation of patients with COPD. Chest 2002;121(4):1092–8. [CrossRef]

8. Karadallı MN, Boşnak-Güçlü M, Camcıoğlu B, Kokturk N, Türktaş H. Effects of Inspiratory Muscle Training in Subjects With Sarcoidosis: A Randomized Controlled Clinical Trial. Respir Care 2016;61(4):483–94. [CrossRef]

9. Hamblin M, Prosch H, Vašáková M. Diagnosis, course and management of hypersensitivity pneumonitis. Eur Respir Rev 2022;31(163):210169. [CrossRef]

10. Hoffman M. Inspiratory muscle training in interstitial lung disease: a systematic scoping review. J Bras Pneumol 2021;47(4):e20210089. [CrossRef]

11. Boushel R. Muscle metaboreflex control of the circulation during exercise. Acta Physiol (Oxf) 2010;199(4):367–83. [CrossRef]

12. Chen C, Kolbe J, Wilsher ML, De Boer S, Paton JFR, Fisher JP. Cardiorespiratory responses to muscle metaboreflex activation in fibrosing interstitial lung disease. Exp Physiol 2022;107(5):527–40. [CrossRef]

13. Warnier MJ, Rutten FH, de Boer A, Hoes AW, De Bruin ML. Resting heart rate is a risk factor for mortality in chronic obstructive pulmonary disease, but not for exacerbations or pneumonia. PLoS One 2014;9(8):e105152. [CrossRef]

14. Ventura V, Viani M, Bianchi F, d'Alessandro M, Sestini P, Bargagli E. Effect of Ambulatory Oxygen on the Respiratory Pattern during the 6 Min Walking Test in Patients with Interstitial Lung Diseases. Biomedicines 2023;11(7):1834. [CrossRef]

15. Holland AE, Fiore JF Jr, Bell EC, Goh N, Westall G, Symons K, et al. Dyspnoea and comorbidity contribute to anxiety and depression in interstitial lung disease. Respirology 2014;19(8):1215–21. [CrossRef]

16. Luu B, Gupta A, Fabiano N, Wong S, Fiedorowicz JG, Fidler L, et al. Influence of pulmonary rehabilitation on symptoms of anxiety and depression in interstitial lung disease: A systematic review of randomized controlled trials. Respir Med 2023;219:107433. [CrossRef]

17. Hur SA, Guler SA, Khalil N, Camp PG, Guenette JA, Ryerson CJ. Impact of Psychological Deficits and Pain on Physical Activity of Patients with Interstitial Lung Disease. Lung 2019;197(4):415–25. [CrossRef]

18. Watanabe F, Taniguchi H, Sakamoto K, Kondoh Y, Kimura T, Kataoka K, et al. Quadriceps weakness contributes to exercise capacity in nonspecific interstitial pneumonia. Respir Med 2013;107(4):622–8. [CrossRef]

19. Gaunaurd IA, Gómez-Marín OW, Ramos CF, Sol CM, Cohen MI, Cahalin LP, et al. Physical activity and quality of life improvements of patients with idiopathic pulmonary fibrosis completing a pulmonary rehabilitation program. Respir Care 2014;59(12):1872–9. [CrossRef]

20. Perez-Bogerd S, Wuyts W, Barbier V, Demeyer H, Van Muylem A, Janssens W, et al. Short and long-term effects of pulmonary rehabilitation in interstitial lung diseases: a randomised controlled trial. Respir Res 2018;19(1):182. [CrossRef]