

# In-hospital pulmonary rehabilitation after completion of primary respiratory disease treatment improves physical activity and ADL performance

## A prospective intervention study

Masafumi Shimoda, MD<sup>a,\*</sup>, Satoshi Takao<sup>b</sup>, Hiroyuki Kokutou, MD<sup>a</sup>, Naoyuki Yoshida, MD<sup>b</sup>, Keiji Fujiwara, MD<sup>a</sup>, Koji Furuuchi, MD<sup>a</sup>, Takeshi Osawa, MD<sup>a</sup>, Keitaro Nakamoto, MD<sup>a</sup>, Yoshiaki Tanaka, MD<sup>a</sup>, Kozo Morimoto, MD, PhD<sup>a</sup>, Ryozo Yano, MD<sup>a</sup>, Masao Okumura, MD<sup>a</sup>, Takashi Uchiyama, MD<sup>a</sup>, Kozo Yoshimori, MD<sup>a</sup>, Ken Ohta, MD, PhD<sup>a</sup>, Hideaki Senjyu, PhD<sup>b</sup>

## Abstract

**Introduction:** Pulmonary rehabilitation improves the physical condition of patients with chronic respiratory disease; however, there are patients who cannot leave the hospital because of their low activities of daily living (ADLs), despite the completion of primary respiratory disease treatment and rehabilitation during treatment. Therefore, this study demonstrated that those patients recovered their ADLs through in-hospital pulmonary rehabilitation after treatment completion.

**Methods:** We prospectively studied 24 hospitalized patients who had some remaining symptoms and showed low ADL scores of 9 points or less on the short physical performance battery after undergoing treatment for respiratory disease in Fukujuji Hospital from October 2018 to October 2019, excluding 2 patients who had re-exacerbation and 1 patient who could not be examined using the incremental shuttle walk test (ISWT). After completion of the primary respiratory disease treatment, patients moved to the regional comprehensive care ward, and they received pulmonary rehabilitation for 2 weeks. In the ward, patients who could not yet leave the hospital could undergo pulmonary rehabilitation for up to 60 days. Data were evaluated three times: upon treatment completion (baseline), postrehabilitation, and 3 months after baseline. The main outcome was an improvement in the incremental shuttle walk test (ISWT) postrehabilitation.

**Results:** The median age of the patients was 80 (interquartile range (IQR): 74.8–84.5), and 14 patients (58.3%) were male. The ISWT distance significantly increased postrehabilitation (median [IQR]: 60 m [18–133] vs 120 m [68–203], P < .001). The Barthel Index (BI) (P < .001), the modified Medical Research Council (P < .001), and other scale scores were also improved. Among patients with acute respiratory diseases such as pneumonia, chronic obstructive pulmonary disease, and interstitial pneumonia, ISWT and other data showed improvement at the postrehabilitation timepoint. Ten patients who could perform examinations at 3 months after baseline were evaluated 3 months after taking baseline data prior to starting rehabilitation. The ISWT showed significant improvement 3 months after baseline (P = .024), and the ISWT distance was maintained after rehabilitation.

**Discussion and conclusions:** Physical activity, symptoms, mental health, and ADL status in patients who had not recovered after primary treatment completion for respiratory diseases could improve through in-hospital pulmonary rehabilitation.

**Abbreviations:** 6MWD = six-minute walk distance, ADL = activity of daily living, BI = Barthel Index, CAT = COPD assessment test, CES-D = center for epidemiologic studies for depression scale, COPD = chronic obstructive pulmonary disease, IP = interstitial

Editor: Maya Saranathan.

Copyright © 2021 the Author(s). Published by Wolters Kluwer Health, Inc.

Received: 21 May 2021 / Received in final form: 4 November 2021 / Accepted: 18 November 2021

http://dx.doi.org/10.1097/MD.00000000028151

The study was approved by the Institutional Review Board of Fukujuji Hospital. Consent was obtained from all patients. The decisions made by this board are based on and in accordance with the Declaration of Helsinki.

The authors have no funding and conflicts of interests to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

<sup>&</sup>lt;sup>a</sup> Respiratory Disease Center, Fukujuji Hospital, Japan Anti-Tuberculosis Association (JATA), Kiyose City, Tokyo, Japan, <sup>b</sup> Respiratory Care and Rehabilitation Center, Fukujuji Hospital, Japan Anti-Tuberculosis Association (JATA), Kiyose City, Tokyo, Japan.

<sup>\*</sup> Correspondence: Masafumi Shimoda, Respiratory Disease Center, Fukujuji Hospital, Japan Anti-Tuberculosis Association (JATA), 3-1-24 Mastuyama, Kiyose City, Tokyo 204-8522, Japan (e-mail: shimodam@fukujuji.org).

This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

How to cite this article: Shimoda M, Takao S, Kokutou H, Yoshida N, Fujiwara K, Furuuchi K, Osawa T, Nakamoto K, Tanaka Y, Morimoto K, Yano R, Okumura M, Uchiyama T, Yoshimori K, Ohta K, Senjyu H. In-hospital pulmonary rehabilitation after completion of primary respiratory disease treatment improves physical activity and ADL performance: a prospective intervention study. Medicine 2021;100:49(e28151).

pneumonia, IQR = interquartile range, ISWT = incremental shuttle walking test, mMRC = modified medical research council, NRADL = Nagasaki University Respiratory ADL questionnaire, QOL = quality of life, SPPB = short physical performance battery.

Keywords: chronic obstructive pulmonary disease assessment test, modified medical research council, physical activity, pulmonary rehabilitation, shuttle walking test

## 1. Introduction

Pulmonary rehabilitation is effective in improving the physical condition of patients with chronic respiratory disease<sup>[1,2]</sup> and reducing the rate of hospital readmission within 4 weeks of prior hospitalization among patients with acute exacerbation of chronic obstructive pulmonary disease (COPD).<sup>[3]</sup> Regarding pulmonary rehabilitation during hospitalization, after treatment completion for acute exacerbation of COPD, patients improved their six-minute walk distance (6MWD) outcome after 4 or more weeks of rehabilitation.<sup>[4]</sup> However, there have been no reports demonstrating the benefits of rehabilitation for respiratory diseases other than COPD and the appropriate duration of inhospital pulmonary rehabilitation after treatment completion for an exacerbation of chronic pulmonary disease. We observed some patients who could not leave our hospital due to their low activities of daily living (ADLs), despite completion of primary respiratory disease treatment and underwent rehabilitation during treatment. Those patients often move to a long-term care bed in a sanatorium, such as a hospital sanatorium ward or nursing home.<sup>[5,6]</sup> However, many patients want to return to their home, even with a disease,<sup>[7]</sup> and in-hospital pulmonary rehabilitation after treatment completion might help improve their physical conditions and leave a hospital. If those patients become able to go home, there are many benefits, such as for patient quality of life (QOL) and society, including decreased medical costs. Therefore, this study aimed to demonstrate that patients who had some remaining symptoms and had not yet completely recovered their ability to perform ADLs after treatment completion recovered their ADLs through inhospital pulmonary rehabilitation after treatment completion. In addition, we evaluated patients with various respiratory diseases.

#### 2. Methods

## 2.1. Study design, setting, and sample size

We prospectively studied hospitalized adult patients (age $\geq 20$ years old) who could not leave our hospital due to their low ADLs after treatment completion for respiratory diseases, such as COPD, interstitial pneumonia (IP), pneumonia, bronchial asthma, nontuberculous mycobacteria, and pulmonary hemorrhage, despite receiving rehabilitation in the acute care unit at the Respiratory Disease Center of Japan Anti-Tuberculosis Association (JATA) Fukujuji Hospital from October 2018 to October 2019. They receive pulmonary rehabilitation for 2 weeks after treatment completion for respiratory diseases. Exercise tolerance, respiratory function and other data of the patients were evaluated 3 times: when they moved to the regional comprehensive care ward (baseline), after 2 weeks of rehabilitation, and 3 months after baseline (Fig. 1). Examinations at 3 months after baseline were performed in outpatients. We statistically compared data from the following timepoints: baseline, postrehabilitation, and 3 months after baseline.

#### 2.2. Participant

The study included patients who had some remaining symptoms and showed a short physical performance battery (SPPB) score of 9 points or less at baseline in the study period. The SPPB can be used to evaluate physical performance for sarcopenia, and the relative risk of ADL disability for those with scores of 7 to 9 ranges from 1.5 to 2.1.<sup>[8,9]</sup> The Asian Working Group for Sarcopenia defines low physical performance as an SPPB score of 9 points or less<sup>[10]</sup>; therefore, our inclusion criteria were formed in consideration of this value. Patients refusing or unable to undergo rehabilitation, those with malignancy, acquired immunodeficiency syndrome, severe dementia, pneumothorax, difficulty performing the ISWT, and disease recurrence in the study periods were excluded. A total of 42 patients who had some remaining symptoms and were difficult to discharge from our hospital immediately after treatment completion for respiratory disease were recruited. Fifteen patients were excluded for SPPB of more than 9 points, 2 patients who had re-exacerbation within 2 weeks of pulmonary rehabilitation, and 1patient who was not able to be examined using the incremental shuttle walk test (ISWT). Therefore, we studied 24 patients.

#### 2.3. Intervention/issue of interest (exposure)

After completion of the primary respiratory disease treatment, patients moved to the regional comprehensive care ward, which was newly established in 2014, following revision of the medical fee scheme in Japan. In the ward, patients who cannot yet leave the hospital because of their poor ability to perform ADLs can undergo pulmonary rehabilitation for up to 60 days.

Pulmonary rehabilitation is a comprehensive intervention based on a thorough patient assessment followed by patienttailored therapies that include exercise training, education, and



behavior change, designed to improve the physical and psychological condition of people with chronic respiratory disease and to promote long-term adherence to health-enhancing behaviors.<sup>[2]</sup> The patients underwent pulmonary rehabilitation 5 days a week for 1 hour each day. Pulmonary rehabilitation exercises included conditioning exercise and limb resistance training for approximately 40 minutes and endurance exercise training with a load of 60% to 80% of the exercise tolerance obtained from the ISWT for 20 minutes. An education component regarding self-training during hospitalization and after discharge was also provided by a physiotherapist.

The evaluated data were ISWT, The Barthel Index (BI), COPD assessment test (CAT), modified Medical Research Council (mMRC), respiratory function tests, Nagasaki University respiratory ADL questionnaire (NRADL), SPPB, and Center for Epidemiologic Studies for Depression Scale (CES-D) scores, grip strength, body weight, pulmonary function, and other relevant findings were collected by a physiotherapist.

This study adopted the ISWT instead of 6MWD as a measurement of exercise training. The ISWT seems to be a better indicator of maximal aerobic power, health status, and pulmonary function, such as forced vital capacity and forced expiratory volume in 1 second, than the 6MWD.<sup>[11,12]</sup> Consequently, the ISWT is considered to be a more standardized test than the 6MWD.<sup>[12]</sup> The ISWT is a test imposing an incremental acceleration as the patient walks round trips on a 10meter course.<sup>[12,13]</sup> The test includes 12 levels, and each level lasts 1 minute.<sup>[12,13]</sup> The walking speed is determined by an audio signal and is increased every minute by 0.17 m/second from 0.50 m/second at the start to a final speed of 2.37 m/second at level 12.<sup>[12,13]</sup> Oxygen saturation and pulse rate are monitored during the test.<sup>[12,13]</sup> The test ends when the patient is too out-of-breath to maintain the required speed or is unable to complete a shuttle for a second consecutive time.<sup>[12,13]</sup> The difference in the ISWT walking distance between the baseline and postrehabilitation timepoints was calculated as  $\Delta$ ISWT (ISWT[postrehabilitation] (m) - ISWT[baseline] (m)).<sup>[12,13]</sup>

We conducted interviews to assess the BI, CAT, mMRC, NRADL, SPPB, and CED-S scores. The BI evaluates the functional status and the level of autonomy in daily life activities through the level of care needed in daily life.<sup>[14]</sup> The CAT and mMRC are scales that are used to evaluate respiratory symptoms such as dyspnea for patients with COPD.<sup>[15-17]</sup> The NRADL is an ADL scale for patients with COPD.<sup>[18]</sup> The SPPB is a measurement of physical performance and extremity functional status.<sup>[8,9]</sup> The CES-D is an assessment of mental state and depression.<sup>[19]</sup> The scale was translated into Japanese by Shima et al and consists of 20 items with a 4-point Likert scale from never=0 to always=3 (for 4 items, the pattern of the reverse rating scale was from never=3 to always=0).<sup>[19,20]</sup> The decrease in the CAT score between the baseline and postrehabilitation timepoints was calculated as  $\Delta CAT$  (CAT[postrehabilitation] -CAT[baseline]).

The pulmonary function test was conducted according to the American Thoracic Society protocol.<sup>[21]</sup> Forced vital capacity and forced expiratory volume in one second were measured from the flow-volume curve obtained by a spirometer (CHESTAC-8900, Chest M.I., Inc., Tokyo, Japan). The predicted pulmonary function values were calculated on the basis of the Japanese Respiratory Society guidelines.<sup>[22]</sup>

The *i*-BODE index was calculated, which was developed for predicting mortality in patients with COPD and is based on

variables including forced expiratory volume in one second% predicted, ISWT distance, mMRC scale score, and body mass index.<sup>[23]</sup> The cut-off values are as follows: quartile 1 (score of 0–2), quartile 2 (score of 3–4), quartile 3 (score of 5–6), and quartile 4 (score of 7–12). Each quartile increase in the score is associated with increased mortality.<sup>[23]</sup>

## 2.4. Comparison

We statistically compared data between the baseline and postrehabilitation timepoints. Among patients with COPD and IP as an underlying disease or patients with pneumonia as the main disease on admission, data were compared as a subanalysis. The ISWT was compared at the following timepoints: baseline, postrehabilitation, and 3 months after baseline. In addition, we evaluated those data in patients with each respiratory disease.

#### 2.5. Ethics and endpoint

The study was approved by the Institutional Review Board of Fukujuji Hospital (Study number: 19014). Consent was obtained from all patients. The decisions made by this board are based on and in accordance with the Declaration of Helsinki. The endpoint of the study was an improvement in the ISWT at postrehabilitation timepoints.

#### 2.6. Statistical analysis

All data were analyzed and processed using EZR, version 1.35 (Saitama Medical Center, Jichi Medical University, Saitama, Japan).<sup>[24]</sup> The Wilcoxon signed-rank test was used to compare data between the baseline and postrehabilitation timepoints. The Mann–Whitney *U* test was used to evaluate the relationship between  $\Delta$ ISWT or  $\Delta$ CAT and other indicators at baseline. The Friedman test was used to compare data among the baseline, postrehabilitation, and 3 months after baseline for multiple comparison procedures. The level of statistical significance was set at *P*=.05 (2-tailed).

## 3. Results

The baseline characteristics of the patients are shown in Table 1. Fourteen patients were male, and the median age of all patients was 80 years old (IQR: 74.8–84.5 years old). The durations of hospitalization, stay in the acute care unit, and stay in the regional comprehensive care ward were 38 days (IQR: 32–67), 20 days (IQR: 15–25), and 18 days (IQR: 15–26), respectively. The duration of rehabilitation in the acute care unit was 9 days (IQR: 6–12 days).

Table 2 shows the patients' ADL status at baseline and postrehabilitation. The ISWT significantly increased postrehabilitation (median [IQR]: baseline 60 m [18–133] vs postrehabilitation 120 m [68–203], P < .001), and 13 patients (54.2%) showed a  $\Delta$ ISWT of more than 50 meters. The BI score significantly increased postrehabilitation (median [IQR]: baseline 80 [63–90] vs postrehabilitation 88 [80–100], P < .001). Ten patients (41.7%) showed BI scores of 70 or less at baseline. After 2 weeks of pulmonary rehabilitation, all patients improved BI scores, and only 3 patients (12.5%) were at moderate risk (BI scores  $\leq$ 70). While the CAT score did not show a significant difference between baseline and postrehabilitation (median [IQR]: baseline 17 [12–21] vs postrehabilitation 14 [9–19],

Table 1

Baseline characteristics of the patients.

	n=24
Age, median (IQR), yr	80 (74.8-84.5)
Sex (male/female)	14/10
Underlying disease	
COPD, n (%)	9 (37.5)
IP, n (%)	8 (33.3)
NTM, n (%)	3 (12.5)
Asthma, n (%)	2 (8.3)
Old healed pulmonary tuberculosis, n (%)	4 (16.7)
Comorbidity without respiratory diseases, n (%)	18 (75.0)
Smoking history, n (%)	16 (66.7)
Brinkman Index, median (IQR)	220 (0-1140)
Main disease on admission	
Pneumonia, n (%)	11 (45.8)
COPD, n (%)	3 (12.5)
IP, n (%)	6 (25.0)
NTM, n (%)	3 (12.5)
Pulmonary hemorrhage, n (%)	1 (4.2)
Duration of hospitalization, median (IQR), day	38 (32-67)
Duration of hospitalization in acute care unit,	20 (15–25)
median (IQR) day	
Duration of hospitalization in regional comprehensive	18 (15–26)
care ward, median (IQR) day	
Duration of rehabilitation in acute care unit,	9 (6-12)
median (IQR) day	
Receiving HOT before admission, n (%)	5 (20.8)
Aggravated respiratory failure after treatment	11 (45.8)
compared to before admission, n (%)	

COPD = chronic obstructive pulmonary disease, HOT = home oxygen therapy, IP = interstitial pneumonia, IQR = interquartile range, NTM = nontuberculous mycobacterial pulmonary infection.

P=.059), the mMRC was increased postrehabilitation (median [IQR]: baseline 3.0 [2.0–4.0] vs postrehabilitation 2.0 [1.0–3.0], P<.001). CES-D (median [IQR]: baseline 16 [6–20] vs postrehabilitation 10 [5–19], P=.016), NRADL (median [IQR]: baseline 53 [40–64] vs postrehabilitation 65 [47–81], P<.001), and SPPB (median [IQR]: baseline 7 [6–9] vs postrehabilitation 8 [6–10], P=.001) scores were also improved. The median baseline *i*-BODE index was 5.0 points (IQR: 2.8–6.3), and it significantly decreased at the time of postrehabilitation (median 3.5 points [IQR: 1.8–6.0], P<.001).

Patients with each respiratory disease were evaluated and are shown in Table 3. Among patients with COPD (n=9) and IP (n=8) as an underlying disease, ISWT (COPD P=.014, IP P=.014), BI (COPD P=.014, IP P=.035), and mMRC (COPD P=.037, IP P=.011) showed improvements at the time of postrehabilitation. IP as an underlying disease showed that NRADL (COPD P=.021) and SPPB (IP P=.033) improved at the time of postrehabilitation. Regarding patients with pneumonia as the main disease on admission (n=11), ISWT (P=.004), BI (P=.005), mMRC (P=.011), and NRADL (P=.023) improved at the time of postrehabilitation.

We examined 10 patients at 3 months after baseline. One patient was excluded due to readmission for an exacerbation of their diseases within 3 months after baseline. Thirteen patients were lost to follow-up because they could not come to our hospital due to their low ADLs, were followed up at a local doctor, or the distance from their house to our hospital was too great. Comparisons of the ISWT results among the3 timepoints (baseline, postrehabilitation, and 3 months after baseline) are

#### Table 2

Comparisons between the baseline and postrehabilitation timepoints.

	Baseline	Postrehabilitation	P value
Body weight, median (IQR), kg	49.6 (42.8–61.2)	49.2 (42.0-61.4)	.807
BMI, n (%), cm²/kg	20.2 (17.6–22.7)	20.4 (17.8–22.6)	.972
ISWT distance, median (IQR), m	60 (18–133)	120 (68–203)	<.001
Barthel Index, median (IQR)	80 (63–90)	88 (80-100)	<.001
CAT score, median (IQR)	17 (12–21)	14 (9–19)	.059
mMRC, median (IQR)	3.0 (2.0-4.0)	2.0 (1.0-3.0)	<.001
CES-D, median (IQR)	16 (6-20)	10 (5–19)	.016
NRADL, median (IQR)	53 (40-64)	65 (47-81)	<.001
SPPB, median (IQR)	7 (6–9)	8 (6-10)	.001
Grip strength			
Right hand, median (IQR), kg	18.0 (10.8–21.5)	17.5 (10.8–21.6)	.958
Left hand, median (IQR), kg	15.0 (13.0–20.0)	16.0 (12.5–20.5)	.863
Respiratory function test			
FVC, median (IQR), L	1.85 (1.30–2.23)	1.98 (1.32–2.61)	.054
FEV1, median (IQR), L	0.95 (0.72–1.46)	1.06 (0.68–1.65)	.286
<i>i</i> -BODE index, median (IQR) <sup>a</sup>	5.0 (2.8–6.3)	3.5 (1.8–6.0)	<.001

BMI = body mass index, CAT = COPD assessment test, CES-D = center for epidemiologic studies for depression scale, FEV1 = forced expiratory volume in one second, FVC = forced vital capacity, ISWT = incremental shuttle walk test, mMRC = modified medical research council, NRADL = Nagasaki University Respiratory ADL questionnaire, SPPB = short physical performance battery.

shown in Figure 2, which showed significant differences (Friedman test; P < .001). The ISWT showed significant improvement 3 months after baseline compared to baseline (P=.024), whereas there was no significant difference between postrehabilitation and 3 months after baseline (P=.459).

#### 4. Discussion

The study demonstrated that the performance of ADLs in patients who had not recovered after primary treatment completion for respiratory diseases could improve through 2 weeks of in-hospital pulmonary rehabilitation after treatment completion for respiratory disease, as reflected in the outcomes of the ISWT, BI, mMRC, CES-D, NRADL, and *i*-BODE index. The subanalysis showed that pulmonary rehabilitation improved ADLs and among patients with diseases other than COPD, such as IP as an underlying disease or pneumonia as the main disease on admission. Three months after taking baseline data prior to starting rehabilitation, physical activity levels had been maintained since discharge.

Several studies have shown that patients with acute exacerbation of COPD have a deteriorated ability to perform physical activity, QOL, and lung function after treatment completion.<sup>[25]</sup> Patients participated in fewer weight-bearing activities due to a decrease in skeletal muscle strength during an acute exacerbation,<sup>[25]</sup> and it is difficult to recover this strength loss even after one month.<sup>[25]</sup> According to Enrico et al, patients who were hospitalized for acute exacerbation of COPD had improved exercise tolerance, such as a greater 6MWD, after 4 weeks of pulmonary rehabilitation.<sup>[4]</sup> Similarly, we demonstrated that after completion of their primary treatment, hospitalized patients showed improvements in physical activity, such as a prolonged distance in the ISWT, after 2 weeks of pulmonary rehabilitation. More than 50% of all patients demonstrated increases in  $\Delta$ ISWT of more than 50 meters, which is greater than the minimal clinically important distance (47.5 meters).<sup>[26]</sup>

Table 3

Comparisons between the baseline and postrehabilitation timepoints among several diseases.											
	COPD as an underlying disease (n=9)			IP as an underlying disease (n=8)			Pneumonia as a main disease on admission (n = 11)				
	Baseline	Postrehabilitation	P value	Baseline	Postrehabilitation	P value	Baseline	Postrehabilitation	P value		
Age, median (IQR), year-old	81.0 (77.0-84.0)			79.0 (76.5-84.8)			80.0 (77.5-84.0)				
Male, n (%)	7 (77.8)			2 (25.0)			8 (72.7)				
ISWT distance, median (IQR), m	30 (20-80)	70 (40-130)	.014	65 (30-153)	140 (68-215)	.014	80 (20-150)	130 (95-205)	.004		
Barthel Index, median (IQR)	70 (55-80)	90 (80-100)	.014	85 (74-90)	90 (85-100)	.035	75 (55-90)	100 (83-100)	.005		
CAT score, median (IQR)	17 (13-21)	15 (13-19)	.726	18 (10-21)	10 (9-16)	.233	17 (13-23)	15 (10-22)	.247		
mMRC, median (IQR)	4.0 (3.0-4.0)	3.0 (2.0-4.0)	.037	3.0 (2.0-3.0)	2.0 (1.8-2.0)	.011	2.0 (2.0-3.5)	2.0 (1.0-2.5)	.011		
CES-D, median (IQR)	15 (6–16)	9 (7-19)	.360	12 (6-20)	6 (4-13)	.059	16 (6-19)	14 (9–19)	.693		
NRADL, median (IQR)	50 (29-55)	53 (52-72)	.075	43 (37-60)	53 (45-86)	.021	55 (51-68)	72 (55–85)	.023		
SPPB, median (IQR)	6 (6-9)	7 (6-9)	.140	7 (6-8)	8 (6-10)	.033	9 (6-9)	9 (7-11)	.089		

CAT = COPD assessment test, CES-D = center for epidemiologic studies for depression scale, ISWT = incremental shuttle walk test, mMRC = modified Medical Research Council, NRADL = Nagasaki University Respiratory ADL questionnaire, SPPB = short physical performance battery.

We also showed that many indicators other than ISWT, such as the BI, mMRC, NRADL, SPPB, and CES-D, were improved after 2 weeks of rehabilitation. The BI can evaluate ADLs and the risk of difficult discharge, and a BI score between 0 and 35 corresponds to a high risk, between 35 and 70 to a medium and over 75 to a low.<sup>[14]</sup> mMRC is useful for a severity assessment of not only COPD but also IP through clinical symptom evaluation.<sup>[27]</sup> ADLs and the mental state of patients are related to physical activity level<sup>[28,29]</sup>; the NRADL and SPPB scores evaluate ADLs, and the CES-D score evaluates mental state.<sup>[19,28]</sup> Eleven patients in our study showed a decrease in quartile of the *i*-BODE index, which predicts mortality, risk of hospitalization, and exacerbation.<sup>[23]</sup> From the above, inhospital pulmonary rehabilitation after treatment completion



Figure 2. The comparison of the ISWT results among 3 timepoints: baseline, postrehabilitation, and 3 months after baseline (Friedman test P < .001). IQR = interquartile range, ISWT = incremental shuttle walk test.

shows many benefits for patients who have not completely recovered their ability.

The particularly important thing in our study was that even 2 weeks of pulmonary rehabilitation was effective for patients with various respiratory diseases. Regarding Pitta et al report, the physical activity levels and lung function of patients with acute exacerbations of COPD were not improved by 7 days of inhospital rehabilitation.<sup>[25]</sup> Several previous studies have also reported results for ADLs in patients with acute exacerbation of COPD studied in 7 to 10-day hospital stays<sup>[16,25,30]</sup>; however, our study enrolled more elderly patients than those reports (median age 80 years vs 67.08 years,<sup>[16]</sup> vs 69 years,<sup>[25]</sup> vs 69.2 years<sup>[30]</sup>); hence, our patients might have involved more frail patients. These patients generally show low physical activity, muscle weakness, anorexia, osteoporosis, and so on.<sup>[31]</sup> Therefore, it would make sense for those patients to receive in-hospital pulmonary rehabilitation after treatment completion.

In Japan, 27% of the population is over 65 years of age, which is a higher percentage than that of any other country.<sup>[32]</sup> Other countries have large aging populations as well, and citizens over age 65 are expected to make up over 25% of the population in many countries by 2050.<sup>[32]</sup> In the future, the number of frail patients may increase in many countries; indeed, many elderly people experience frailty even with advanced medical care in recent years.<sup>[7]</sup> Elderly patients show a poorer ability to perform ADLs after discharge than before admission<sup>[6,33]</sup>; however, frail elderly patients can perform ADLs after 8 weeks of rehabilitation.<sup>[31]</sup> Therefore, patients with remaining symptoms after treatment completion might require a longer period of pulmonary rehabilitation. We can continue pulmonary rehabilitation for up to 60 days for patients who cannot leave the hospital upon finishing their primary treatment because our hospital established a regional comprehensive care ward in June 2017. However, only a few hospitals have this type of ward. Patients who cannot perform ADLs and who cannot leave the hospital after treatment completion in an acute care unit often move to a long-term care bed in a sanatorium, such as a hospital sanatorium ward or nursing home.<sup>[5,6]</sup> However, many elderly patients want to return to their home, even with a disease.<sup>[7]</sup> If those patients become able to go home after pulmonary rehabilitation subsequent to their treatment, there are many benefits, such as for patient QOL and society, including decreased medical costs. Hence, we consider that the social system should be coordinated, such as a regional comprehensive care ward for patients who need additional rehabilitation after treatment completion.

This investigation had several limitations. The study was performed as a single-center trial and included a relatively small number of patients. The study subject is heterogeneous with various pathologies and diagnoses. We thought proper periods of in-hospital pulmonary rehabilitation were different for each respiratory disease. Regarding the data from 3 months after taking baseline data prior to starting rehabilitation, approximately half of the patients were lost to follow-up. CAT, mMRC, and NRADL scores are used for the evaluation of patients with COPD; however, in our study, we also adopted these scores for patients with other respiratory diseases. The study could not set a control group; therefore, improvements in our patients could not be denied related to spontaneous resolution after treatment completion. However, a previous study demonstrated that the CAT score of patients with acute exacerbation of COPD returns to baseline a median of 11 days after exacerbation.<sup>[34]</sup> Patients in our study were included after treatment completion, and the median duration of hospitalization in the acute care unit was 18 days. Therefore, we considered that our patients had stayed enough time for spontaneous resolution before starting pulmonary rehabilitation for 2 weeks.

## 5. Conclusion

We demonstrated that patients who had remaining symptoms after primary treatment completion for respiratory diseases could improve their exercise capacity, symptoms, ADL, and mental status following 2 weeks of in-hospital pulmonary rehabilitation.

#### **Author contributions**

Conceptualization: Masafumi Shimoda.

- Data curation: Masafumi Shimoda, Satoshi Takao, Hiroyuki Kokutou, Naoyuki Yoshida, Keiji Fujiwara, Koji Furuuchi, Takeshi Osawa, Keitaro Nakamoto, Yoshiaki Tanaka, Kozo Morimoto, Ryozo Yano, Masao Okumura, Takashi Uchiyama, Kozo Yoshimori.
- Formal analysis: Masafumi Shimoda.
- Investigation: Masafumi Shimoda.
- Methodology: Masafumi Shimoda, Satoshi Takao.
- Project administration: Kozo Yoshimori.
- Software: Masafumi Shimoda.

Supervision: Masafumi Shimoda, Ken Ohta, Hideaki Senjyu.

Visualization: Masafumi Shimoda.

Writing - original draft: Masafumi Shimoda.

Writing – review & editing: Masafumi Shimoda, Satoshi Takao, Hideaki Senjyu.

## References

- [1] Spruit MA. Pulmonary rehabilitation. Eur Respir Rev 2014;23:55-63.
- [2] Rochester CL, Vogiatzis I, Holland AE, et al. An official American thoracic society/European respiratory society policy statement: enhancing implementation, use, and delivery of pulmonary rehabilitation. Am J Respir Crit Care Med 2015;192:1373–86.
- [3] Puhan MA, Gimeno-Santos E, Cates CJ, Troosters T. Pulmonary rehabilitation following exacerbations of chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2016;12:CD005305.
- [4] Clini EM, Crisafulli E, Costi S, et al. Effects of early inpatient rehabilitation after acute exacerbation of COPD. Respir Med 2009;103:1526–31.
- [5] De Saint-Hubert M, Schoevaerdts D, Cornette P, D'Hoore W, Boland B, Swine C. Predicting functional adverse outcomes in hospitalized older patients: a systematic review of screening tools. J Nutr Health Aging 2010;14:394–9.

- [6] Helvik AS, Selbaek G, Engedal K. Functional decline in older adults one year after hospitalization. Arch Gerontol Geriatr 2013;57:305–10.
- [7] Arai H, Ouchi Y, Toba K, et al. Japan as the front-runner of super-aged societies: Perspectives from medicine and medical care in Japan. Geriatr Gerontol Int 2015;15:673–87.
- [8] Guralnik JM, Ferrucci L, Pieper CF, et al. Lower extremity function and subsequent disability: consistency across studies, predictive models, and value of gait speed alone compared with the short physical performance battery. J Gerontol A Biol Sci Med Sci 2000;55:M221–31.
- [9] Phu S, Kirk B, Bani Hassan E, et al. The diagnostic value of the Short Physical Performance Battery for sarcopenia. BMC Geriatr 2020;20:242.
- [10] Chen LK, Woo J, Assantachai P, et al. Asian working group for sarcopenia: 2019 consensus update on sarcopenia diagnosis and treatment. J Am Med Dir Assoc 2020;21:300–7. e302.
- [11] Leone M, Duverge S, Kalinova E, Bui HT, Comtois AS. Comparison of bioenergetics of walking during a multistage incremental shuttle walk test and a 6-min walk test in active older adults. Aging Clin Exp Res 2017;29:239–46.
- [12] Ushiki A, Nozawa S, Yasuo M, et al. Associations between the distance covered in the incremental shuttle walk test and lung function and health status in patients with chronic obstructive pulmonary disease. Respir Investig 2017;55:33–8.
- [13] Parreira VF, Janaudis-Ferreira T, Evans RA, Mathur S, Goldstein RS, Brooks D. Measurement properties of the incremental shuttle walk test. a systematic review. Chest 2014;145:1357–69.
- [14] Strini V, Piazzetta N, Gallo A, Schiavolin R. Barthel Index: creation and validation of two cut-offs using the BRASS Index. Acta Biomed 2020;91 (2-S):19–26.
- [15] Garcia-Sidro P, Naval E, Martinez Rivera C, et al. The CAT (COPD Assessment Test) questionnaire as a predictor of the evolution of severe COPD exacerbations. Respir Med 2015;109:1546–52.
- [16] Zhou A, Zhou Z, Peng Y, Zhao Y, Duan J, Chen P. The role of CAT in evaluating the response to treatment of patients with AECOPD. Int J Chron Obstruct Pulmon Dis 2018;13:2849–58.
- [17] Zhou Z, Zhou A, Zhao Y, Chen P. Evaluating the Clinical COPD Questionnaire: a systematic review. Respirology 2017;22:251–62.
- [18] Takigawa N, Tada A, Soda R, et al. Comprehensive pulmonary rehabilitation according to severity of COPD. Respir Med 2007;101: 326–32.
- [19] Jiang L, Wang Y, Zhang Y, et al. The reliability and validity of the center for epidemiologic studies depression scale (CES-D) for Chinese University Students. Front Psychiatry 2019;10:315.
- [20] Shima S, Shikano T, Kitamura T, Asai M. New self-rating scale for depression. Seishin Igaku (Clinical Psychiatry) 1985;27:717–23. (Japanese).
- [21] Graham BL, Steenbruggen I, Miller MR, et al. Standardization of Spirometry 2019 Update. An Official American Thoracic Society and European Respiratory Society Technical Statement. Am J Respir Crit Care Med 2019;200:e70–88.
- [22] Kubota M, Kobayashi H, Quanjer PH, et al. Reference values for spirometry, including vital capacity, in Japanese adults calculated with the LMS method and compared with previous values. Respir Investig 2014;52:242–50.
- [23] Williams JE, Green RH, Warrington V, Steiner MC, Morgan MD, Singh SJ. Development of the i-BODE: validation of the incremental shuttle walking test within the BODE index. Respir Med 2012;106:390–6.
- [24] Kanda Y. Investigation of the freely available easy-to-use software 'EZR' for medical statistics. Bone Marrow Transplant 2013;48:452–8.
- [25] Pitta F, Troosters T, Probst VS, Spruit MA, Decramer M, Gosselink R. Physical activity and hospitalization for exacerbation of COPD. Chest 2006;129:536–44.
- [26] Singh SJ, Jones PW, Evans R, Morgan MD. Minimum clinically important improvement for the incremental shuttle walking test. Thorax 2008;63:775–7.
- [27] Rajala K, Lehto JT, Sutinen E, Kautiainen H, Myllarniemi M, Saarto T. mMRC dyspnoea scale indicates impaired quality of life and increased pain in patients with idiopathic pulmonary fibrosis. ERJ Open Res 2017;3(4.):84-2017.
- [28] Yoza Y, Ariyoshi K, Honda S, Taniguchi H, Senjyu H. Development of an activity of daily living scale for patients with COPD: the activity of daily living dyspnoea scale. Respirology 2009;14:429–35.
- [29] Pierobon A, Sini Bottelli E, Ranzini L, et al. COPD patients' self-reported adherence, psychosocial factors and mild cognitive impairment in pulmonary rehabilitation. Int J Chron Obstruct Pulmon Dis 2017; 12:2059–67.

- [30] He M, Yu S, Wang L, Lv H, Qiu Z. Efficiency and safety of pulmonary rehabilitation in acute exacerbation of chronic obstructive pulmonary disease. Med Sci Monit 2015;21:806–12.
- [31] Maddocks M, Kon SS, Canavan JL, et al. Physical frailty and pulmonary rehabilitation in COPD: a prospective cohort study. Thorax 2016;71:988–95.
- [32] Wan He DG, and Paul Kowel. An Aging World: 2015 International Population Reports. United States Census Bureau, International population reports., Series P-95, 16-1, 2016.
- [33] Seemungal TA, Donaldson GC, Bhowmik A, Jeffries DJ, Wedzicha JA. Time course and recovery of exacerbations in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2000;161:1608–13.
- [34] Mackay AJ, Donaldson GC, Patel AR, Jones PW, Hurst JR, Wedzicha JA. Usefulness of the chronic obstructive pulmonary disease assessment test to evaluate severity of COPD exacerbations. Am J Respir Crit Care Med 2012;185:1218–24.