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

A prospective intervention study

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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 5 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 compared to 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 pneumonia.
1. Introduction

Pulmonary rehabilitation is effective in improving the physical condition of patients with chronic respiratory disease \(^1,2\) and reducing the rate of hospital readmission within 4 weeks of prior hospitalization among patients with acute exacerbation of chronic obstructive pulmonary disease (COPD).\(^3\) 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.\(^4\) However, there have been no reports demonstrating the benefits of rehabilitation for respiratory diseases other than COPD and the appropriate duration of in-hospital 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.\(^5,6\) However, many patients want to return to their home, even with a disease,\(^7\) 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 in-hospital 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 ≥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.\(^8,9\) The Asian Working Group for Sarcopenia defines low physical performance as an SPPB score of 9 points or less;\(^10\) 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 1 patient 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 patient-tailored therapies that include exercise training, education, and

![Figure 1. Study flowchart of this study.](image-url)
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.[2] 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 one second, than the 6MWD.[11,12] Consequently, the ISWT is considered to be a more standardized test than the 6MWD.[12] The ISWT is a test imposing an incremental acceleration as the patient walks round trips on a 10-meter course.[12,13] The test includes 12 levels, and each level lasts 1 minute.[12,13] 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.[12,13] Oxygen saturation and pulse rate are monitored during the test.[12,13] 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.[12,13] The difference in the ISWT walking distance between the baseline and postrehabilitation timepoints was calculated as ΔISWT (ISWT[postrehabilitation] (m) – ISWT[baseline] (m)).[12,13]

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.[14] The CAT and mMRC are scales that are used to evaluate respiratory symptoms such as dyspnea for patients with COPD.[15–17] The NRADL is an ADL scale for patients with COPD.[18] The SPPB is a measurement of physical performance and extremity functional status.[19] The CES-D is an assessment of mental state and depression.[19] 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).[19,20] The decrease in the CAT score between the baseline and postrehabilitation timepoints was calculated as ΔCAT (CAT[postrehabilitation] - CAT[baseline]).

The pulmonary function test was conducted according to the American Thoracic Society protocol.[21] 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.[22]

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.[23] 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.[23]

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).[24] 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 ΔISWT or ΔCAT 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 ΔISWT 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 ≤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],
Aggravated respiratory failure after treatment
Receiving HOT before admission, n (%) 5 (20.8)

Duration of rehabilitation in acute care unit, median (IQR) day 20 (15–26)
Duration of hospitalization in regional comprehensive care ward, median (IQR) day 18 (15–26)
Duration of rehabilitation in acute care unit, median (IQR) day 9 (6–12)
Receiving HOT before admission, n (%) 5 (20.8)
Aggravated respiratory failure after treatment compared to before admission, n (%) 11 (45.8)

Table 2

Comparisons between the baseline and postrehabilitation time-points.

|                        | 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 (88–203) | <.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 (6–19) | .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-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.

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. Patents participated in fewer weight-bearing activities due to a decrease in skeletal muscle strength during an acute exacerbation, and it is difficult to recover this strength loss even after one month. 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. 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 ∆ISWT of more than 50 meters, which is greater than the minimal clinically important distance (47.5 meters).

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.

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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.\textsuperscript{14} mMRC is useful for a severity assessment of not only COPD but also IP through clinical symptom evaluation.\textsuperscript{27} ADLs and the mental state of patients are related to physical activity level\textsuperscript{28,29}; the NRADL and SPPB scores evaluate ADLs, and the CES-D score evaluates mental state.\textsuperscript{19,28} Eleven patients in our study showed a decrease in quartile of the i-BODE index, which predicts mortality, risk of hospitalization, and exacerbation.\textsuperscript{25} From the above, in-hospital pulmonary rehabilitation after treatment completion 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 in-hospital rehabilitation.\textsuperscript{25} Several previous studies have also reported results for ADLs in patients with acute exacerbation of COPD studied in 7 to 10-day hospital stays\textsuperscript{16,25,30}; however, our study enrolled more elderly patients than those reports (median age 80 years vs 67.08 years,\textsuperscript{16} vs 69 years,\textsuperscript{25} vs 69.2 years\textsuperscript{30}); hence, our patients might have involved more frail patients. These patients generally show low physical activity, muscle weakness, anorexia, osteoporosis, and so on.\textsuperscript{31} 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.\textsuperscript{32} 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.\textsuperscript{125} 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.\textsuperscript{7} Elderly patients show a poorer ability to perform ADLs after discharge than before admission\textsuperscript{6,33}; however, frail elderly patients can perform ADLs after 8 weeks of rehabilitation.\textsuperscript{141} 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.\textsuperscript{5,6} However, many elderly patients want to return to their home, even with a disease.\textsuperscript{7} 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.

### 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 (76.5–84.5) | .001     | 80.0 (77.5–84.0) | 8 (72.7) | .001     | 80 (75–205) | .004 |
| Male, n (%)                   | 7 (77.8) | 2 (25.0) | .141     | 8 (72.7) | 2 (25.0) | .141     | 120 (95–205) | .004 |
| mMRC, median (IQR), m         | 30 (20–80) | 65 (30–153) | .014     | 85 (74–90) | 10 (8–16) | .233     | 100 (83–100) | .005 |
| Barthel Index, median (IQR)   | 70 (55–80) | 85 (74–90) | .014     | 75 (55–90) | 10 (8–16) | .233     | 15 (10–22) | .247 |
| CAT score, median (IQR)       | 17 (13–21) | 18 (10–21) | .726     | 17 (13–21) | 10 (8–16) | .233     | 15 (10–22) | .247 |
| SPPB, median (IQR)            | 6 (6–9) | 6 (6–9) | .140     | 6 (6–9) | 6 (6–9) | .140     | 6 (6–9) | .140 |
| NRADL, median (IQR)           | 50 (29–55) | 43 (37–60) | .075     | 55 (51–68) | 53 (45–86) | .021     | 72 (55–85) | .023 |
| ISWT distance, median (IQR), m| 30 (20–80) | 65 (30–153) | .014     | 85 (74–90) | 10 (8–16) | .233     | 100 (83–100) | .005 |

**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.

![Figure 2](image-url) 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.
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 were 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. 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
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