ORIGINAL ARTICLE Probable Respiratory Sarcopenia Decreases Activities of Daily Living in Older Patients Hospitalized with **Respiratory Diseases: A Cross-sectional Study**

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Objectives: Respiratory sarcopenia is characterized by low respiratory muscle mass and respiratory muscle strength, but its impact on activities of daily living (ADL) remains unknown. We aimed to investigate the association between respiratory sarcopenia and decreased ADL. **Methods:** This retrospective cross-sectional study included older inpatients (\geq 65 years old) with respiratory diseases who underwent rehabilitation. Because the evaluation of respiratory muscle mass is challenging, probable respiratory sarcopenia was defined according to low appendicular skeletal muscle index ($<7 \text{ kg/m}^2$ for men, $<5.7 \text{ kg/m}^2$ for women) and peak expiratory flow rate (<4.4 L/s for men, <3.21 L/s for women). ADL was assessed on the first day of rehabilitation using the baseline Barthel Index (BI). Results: Of 111 inpatients (median age 75 years; 57 women), 13 (11.7%) had probable respiratory sarcopenia. Forty-five patients (40.5%) had sarcopenia and 12 of these had probable respiratory sarcopenia. Pulmonary functions (Forced Vital Capacity and expiratory volume in 1 s) were significantly lower in patients with probable respiratory sarcopenia than those without. Spearman's rank coefficient analysis showed probable respiratory sarcopenia did not significantly correlate with age, phase angle, Charlson Comorbidity Index (CCI), or hemoglobin (Hb). Multivariate linear regression analysis with baseline BI revealed probable respiratory sarcopenia (β -0.279 and P=0.004) was the significant factor after adjusting for age, sex, body mass index, chronic obstructive pulmonary disease, CCI, and Hb. Conclusions: Probable respiratory sarcopenia was independently associated with decreased ADL in patients aged 65 years and older who were hospitalized with respiratory diseases.

Key Words: activities of daily living; respiratory diseases; respiratory sarcopenia; sarcopenia

INTRODUCTION

Respiratory sarcopenia is a medical condition characterized by low respiratory muscle mass and strength.^{1,2)} It differs from sarcopenia, which is characterized by low appendicular skeletal muscle mass, muscle strength, and physical function.³⁾ Shortness of breath, dyspnea, reduced coughing ability, and aspiration pneumonia caused by respiratory sarcopenia can result in decreased activities of daily living (ADL). Therefore, it is crucial to assess respiratory

sarcopenia because of the unfavorable impact of low ADL on mortality.4,5)

Sarcopenia is a risk factor for decreased ADL.³⁾ The prevalence of sarcopenia in patients with primary lung cancer, interstitial pneumonia, and chronic obstructive pulmonary disease (COPD) is 45%,⁶⁾ 32.1%,⁷⁾ and 21.6%,⁸⁾ respectively. Low respiratory function, which reflects low respiratory muscle strength,¹⁾ is associated with decreased ADL⁹⁾ and sarcopenia in older adults.¹⁰⁾ One study found that ADL independence was lower in older adults with sarcopenia and

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low respiratory function than in those with only low respiratory function or robust groups.¹¹⁾ These findings suggest that some older patients with respiratory diseases have decreased appendicular skeletal muscle mass and low respiratory function, similar to older patients with sarcopenia. Therefore, respiratory sarcopenia could likely lead to a decline in ADL in patients with respiratory diseases, because many patients may exhibit low respiratory function. In the current study, we aimed to investigate the association between respiratory sarcopenia and decreased ADL in older hospitalized patients with respiratory diseases.

MATERIALS AND METHODS

Patients

This retrospective cross-sectional study included 122 patients (aged \geq 65 years) who were hospitalized with respiratory diseases and underwent pulmonary rehabilitation at the University of Occupational and Environmental Health Hospital between February 2022 and January 2023. Typically, patients received rehabilitation for airway clearance, improvement of muscle strength, or improvement in ADL ability. All data were collected from medical records. We considered only hospitalized patients who underwent a physical function evaluation a few days after rehabilitation started and a pulmonary function test within 60 days before or 7 days after rehabilitation started. All patients underwent rehabilitation within 2 weeks after hospitalization. Hospitalized patients with missing data or a history of lung surgery were excluded. This study followed the Declaration of Helsinki and was approved by the Ethics Committee of the University of Occupational and Environmental Health [UOEHCRB20-155]. The study's retrospective nature did not require written consent, but patients were provided with the option to withdraw from the study at any time.

Spirometry

Physicians in primary departments requested medical technologists to assess the adequacy of respiratory function for surgery, disease severity, and treatment efficacy. Medical technologists conducted the pulmonary function tests using an electronic spirometer (FUDAC-7, Fukuda Denshi, Tokyo, Japan) based on the official guidelines of the Japanese Respiratory Society.¹²⁾ Patients were instructed to firmly hold the mouthpiece connected to the spirometer with their lips and clamp their noses to prevent air leakage. After normal breathing, they were instructed to take a deep inhalation from the maximal expiratory level to the maximal inspira-

tory level and then forcefully exhale in one continuous breath back to the maximal expiratory level. Practice trials preceded the test, and re-measurements were taken as necessary. The use of bronchodilators or inhaled steroids during the test was documented in the medical records. The forced vital capacity (FVC), forced expiratory volume in 1 s (FEV₁), and peak expiratory flow rate (PEFR) were assessed. PEFR represents the peak of the flow-volume curve captured by the spirometer, reflecting the highest airflow rate achieved during a forceful exhalation. PEFR is known to decline with age¹³⁾ and is related to respiratory muscle strength¹⁴⁾ and sarcopenia.¹⁵⁾

Assessment of Physical Function

Physical rehabilitation was prescribed according to the patient's condition and was started on the day of the visit to the Department of Rehabilitation Medicine. Physical function evaluation included handgrip strength, physical function (gait speed, short physical performance battery, or five-time chair stand test), and body composition using a bioimpedance device (InBody S10, InBody, Tokyo, Japan) at least 2 h after eating and after 10 min of rest in the supine position. The InBody S10 enabled the evaluation of the appendicular skeletal muscle index (SMI) and phase angle (PhA) by incorporating age, sex, height, and weight. PhA reflects the resistance and reactance of the whole body and is related to sarcopenia.¹⁶⁾ The Barthel Index (BI)¹⁷⁾ was used to evaluate ADL on the day rehabilitation started (baseline BI). The BI comprises scores on a scale of 0-100, with higher scores indicating better ADL functioning. The BI items included (1) feeding, (2) grooming, (3) dressing, (4) transferring, (5) bladder management, (6) bowel management, (7) toileting, (8) bathing, (9) walking, and (10) climbing up and down.

Definition of Probable Respiratory Sarcopenia and Sarcopenia

Given the paucity of data defining respiratory muscle mass, a more definitive diagnosis of respiratory sarcopenia is needed. However, while it is known that respiratory muscle mass is associated with trunk muscle mass,¹⁸⁾ there is no clear cutoff value that indicates a reduction in trunk muscle mass. According to a position paper published by four Japanese professional organizations (Society for Respiratory Care and Rehabilitation, Association for Sarcopenia and Frailty, Society of Respiratory Physical Therapy, and Association of Rehabilitation Nutrition),¹⁾ probable respiratory sarcopenia rather than respiratory sarcopenia can be defined in cases where the appendicular skeletal muscle mass falls

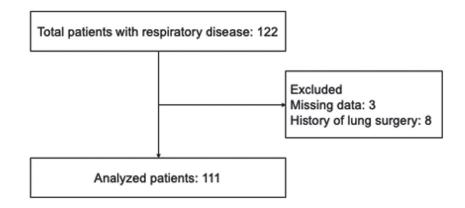


Fig. 1. Flowchart of patient recruitment.

below cutoff values defined by the Asian-Working Group for Sarcopenia (AWGS) 2019, which are used as a surrogate for the decline in respiratory muscle mass. To define probable respiratory sarcopenia, we adopted the cutoff values of SMI from AWGS 2019 (SMI $<7 \text{ kg/m}^2$ for men and $<5.7 \text{ kg/m}^2$ for women)³⁾ and cutoff values of low respiratory muscle strength (PEFR <4.4 L/s for men and <3.21 L/s for women) according to a previous report.¹⁵⁾ To define sarcopenia, we also used the AWGS 2019,³ with low appendicular skeletal muscle mass indicated by SMI less than 7 kg/m² for men and less than 5.7 kg/m² for women, in combination with low muscle strength as indicated by at least one of the following: low handgrip strength (<28 kg for men or <18 kg for women), low physical performance (gait speed <1 m/s), short physical performance battery (≤9 points), or slow five-time chair stand test (≥ 12 s).

Collecting Other Data

Respiratory disease types were categorized into primary lung cancer, interstitial pneumonia, COPD, asthma, and other diseases. We investigated age, sex, body mass index (BMI), comorbidities, history of stroke, the Charlson Comorbidity Index (CCI),¹⁹⁾ Brinkman Index,²⁰⁾ serum albumin, hemoglobin (Hb), C-reactive protein levels (CRP), and preadmission orientation. The CCI, serum albumin, Hb, and CRP were recorded at admission.

Statistical Analysis

Statistical analyses were performed using SPSS Version 27 (IBM SPSS Japan, Tokyo, Japan); the bilateral test set P<0.05 as statistically significant. Categorical variables were expressed as number (percentage), whereas quantitative variables were expressed as median [interquartile range] or mean (standard deviation) according to the normality of

the Shapiro–Wilk test. Categorical variables were analyzed using the chi-square test and Fisher's test to compare older patients with and without probable respiratory sarcopenia. Quantitative variables were subjected to the t-test and Mann– Whitney U test based on the normality of the Shapiro–Wilk test.

Spearman's rank correlation coefficient analysis evaluated the association among probable respiratory sarcopenia, age, BMI, CCI, PhA, Hb, and baseline BI. Age,³⁾ BMI,³⁾ CCI,²¹⁾ PhA,¹⁶) and Hb²²) have been reported to be associated with sarcopenia. To investigate the association between ADL and probable respiratory sarcopenia, we performed multivariate linear regression analysis of baseline BI with age, sex, BMI, COPD, CCI, Hb, and probable respiratory sarcopenia. The Variance Inflation Factor (VIF) among factors in the multivariate linear regression model was then calculated. Comorbidity is associated with decreased ADL in older adults.²³⁾ BMI²⁴⁾ and Hb²⁵⁾ are also associated with decreased ADL. Given that multivariate linear regression analysis necessitates a minimum of 15 cases per independent variable, this study required at least 105 cases to accommodate the seven variables in the model. Multicollinearity was assessed using the VIF, where a VIF value between 1 and 3 indicates the absence of multicollinearity.

RESULTS

A total of 122 hospitalized patients (aged \geq 65 years) with respiratory diseases were evaluated; 3 patients were excluded because of missing data and 8 were excluded because of previous lung surgery (**Fig. 1**). Therefore, this study included 111 patients with respiratory diseases [median age, 75 years; 57 women (51.4%)]. Respiratory disease types included primary lung cancer (n=59), interstitial pneumonia (n=52), COPD (n=10), asthma (n=6), and others (n=9). Others were metastatic lung tumors (n=5), benign lung tumors (n=2), and mediastinal tumors (n=2).

Seven patients had primary lung cancer and interstitial pneumonia, and 9 patients had primary lung cancer and COPD. Twenty patients regularly used bronchodilators or inhaled steroids at the time of the pulmonary function test, but no patients used them during the pulmonary function test to assess airway reversibility. In total, 68 patients were in the preoperative stage for surgery. The number of patients with probable respiratory sarcopenia was 13 (11.7%), and 12 of them had sarcopenia. Forty-five (40.5%) had sarcopenia, and 27 of them had low PEFR.

Table 1 shows the characteristics and comparisons of patients with probable respiratory sarcopenia and those without probable respiratory sarcopenia. Patients with probable respiratory sarcopenia had a higher incidence of COPD (P=0.022), lower BMI (P=0.004), more regular use of bronchodilators or inhaled steroids (P=0.002), lower handgrip strength (P<0.001), lower SMI (P<0.001), more cases of sarcopenia (P<0.001), and lower scores on the baseline BI (P=0.007)than patients without probable respiratory sarcopenia. PhA tended to be lower in patients with probable respiratory sarcopenia than in patients without (P=0.068). In the pulmonary function tests, patients with probable respiratory sarcopenia exhibited lower FVC, FEV₁, and PEFR (P<0.013, P<0.001, and P<0.001, respectively) than patients without probable respiratory sarcopenia. However, no significant difference was observed in the FEV₁/FVC ratio between patients with and without probable respiratory sarcopenia (P=0.155).

Spearman's rank correlation coefficient analysis showed that probable respiratory sarcopenia had a significant correlation with BMI (ρ –0.274, P=0.004) and baseline BI (ρ –0.255, P=0.007) but no significant correlation with sarcopenia-related factors such as age (ρ 0.13, P=0.174), CCI (ρ 122, P=0.205), PhA (ρ –0.174, P=0.068), and Hb (ρ –0.066, P=0.494). A multivariate linear regression analysis with the baseline BI (adjusted R²=0.173, P<0.001) revealed that probable respiratory sarcopenia (β –0.279, P=0.004) was the significant factor after adjusting for age, sex, BMI, COPD, CCI, and Hb (**Table 2**). Multicollinearity was not observed among them.

DISCUSSION

This study investigated the association between probable respiratory sarcopenia and ADL in patients aged 65 years or over who were referred to our Department of Rehabilitation Medicine for treatment of respiratory diseases. The prevalence of probable respiratory sarcopenia in these patients was 11.7%, based on our operational definition. We found that probable respiratory sarcopenia was independently associated with decreased ADL. Based on our definition of probable respiratory sarcopenia that we adopted from a position paper by four Japanese health organizations,¹⁾ we believe this study to be the first to associate probable respiratory sarcopenia with decreased ADL in older inpatients with respiratory diseases.

The position paper on the diagnosis of respiratory sarcopenia¹⁾ recommends evaluating respiratory muscle mass by ultrasonography or computed tomography and respiratory muscle strength based on the maximal inspiratory and/or expiratory pressure in the pulmonary function test. For cases in which the assessment of respiratory muscle mass is challenging, the appendicular skeletal muscle mass can be used to determine respiratory muscle mass, and probable respiratory sarcopenia can be diagnosed. PEFR, peak cough flow, and sniff nasal inspiratory pressure can be used to evaluate respiratory muscle strength. However, low respiratory muscle strength cutoff values still need to be established. There are few studies on the association between sarcopenia and low PEFR^{9,15)} in older adults. Kera et al.¹⁵⁾ set the cutoff values in the PEFR for respiratory sarcopenia (4.4 L/s for men and 3.21 L/s for women) as the only indicator of respiratory muscle strength to confirm sarcopenia and long-term care insurance among community-dwelling older adults. Therefore, following the algorithm definition of four Japanese health organizations for probable respiratory sarcopenia,¹⁾ we used SMI cutoff values for low appendicular skeletal muscle mass (7 kg/m² for men and 5.7 kg/m² for women) and PEFR cutoff values for low respiratory function (4.4 L/s for men and 3.21 L/s for women) based on previous reports.^{3,15)}

PEFR is influenced by airway stenosis.²⁶⁾ Our study showed no difference in the FEV₁/FVC ratio between patients with and without probable respiratory sarcopenia. Furthermore, FVC and FEV₁ were lower in patients with probable respiratory sarcopenia. Therefore, despite the impact of airway obstruction on PEFR, the findings suggest that respiratory muscle strength is lower in patients with probable respiratory sarcopenia than those without it.

The prevalence of sarcopenia among those with probable respiratory sarcopenia is expected, given that SMI is used as a surrogate for respiratory muscle mass. However, this study revealed that probable respiratory sarcopenia did not significantly correlate with potential factors associated with sarcopenia, such as age, PhA, or Hb. PhA has been reported

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	Overall (n=111)	With probable RS (n=13)	Without probable RS (n=98)	P value	
Age, years	75 [71–81]	78 [74.5–81.5]	75 [70.5–81]	0.172	
Sex, female	57 (51.4%)	7 (53.8%)	50 (51%)	0.848	
BMI, kg/m ²	23 [20.6–25.2]	20.1 [19.1–22.3]	23.3 [21–25.4]	0.004	
Respiratory disease					
Primary lung cancer	59 (53.2%)	9 (69.2%)	50 (51%)	0.23	
Interstitial pneumonia	52 (46.8%)	3 (23%)	49 (50%)	0.063	
COPD	10 (14.4%)	3 (23%)	7 (7.1%)	0.022	
Asthma	6 (5.4%)	2 (11.7%)	4 (3.6%)	0.147	
Others	9 (8.1%)	1 (0.9%)	8 (8.1%)	0.712	
Comorbidities					
Hypertension	52 (46.8%)	6 (46.2%)	46 (46.9%)	1	
Diabetes mellitus	27 (24.3%)	2 (15.4%)	25 (25.5%)	0.731	
Chronic heart failure	7 (6.3%)	1 (7.7%)	6 (6.1%)	0.593	
Atrial fibrillation	8 (7.2%)	1 (7.7%)	7 (7.1%)	1	
Kidney failure	12 (10.8%)	2 (15.4%)	10 (10.2%)	0.631	
Cancer, other than lung	15 (13.5%)	1 (7.7%)	14 (14.3%)	1	
Connective tissue disease	50 (45%)	4 (30.8%)	46 (46.9%)	0.271	
History of stroke	9 (8.1%)	3 (23.1%)	6 (6.1%)	0.07	
CCI	2 [1–3]	3 [0.5–3.5]	2 [1–3]	0.203	
Bronchodilators or inhaled steroids use	20 (18%)	7 (53.8%)	13 (13.3%)	0.002	
Brinkman Index	495 [0-992]	660 [367–1240]	400 [0-900]	0.058	
Low handgrip strength	69 (62.1%)	12 (17.4%)	57 (82.6%)	0.017	
Low SMI	51 (45.9%)	13 (100%)	38 (38.8%)	< 0.001	
Sarcopenia	45 (40.5%)	12 (92.3%)	33 (33.7%)	< 0.001	
PhA, °	4.5 [3.7–5.1]	4.2 [3.6-4.4]	4.5 [3.7–5.2]	0.068	
FVC, L	2.34 (0.89)	1.76 (0.57)	2.41 (0.88)	0.013	
FEV ₁ , L	1.69 (0.59)	1.09 [0.76–1.37]	1.72 [1.34–2.19]	< 0.001	
FEV ₁ /FVC, %	75.1 (13.6)	79.8 [72.6-88.6]	71.6 [65.8-82.6]	0.155	
PEFR, L/s	5.24 [3.93-6.82]	2.96 [2.43-3.04]	5.55 [4.28-7.41]	< 0.001	
Low PEFR	40 (36%)	13 (100%)	27 (27.5%)	< 0.001	
Serum albumin, g/dL	3.8 [3.5-4.2]	3.7 [3.4–4.1]	3.9 [3.5–4.2]	0.541	
Hb, g/dL	12.3 [11–13.8]	12.3 [10.3–13.6]	12.4 [11.1–13.9]	0.491	
CRP, mg/dL	0.24 [0.06-0.88]	0.24 [0.13-0.66]	0.24 [0.06-0.94]	0.945	
Baseline Barthel Index	95 [85–100]	65 [55–100]	100 [90–100]	0.007	
Preadmission orientation					
Home	106 (95.6%)	11 (84.6%)	95 (96.9%)	0.104	
Nursing home	3 (2.7%)	1 (7.7%)	2 (2%)	0.104	
Another hospital	2 (1.8%)	1 (7.7%)	1 (1%)		

Table 1. Patie	ent characteristics and	l comparison l	between patients	with and withou	t probable r	espiratory s	arcopenia
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Categorical variables are given as number (percentage); quantitative variables are given as median [interquartile range]; some data for FVC and FEV_1 given as mean (standard deviation). CCI, serum albumin, Hb, and CRP were assessed at admission. BMI, handgrip strength, SMI, and PhA were assessed a few days after rehabilitation started. Baseline BI was assessed on the first day of rehabilitation.

RS, respiratory sarcopenia.

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	В	ß	95% confidence interval	P value	VIF
	D	p	93% confidence filter var	r value	V II
Probable respiratory sarcopenia	-16.118	-0.279	-26.904 to -5.333	0.004	1.155
Age	-0.365	-0.123	-0.889 to 0.158	0.169	1.031
Female	-6.732	-0.179	-13.502 to 0.037	0.051	1.08
BMI	0.627	0.126	-0.276 to 1.530	0.917	1.091
COPD	6.558	0.101	-5.260 to 18.376	0.274	1.10
CCI	-1.174	-0.095	-3.366 to 1.017	0.290	1.052
Hb	0.342	0.136	-0.099 to 0.784	0.127	1.052

Table 2. Multivariate linear regression analysis of probable respiratory sarcopenia with baseline BI

Adjusted $R^2=0.173$, P<0.001. CCI and Hb were recorded at admission. Baseline BI was assessed on the first day of rehabilitation.

as a useful indicator of sarcopenia in various studies.^{16,27)} In our results, patients with probable respiratory sarcopenia tended to have lower PhA values than those without, indicating a potential negative association. However, these trends did not reach statistical significance. Although PhA is associated with grip strength and skeletal muscle mass,^{16,27)} its relationship with respiratory function remains to be elucidated. Consequently, our findings did not conclusively determine the relevance of PhA to PEFR. This highlights the need for further research to clarify the role of PhA in assessing respiratory muscle strength and function.

Patients with respiratory diseases experience a limited capacity to perform ADL because of respiratory symptoms.^{28,29)} However, it is difficult to demonstrate a decline in ADL using comprehensive ADL assessment scales,³⁰⁾ such as the BI. Because of the adverse effects of severe dyspnea on motor endurance and subsequent decreased ADL, assessment tools that incorporate the degree of dyspnea have been developed.^{31,32)} Given that respiratory function reflects respiratory symptoms, probable respiratory sarcopenia might indicate respiratory symptoms and help detect a statistically significant decline in the comprehensive ADL. Although the adjusted coefficient of determination of the multivariate regression model in this study did not fit well, the standardized partial regression coefficient for probable respiratory sarcopenia indicated that it was closely related to decreased ADL.

"Sarcopenic respiratory disability" defines functional disability resulting from reduced respiratory function caused by respiratory sarcopenia.²⁾ However, our study has not conclusively shown significant impairment caused by respiratory muscle sarcopenia. More research is needed to understand its impact on respiratory function and functional disability.

LIMITATIONS

This study has some limitations. First, the diagnosis of respiratory sarcopenia in this study was probable rather than definitive. The concept of "probable respiratory sarcopenia" was operationalized because of the need for established diagnostic criteria and the paucity of data directly defining respiratory muscle mass. As a result, our results should be interpreted with the understanding that they do not provide a definitive diagnosis of respiratory sarcopenia but rather an association with ADL limitations based on a probable condition associated with decreased respiratory muscle mass and function. Further research is required to refine the diagnostic criteria for respiratory sarcopenia, allowing for a more definitive respiratory muscle mass and understanding its impact on ADL. Second, the generalizability of the study is limited because of its retrospective and single-center design. Third, the causal association between probable respiratory sarcopenia and decreased ADL was not addressed because of the retrospective cross-sectional nature of the study. Fourth, many of the included patients were in the preoperative stages of lung cancer. This may have introduced a potential selection bias because these patients differ from patients with common respiratory diseases. Fifth, because not all evaluations were conducted within a few days, each evaluation might have incurred pathological alterations.

CONCLUSION

The results of this study showed that probable respiratory sarcopenia was independently associated with decreased ADL in patients aged 65 years and over who were hospitalized with respiratory diseases. Further investigations are warranted to establish the parameters and threshold values from pulmonary function tests that can accurately delineate low respiratory muscle strength, thereby providing definitive diagnostic criteria for respiratory sarcopenia.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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