

# Effect of Pulmonary Rehabilitation on Erector Spinae Muscles in Individuals With COPD

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**BACKGROUND:** A recent paper reported that low muscle mass in the erector spinae muscles (ESM) was strongly associated with poor prognosis and declining muscle mass over time in subjects with COPD. However, effects of pulmonary rehabilitation (PR), if any, on ESM mass have not been reported. We hypothesized that PR reduces the annual decline in ESM mass. **METHODS:** This was a retrospective cohort study. Thirty-nine subjects with COPD who received PR and underwent chest computed tomography before and after PR were evaluated (rehabilitation group). We also evaluated 39 age-matched subjects with COPD who did not receive PR (nonrehabilitation group). Data were collected from August 2010 until March 2020 in both groups. The ESM cross-sectional area ( $ESM_{CSA}$ ) was measured using axial computed tomography images, and annual changes were calculated. The 6-min walk distance (6MWD) was measured before and after PR; the minimum clinically important difference was defined as 30 m. **RESULTS:**  $ESM_{CSA}$  declined in the nonrehabilitation group over time ( $-116.0 \pm 141.2 \text{ mm}^2/\text{y}$ ) but increased in the PR group ( $51.0 \pm 95.3 \text{ mm}^2/\text{y}$ ;  $P < .001$ ). The annual increase in  $ESM_{CSA}$  was significantly higher among subjects with an increase in 6MWD that exceeded the minimum clinically important difference compared with nonresponders in the rehabilitation group. The annual change in  $ESM_{CSA}$  was negatively correlated with comorbidity index, and triple therapy (long-acting  $\beta_2$ -agonist/long-acting muscarinic antagonist/inhaled corticosteroid) had a favorable effect on annual change in  $ESM_{CSA}$ . Multiple regression analysis revealed that only PR was an independent factor for annual change in  $ESM_{CSA}$ . **CONCLUSIONS:** ESM mass was shown to decline yearly in subjects with COPD. The annual decline in muscle mass was reduced by PR. *Key words:* COPD; rehabilitation; skeletal muscle; computed tomography; rehabilitation outcome. [Respir Care 0;0(0):1–●. © 0 Daedalus Enterprises]

## Introduction

Skeletal muscle dysfunction and atrophy are key systemic consequences of COPD and have important clinical implications, such as reduced exercise tolerance, quality of life, and even survival.<sup>1</sup> Sarcopenia describes age-related loss of skeletal muscle. The prevalence of sarcopenia is 14.5–24% in patients with COPD and increases with age and disease severity.<sup>2,3</sup> Although body mass index (BMI) is indicative of basic nutritional status and has been reported to predict mortality in subjects with COPD,<sup>4</sup> BMI is not sensitive to changes in body composition as it can be normal or even increased despite the occurrence of muscle wasting.<sup>5,6</sup> McDonald et al<sup>7</sup> reported that the pectoralis muscle area was more significantly associated with COPD-related traits,

including pulmonary function, dyspnea sensation, and exercise capacity, compared with BMI using existing computed tomography (CT) scans in a previous epidemiologic study. The pectoralis muscle is an accessory respiratory muscle that contributes to inspiration,<sup>8</sup> and the cross-sectional area (CSA) of muscles is correlated with pulmonary function parameters, such as FEV<sub>1</sub> and FVC.<sup>7</sup> Tanimura et al<sup>9</sup> reported that the CSA of the mass of the erector spinae muscles ( $ESM_{CSA}$ ) is the strongest risk factor for mortality compared with other clinical parameters including lung function,  $P_{aO_2}$ , BMI, modified Medical Research Council (mMRC) dyspnea scale, comorbidity indexes, St George Respiratory Questionnaire score, prior COPD exacerbations, and smoking history in subjects with COPD. These investigators also reported that  $ESM_{CSA}$  decreased yearly in subjects with

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COPD.<sup>10</sup> Because the trunk muscles, including ESM, have an important role in stabilizing the body, maintaining posture, and controlling spinal and pelvic movement, atrophy of these muscles may lead to an increase in the risk of falling and disability in activities of daily living in elderly people and patients with COPD.<sup>11,12</sup>

Both pectoralis muscles and ESMs can be assessed with chest CT. Because chest CT is usually performed to diagnose and evaluate emphysema and to exclude other critical pulmonary diseases, such as lung cancer and pulmonary fibrosis, these images may simultaneously be used to evaluate local skeletal muscle mass without a need for additional radiation exposure.

A previous study reported that pulmonary rehabilitation (PR) enhanced lower limb muscle function and increased muscle mass<sup>13</sup>; however, the effect of PR on ESMs or pectoralis muscles has not been evaluated. We hypothesized that PR increases muscle mass for both ESM and pectoralis muscles and reduces the annual decline in muscle mass.

## Methods

### Subjects and Study Design

This was a retrospective cohort study. The Ethics Committee of Kindai University approved this study (approval number, R02-012) and authorized a waiver of consent. Confidentiality of subject information was guaranteed. The study was conducted in accordance with the Declaration of Helsinki. The basic information in this study has been registered with the University Hospital Medical Information Network Clinical Trials Registry (UMIN 00042233).

Medical records were reviewed to evaluate the effect of PR on ESM mass in subjects with COPD. A total of 89 subjects (age range, 51–91 y) with COPD were referred to the

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Supplementary material related to this paper is available at <http://www.rcjournal.com>.

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## QUICK LOOK

### Current knowledge

Skeletal muscle dysfunction and atrophy are key systemic consequences of COPD and have important clinical implications, such as reduced exercise tolerance, quality of life, and survival. Erector spinae muscle (ESM) mass is the strongest risk factor for mortality and decreases year by year.

### What this paper contributes to our knowledge

We used computed tomography to evaluate the effect of pulmonary rehabilitation (PR) on the annual change of ESM mass in subjects with COPD. ESM cross-sectional areas declined in subjects who did not receive PR and increased in subjects who received PR. Our results indicate that PR can effectively improve ESM in subjects with COPD.

out-patient PR program at Kindai University Hospital (Osaka, Japan) from August 2010 until March 2020. Seventy-one subjects completed the PR program (Fig. 1). Subjects were considered to have completed the program if they attended at least 12 sessions, given that most professional society guidelines recommend a minimum of 12 supervised sessions.<sup>14,15</sup> Among the 71 subjects, 41 had 2 CT scans (before and after the PR program). Chest CT scans were performed at the physician's discretion to evaluate emphysema or to exclude the possibility of lung cancer, irrespective of this study. Therefore, a CT scan was not performed routinely in PR program attendees, and the interval between CT scans varied because of the retrospective nature of this observational study. Two subjects were excluded from the analysis because the CT scans were performed at the time of admission during a COPD exacerbation. A previous study reported that ESMs are affected by such exacerbations.<sup>10</sup> Therefore, 39 subjects who completed the PR program were evaluated in this study (rehabilitation group). We also evaluated 39 age-matched out-patients with COPD who did not participate in the PR program and had 2 CT scans (non-rehabilitation group). All subjects in both groups were diagnosed with COPD and treated in the Department of Respiratory Medicine and Allergology of Kindai University Hospital. The diagnosis and classification of COPD were made according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines.<sup>16</sup>

The out-patient PR program was conducted twice a week for 12 weeks (24 sessions), and the PR maintenance program consisted of supervised endurance training once or twice per month. Each session consisted of respiratory muscle stretch gymnastics,<sup>17</sup> followed by endurance training involving the lower limbs through exercise on a treadmill

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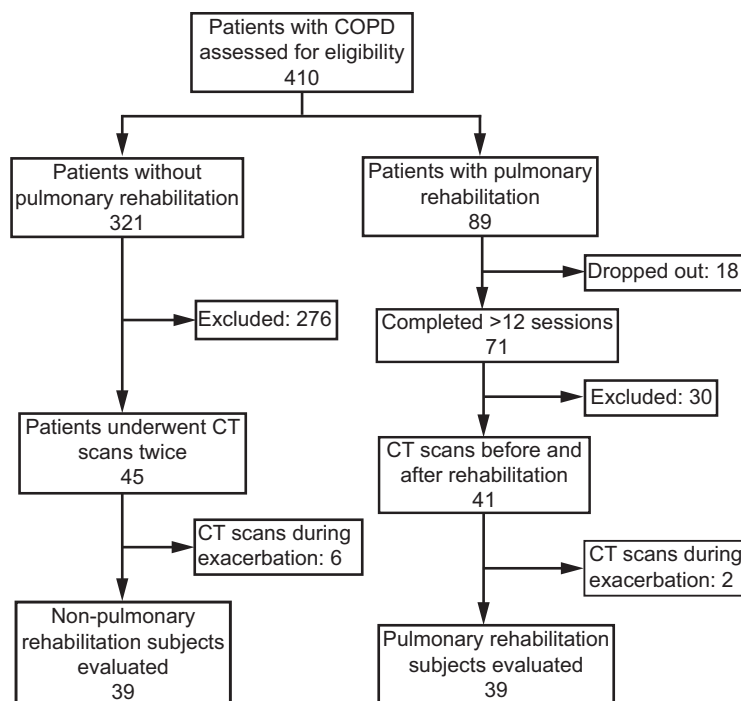


Fig. 1. Flow chart. CT = computed tomography.

or ergometric bicycling at 60–70% of peak work load for 20–40 min, and strength training of the upper and lower limbs for 10–20 min, as previously described in previous study.<sup>14</sup> Respiratory muscle stretch gymnastics is designed to decrease chest wall stiffness, particularly of the respiratory muscles, because the majority of subjects with COPD had reduced chest wall mobility.<sup>17,18</sup>

### Clinical Variables

Clinical data were retrieved from the medical files and included pulmonary function, current medications, smoking history, medical history, past COPD exacerbations, and comorbidities. Comorbidity indices (Charlson comorbidity index and COPD-specific comorbidity test) were calculated, as reported previously.<sup>14,19,20</sup> We monitored severe exacerbations requiring hospitalization. All patients included in the study underwent spirometry (CHEST AC-55V; Chest, Tokyo, Japan), according to the method described in the American Thoracic Society guidelines.<sup>21</sup> The single-breath diffusing capacity of the lung for carbon monoxide ( $D_{LCO}$ ) was also measured.<sup>22</sup> The values for total lung capacity, FVC, residual volume, FEV<sub>1</sub>, and  $D_{LCO}$  were related to the percentage of the predicted values.<sup>23,24</sup> Exercise tolerance was assessed before and after the PR program by measuring the 6-min walk distance (6MWD) in accordance with the American Thoracic Society guidelines.<sup>25</sup> The 6MWD was measured in the rehabilitation group, but not in the non-rehabilitation group. The minimum clinically important difference

in the 6MWD was defined as an increase > 30 m.<sup>26</sup> Responders to pulmonary rehabilitation for exercise capacity were defined as having a 30-m increase in the 6MWD.

### CT Scan Acquisition and Analysis

ESM<sub>CSA</sub> was measured using axial chest CT images at the level of the lower margin of the 12th thoracic vertebra with a manually drawn line depicting the ESM<sub>CSA</sub>.<sup>9,10,27</sup> ESM<sub>CSA</sub> is presented as the sum of the bilateral sectional areas calculated using the medical imaging and information management system (SYNAPSE 4.4.3, Fujifilm Medical, Tokyo, Japan; see the supplementary materials at <http://www.rcjournal.com>).<sup>9,10,27</sup> The CSA of the pectoralis muscle (PM<sub>CSA</sub>) was also determined based on a single axial CT scan slice above the aortic arch, as described previously.<sup>7,9</sup> (see the supplementary materials at <http://www.rcjournal.com>). Emphysema was quantified by calculating the percentage of the low-attenuation area, determined using a cutoff value of –950 HU on whole-lung CT images using Synapse Vincent (Fujifilm Medical).<sup>9</sup> Annual changes in the CSA of muscles were calculated from 2 CT scans using the following formula: (CSA in second CT scan – CSA in first CT scan)/(interval between two CT scans [in years]).

### Statistical Analysis

Descriptive statistics were calculated for continuous variables, as represented by mean ± SD (assumed to follow a

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normal distribution), median (interquartile range [IQR]; assumed to follow a non-normal distribution), and categorical variables by  $n$  (%). To compare 2 groups for parameters, we used the Student  $t$  test (for continuous variables with normal distributions), the Wilcoxon rank-sum test (for non-normal distributions), and the chi-square test (for categorical variables). The Shapiro-Wilk test was used to determine whether the distribution was normal. For comparison of the annual change of muscle CSA between groups (with vs without PR; responders vs non-responders), we performed linear regression using study groups and baseline values as explanatory variables. Correlations between parameters were assessed using Spearman's correlation analysis. Correlation coefficients  $< 0.4$  were considered to be weak, and those from 0.4 to 0.69 were considered to be moderate.<sup>28</sup> We also used standard least squares fitting with the restricted maximum likelihood method for multiple regression analyses. Comparisons between COPD stages or mMRC dyspnea scales were performed using analysis of variance. The minimum clinically important difference for 6MWD was defined as an increase  $> 30$  m.<sup>26</sup> Analyses were performed using JMP 11.2.0 software (SAS Institute, Tokyo, Japan).

## Results

### Subject Characteristics

There were no significant differences between the rehabilitation and nonrehabilitation groups with respect to age, gender, BMI, smoking history, percent of predicted FEV<sub>1</sub>, percent of predicted FVC, and drug treatment (Table 1). However, the rehabilitation group had more severe dyspnea (per the mMRC), more advanced GOLD stage, a greater proportion requiring long-term oxygen therapy, and more frequent exacerbations, while the nonrehabilitation group had a greater prevalence of asthma-COPD overlap and higher comorbidity indices (ie, Charlson comorbidity index). The proportion of prescriptions for inhaled drugs did not differ between the groups. With the exception of 1 subject in the nonrehabilitation group, the subjects were treated with a long-acting  $\beta_2$  agonist (LABA) or a long-acting muscarinic antagonist (LAMA). The interval between the first and second CT scans did not differ between the groups (rehabilitation group  $2.3 \pm 1.3$  y vs nonrehabilitation group  $2.1 \pm 1.2$  y;  $P = .24$ ). In the PR group, the interval between the first CT and the start of PR was  $1.4 \pm 1.0$  y, and between the end of PR and the second CT the interval was  $0.9 \pm 0.7$  y.

### Effect of PR on Annual Changes in Muscle CSA

There were no significant differences between the rehabilitation and nonrehabilitation groups with respect to the

mean values of ESM<sub>CSA</sub> or PM<sub>CSA</sub> at the time of the first or second CT scan (Table 1). ESM<sub>CSA</sub> decreased in 13 subjects in the rehabilitation group and in 33 subjects in the nonrehabilitation group. The annual changes in ESM<sub>CSA</sub> and PM<sub>CSA</sub> of the rehabilitation group ( $51.0 \pm 95.3$  and  $15.3 \pm 171.9$  mm<sup>2</sup>/y, respectively) were significantly higher than the changes in ESM<sub>CSA</sub> and PM<sub>CSA</sub> of the nonrehabilitation group ( $-116.0 \pm 141.2$  mm<sup>2</sup>/y,  $P < .001$ ; and  $-138.4 \pm 317.4$  mm<sup>2</sup>/y,  $P = .02$ , compared with the rehabilitation group) (Fig. 2, Table 2). We could not measure PM<sub>CSA</sub> in 2 subjects during the second CT scan because it was an abdominal CT scan. The annual changes in ESM<sub>CSA</sub> were significantly greater in subjects for whom the 6MWD increased more than the minimum clinically important difference (responders) ( $n = 17$ ) compared with the other subjects ( $n = 22$ ) in the rehabilitation group (responders  $94.0 \pm 88.0$  vs nonresponders  $17.0 \pm 88.4$  mm<sup>2</sup>/y,  $P < .001$ ) (Fig. 3; see the supplementary materials at <http://www.rcjournal.com>). The annual changes in PM<sub>CSA</sub> were not different between responders and nonresponders (responders  $52.1 \pm 206.4$  vs nonresponders  $-15.9 \pm 133.7$  mm<sup>2</sup>/y,  $P = .18$ ). There was no significant difference between responders and nonresponders in terms of background characteristics (see the supplementary materials at <http://www.rcjournal.com>).

### Effect of Clinical Background on Annual Changes in Muscle CSA

The annual changes in ESM<sub>CSA</sub> or PM<sub>CSA</sub> were not affected by treatment with inhaled corticosteroids (ICS) ( $P = .26$  and  $.28$ , respectively; see the supplementary materials at <http://www.rcjournal.com>). The annual changes in ESM<sub>CSA</sub> were significantly greater in the 29 subjects who received triple therapy (LABA/LAMA/ICS) compared with the 49 subjects who did not ( $23.6 \pm 131.8$  vs  $-66.4 \pm 145.2$  mm<sup>2</sup>/y, respectively;  $P < .001$ ). The median (IQR) of past COPD exacerbations was greater in subjects treated with triple therapy compared with other therapies, but this difference was not statistically significant ( $0$  [IQR  $0-2$ ] vs  $0$  [IQR  $0-1$ ], respectively;  $P = .22$ ), and a higher percentage of subjects with asthma-COPD overlap were treated with triple therapy (62.1%) compared with other therapies (16.3%) ( $P < .001$ ). The annual changes in PM<sub>CSA</sub> were unaffected by triple therapy ( $P = .26$ ). When combined with asthma (ie, asthma-COPD overlap), the annual changes in ESM<sub>CSA</sub> or PM<sub>CSA</sub> were unaffected ( $P = .81$  and  $.21$ , respectively). Likewise, annual changes in ESM<sub>CSA</sub> or PM<sub>CSA</sub> were unaffected by long-term oxygen therapy ( $P = .82$  and  $.40$ , respectively), nor were they different as a function of the GOLD stage ( $P = .82$  and  $.40$ , respectively) or mMRC dyspnea scale ( $P = .12$  and  $.68$ , respectively) (see the supplementary materials at <http://www.rcjournal.com>).

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Table 1. Subject Characteristics

	Rehabilitation ( <i>n</i> = 39)	No Rehabilitation ( <i>n</i> = 39)	<i>P</i>
Gender, male/female, <i>n</i>	38/1	38/1	> .99 <sup>‡</sup>
Age, y	76.1 ± 7.1	76.7 ± 5.1	.53*
Body mass index, kg/m <sup>2</sup>	22.1 ± 3.4	23.1 ± 3.1	.22*
Smoking history			
Former/current smoker, <i>n</i>	35/4	29/10	.07 <sup>‡</sup>
Pack-years	75.4 ± 35.5	64.5 ± 34.8	.30*
mMRC dyspnea scale, <i>n</i>			.02 <sup>‡</sup>
1	9	20	
2	22	12	
3	6	7	
4	2	0	
LTOT, <i>n</i> (%)	9 (23.1)	2 (5.1)	.02 <sup>‡</sup>
GOLD stage I/II/III/IV, <i>n</i>			< .001 <sup>‡</sup>
I	8	2	
II	8	21	
III	13	15	
IV	10	1	
Asthma-COPD overlap, <i>n</i> (%)	6 (15.4)	17 (43.6)	.001 <sup>‡</sup>
FEV <sub>1</sub> , % predicted	51.4 ± 23.7	56.6 ± 17.0	.43*
FVC, % predicted	51.4 ± 23.7	56.6 ± 16.9	.18*
Inspiratory capacity, L	2.3 ± 0.5	2.1 ± 0.4	.25*
Residual volume, L	2.7 ± 0.7	2.2 ± 0.5	.01*
Total lung capacity, L	6.1 ± 1.1	5.4 ± .7	.02*
D <sub>LCO</sub> , mL/min/mm Hg	12.5 ± 4.0	14.0 ± 4.3	.22*
LAA%, < -950 HU, %	25.2 ± 15.8	24.9 ± 10.8	.85*
Past COPD exacerbations	1 (0–2)	0 (0–0)	< .001 <sup>†</sup>
Exacerbation(s) in period between 2 CT scans	0 (0–1)	0 (0–0)	.02 <sup>†</sup>
Charlson comorbidity index	2 (1–3)	3 (2–4)	.01 <sup>†</sup>
COTE index	0 (0–2)	1 (0–2)	.19 <sup>†</sup>
Therapy, <i>n</i> (%)			
LABA or LAMA	39 (100)	38 (97.4)	.31 <sup>‡</sup>
Triple therapy	18 (46.1)	20 (51.3)	.65 <sup>‡</sup>
Inhaled corticosteroids	18 (46.2)	11 (28.2)	.10 <sup>‡</sup>
ESM <sub>CSA</sub> , mm <sup>2</sup>			
First CT scan	3,217 ± 737	3,452 ± 737	.28*
Second CT scan	3,291 ± 748	3,284 ± 771	.77*
PM <sub>CSA</sub> , mm <sup>2</sup>			
First CT scan	2,626 ± 890	2,867 ± 827	.30*
Second CT scan	2,672 ± 748	2,693 ± 776	.98*

Data are presented as mean ± SD or median (interquartile range) unless otherwise noted.

\* Student *t* test.

<sup>†</sup> Wilcoxon rank-sum test.

<sup>‡</sup> Chi-squared test.

mMRC = modified Medical Research Council

LTOT = long-term oxygen therapy

GOLD = Global Initiative for Chronic Obstructive Lung Disease

D<sub>LCO</sub> = diffusing capacity of the lung for carbon monoxide

LAA% = percentage of the lung field occupied by low-attenuation area

HU = Hounsfield units

COTE = COPD-specific comorbidity test

LABA = long-acting β<sub>2</sub> agonist

LAMA = long-acting muscarinic antagonist

Triple therapy = LABA/LAMA/ICS

ESM<sub>CSA</sub> = cross-sectional area of the erector spinae muscles

PM<sub>CSA</sub> = cross-sectional area of the pectoralis muscles

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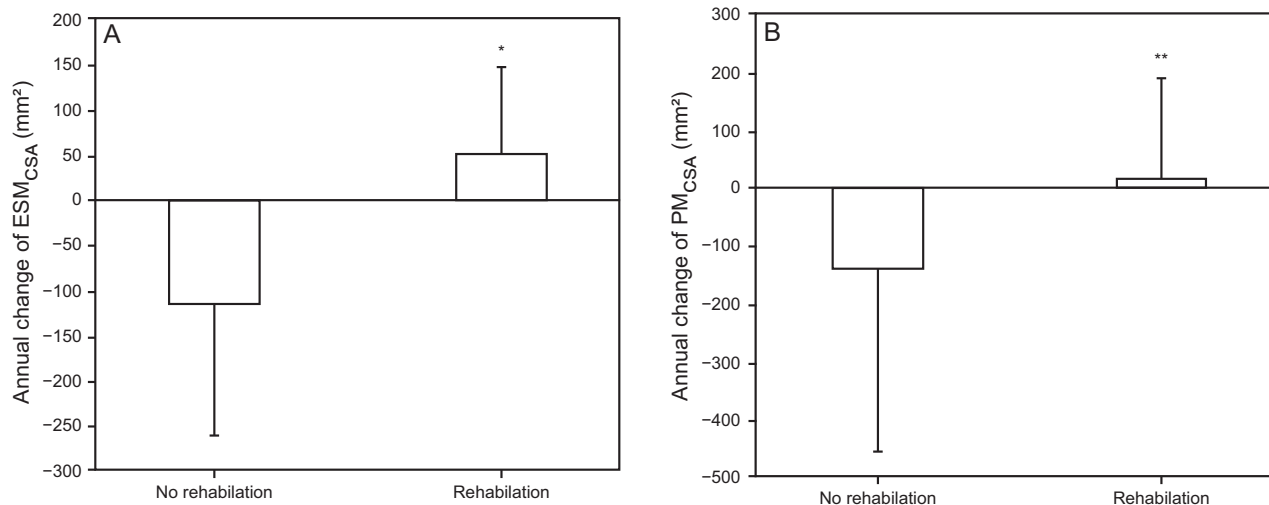


Fig. 2. Annual changes in the cross-sectional area of (A) the erector spinae muscles ( $ESM_{CSA}$ ) and (B) the pectoralis muscles ( $PM_{CSA}$ ) in subjects with COPD. Rehabilitation group ( $n = 39$ ): subjects who participated in the out-patient pulmonary rehabilitation program. No rehabilitation group ( $n = 39$ ): subjects did not participate in the pulmonary rehabilitation program.  $ESM_{CSA}$  and  $PM_{CSA}$  declined in the nonrehabilitation group over time and increased in the rehabilitation group. Data are mean  $\pm$  SD. \* $P < .001$  and \*\* $P = .02$ .

Table 2. Linear Regression for Annual Changes in  $ESM_{CSA}$  and  $PM_{CSA}$  Using Study Groups (With or Without PR) and Baseline Values as Explanatory Variables

Factors	<i>P</i>	Factors	<i>P</i>
PR	< .001	PR	.02
Baseline $ESM_{CSA}$	.35	Baseline $PM_{CSA}$	< .001

$ESM_{CSA}$  = cross-sectional area of erector spinae muscles  
 $PM_{CSA}$  = cross-sectional area of pectoralis muscles  
 PR = pulmonary rehabilitation

In summary, in terms of clinical background, other than PR, only triple therapy affected annual changes in  $ESM_{CSA}$ .

### Correlation Between Clinical Parameters and Muscle CSA

$ESM_{CSA}$  at the first CT scan (baseline) was moderately and positively correlated with BMI, 6MWD, and  $PM_{CSA}$ ; a weak positive correlation was observed with inspiratory capacity; and a weak negative correlation was evident with residual volume (Table 3).  $PM_{CSA}$  at baseline was moderately and positively correlated with BMI; there was a weak positive correlation with percent of predicted  $FEV_1$ ; and weak negative correlations were observed with residual volume and low-attenuation area percentage.

The annual changes in  $ESM_{CSA}$  were weakly and positively correlated with mMRC dyspnea scale and COPD exacerbations during the period between the 2 CT scans; a moderate positive correlation was observed with annual changes in  $PM_{CSA}$ ; and a weak negative correlation existed with the Charlson comorbidity index (Table 4).

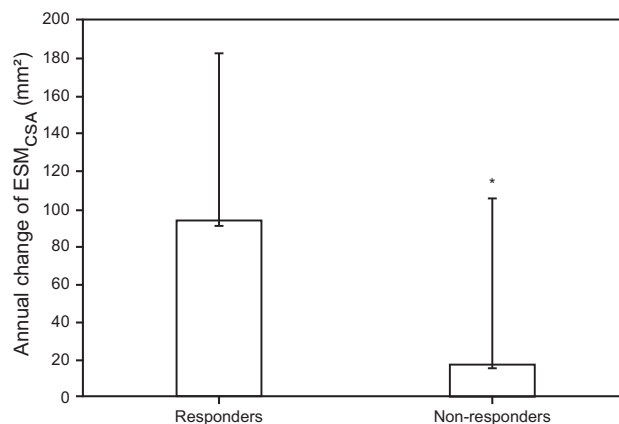


Fig. 3. Annual changes in the cross-sectional area of the erector spinae muscles ( $ESM_{CSA}$ ) in subjects with COPD who participated in the out-patient pulmonary rehabilitation program. Responders ( $n = 17$ ): subjects in whom the 6MWD increased more than the minimum clinically important difference (30 m) after the rehabilitation program. Nonresponders ( $n = 22$ ): subjects in whom the 6MWD did not increase. The annual changes in  $ESM_{CSA}$  were significantly greater in responders compared with nonresponders. Data are the mean  $\pm$  SD. \* $P < .001$ . 6MWD = 6-min walk distance.

We performed multiple regression analysis of the annual changes in  $ESM_{CSA}$  and determined that PR alone was an independent variable (Table 5).

### Discussion

Our results indicate that  $ESM_{CSA}$  and  $PM_{CSA}$  decreased year by year, and the annual changes of  $ESM_{CSA}$  and  $PM_{CSA}$  were different between the PR group and the nonrehabilitation group, in favor of the PR group. This is the first

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Table 3. Correlation Coefficients for ESM<sub>CSA</sub> and PM<sub>CSA</sub> at the Baseline CT Scan\*

	ESM <sub>CSA</sub>			PM <sub>CSA</sub>		
	Correlation Coefficient	<i>n</i>	<i>P</i>	Correlation Coefficient	<i>n</i>	<i>P</i>
Age	−0.02	78	.89	−0.02	76	.89
Smoking pack-years	−0.15	78	.19	0.06	76	.58
Body mass index, kg/m <sup>2</sup>	0.45	78	< .001	0.53	76	< .001
mMRC dyspnea scale	−0.04	78	.75	−0.19	76	.10
FEV <sub>1</sub> , % predicted	0.22	78	.054	0.24	76	.033
FVC, % predicted	0.07	78	.54	−0.02	76	.89
Inspiratory capacity	0.31	49	.033	0.28	76	.055
Residual volume	−0.29	49	.046	−0.39	49	< .001
Total lung capacity	0.03	49	.85	−0.16	49	.27
D <sub>LCO</sub>	0.09	47	.53	0.28	47	.055
LAA%	−0.14	53	.30	−0.38	53	< .001
Past COPD exacerbations	−0.09	78	.44	−0.02	76	.85
Exacerbation(s) in period between 2 CT scans	−0.02	78	.84	0.06	76	.60
Charlson comorbidity index	−0.08	78	.51	0.05	76	.65
COTE index	0.10	78	.40	0.20	76	.08
6MWD at baseline	0.42	39	< .01	0.31	37	.060
ESM <sub>CSA</sub>	No data	No data	No data	0.46	76	< .001
PM <sub>CSA</sub>	0.46	76	< .001	No data	No data	No data

\* Spearman's correlation coefficient.

ESM<sub>CSA</sub> = cross-sectional area of erector spinae musclesPM<sub>CSA</sub> = cross-sectional area of pectoralis muscles

CT = computed tomography

mMRC = modified Medical Research Council

D<sub>LCO</sub> = diffusing capacity of the lung for carbon monoxide

LAA% = percentage of the lung field occupied by low-attenuation area

COTE = COPD-specific comorbidity test

6MWD = 6-min walk distance

study to report the effect of PR on the annual changes in ESMs, which are major trunk muscles. Skeletal muscle mass is an independent predictor of mortality and frailty.<sup>1,29</sup> Exercise training alone or when combined with other treatments have favorable effects on muscle mass and function.<sup>13</sup> However, there are no reports on the effect of PR on trunk muscle mass in subjects with COPD. A recent study reported that ESM<sub>CSA</sub> is the strongest predictor of mortality in subjects with COPD and declines year by year.<sup>10</sup> The CSA of ESMs has also been reported to predict mortality after liver transplants and vascular surgery.<sup>30,31</sup> The health trajectory of subjects with COPD may be improved as a result of a PR program that maintains ESM<sub>CSA</sub>. A recent report showed that PR after hospitalization improved survival in subjects with COPD.<sup>32</sup> The mechanism by which a usual PR program can improve ESM<sub>CSA</sub> remains unclear. However, reports indicate that PR for subjects with COPD improves balancing ability,<sup>33-35</sup> which suggests that trunk muscle improvement may be implicated. Usual PR programs that include endurance training may be able to improve trunk muscles similarly to a more specific trunk flexor rehabilitation program.<sup>36</sup>

ESM<sub>CSA</sub> and PM<sub>CSA</sub> declined in some subjects even after completing the PR program. The magnitude of response

to exercise training in COPD is highly variable, with some subjects achieving little or no benefit in terms of strengthening of the lower limb muscles.<sup>37</sup> The lack of response to exercise training may relate to the inability to tolerate sufficient intensity or duration of training, or to poor adherence to the training intervention.<sup>37</sup> We measured the CSA of muscles before and after the PR program; however, because this was a retrospective study, the measurements were performed several months after the PR program in some subjects, and the CT scans were performed regardless of the PR. Therefore, the effect of the PR program might have diminished by the time measurements were recorded for some subjects.

Triple therapy (ICS/LABA/LAMA) had a favorable effect on the annual change in ESM<sub>CSA</sub>, although the effect was not significant based on multiple regression analysis. Triple therapy was prescribed for subjects with COPD and a concomitant asthmatic component or frequent COPD exacerbations.<sup>16</sup> In other words, triple therapy was prescribed for subjects who had more severe disease and symptoms. We reasoned that the annual decline in ESM<sub>CSA</sub> was greater in subjects with severe COPD complicated by frequent exacerbations,<sup>10</sup> but the annual change in ESM<sub>CSA</sub> was not correlated with the presence of asthma-COPD

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Table 4. Correlation Coefficients for Annual Changes in ESM<sub>CSA</sub> and PM<sub>CSA</sub>\*

	ESM <sub>CSA</sub>			PM <sub>CSA</sub>		
	Correlation Coefficient	<i>n</i>	<i>P</i>	Correlation Coefficient	<i>n</i>	<i>P</i>
Age	−0.04	78	.71	−0.10	76	.41
Smoking, pack-years	0.02	78	.90	0.11	76	.37
Body mass index, kg/m <sup>2</sup>	−0.12	78	.28	−0.09	76	.44
mMRC dyspnea scale	0.22	78	.049	0.10	76	.41
FEV <sub>1</sub> , % predicted	−0.06	78	.62	−0.02	76	.88
FVC, % predicted	0.03	78	.81	0.06	76	.60
Inspiratory capacity	0.10	49	.50	−0.06	49	.67
Residual volume	0.17	49	.25	0.08	49	.57
Total lung capacity	0.18	49	.22	−0.02	49	.88
D <sub>LCO</sub>	0.01	47	.98	0.11	47	.45
LAA%	−0.01	53	.93	−0.03	53	.82
Past exacerbations	0.21	78	.060	0.09	76	.46
Exacerbation(s) in period between 2 CT scans	0.27	78	.02	0.12	76	.30
Charlson comorbidity index	−0.24	78	.032	−0.14	76	.21
COTE index	−0.15	78	.19	−0.17	76	.15
6MWD at baseline	−0.07	39	.69	−0.12	37	.48
ESM <sub>CSA</sub>	No data	No data	No data	0.41	76	< .001
PM <sub>CSA</sub>	0.41	76	< .001	No data	No data	No data
Interval between 2 CT scans	0.16	76	.16	0.07	76	.55

\* Spearman's correlation coefficient.

ESM<sub>CSA</sub> = cross-sectional area of erector spinae musclesPM<sub>CSA</sub> = cross-sectional area of pectoralis muscles

CT = computed tomography

mMRC = modified Medical Research Council

D<sub>LCO</sub> = diffusing capacity of the lung for carbon monoxide

LAA% = percentage of the lung field occupied by low-attenuation area

COTE = COPD-specific comorbidity test

6MWD = 6-min walk distance

Table 5. Least-Squares Regression Model to Annual Changes in ESM<sub>CSA</sub>

Factors	<i>P</i>
Pulmonary rehabilitation	< .001
Triple therapy	.24
Charlson comorbidity index	.28
Past COPD exacerbations	.45
Exacerbation(s) in period between 2 CT scans	.20
Asthma-COPD overlap	.44
LTOT	.08
GOLD stages	.39
mMRC dyspnea scale	.14

ESM<sub>CSA</sub> = cross-sectional area of erector spinae musclesTriple therapy = long-acting  $\beta_2$  agonist/long-acting muscarinic antagonist/inhaled corticosteroid

CT = computed tomography

LTOT = long-term oxygen therapy

GOLD = Global Initiative for Chronic Obstructive Lung Disease

mMRC = modified Medical Research Council

overlap or the number of exacerbations. Recent randomized trials have reported the superior effects of triple therapy on pulmonary function, quality of life score, and all-cause mortality compared with LAMA alone, LAMA/LABA, or

LABA/ICS.<sup>38,39</sup> The superiority of triple therapy over single- or double-agent therapy may affect the annual change in ESM<sub>CSA</sub>; however, a randomized controlled trial will be necessary to more definitively prove or disprove this hypothesis.

ESM<sub>CSA</sub> at baseline was moderately correlated with 6MWD, while PM<sub>CSA</sub> was weakly correlated with pulmonary function parameters such as FEV<sub>1</sub>, residual volume, and percentage of the low-attenuation area. This finding is not surprising because ESMs are important for the maintenance of normal posture during walking, and the PMs are important accessory inspiratory muscles of respiration. Because the trunk muscles, including ESMs, have an important role in stabilizing the body, maintaining posture, and controlling spinal and pelvic movements, their atrophy can increase the risk of falling and limitations of activities of daily living in elderly people<sup>11</sup> and in those with COPD.<sup>33</sup> However, these correlations were mostly weak. Muscle CSA does not directly reflect the strength of a particular muscle because no muscle works in isolation, rather groups of muscles are generally recruited to work together. The annual change in ESM<sub>CSA</sub> was weakly and negatively correlated with the Charlson comorbidity index. In this



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study, we included subjects with a history of cancer or cardiovascular disease; therefore, the Charlson comorbidity index was higher than for previous reports in which such patients were excluded.<sup>9,10</sup> Comorbidities may accelerate a decline in ESM<sub>CSA</sub>. Against all expectations, COPD exacerbations during the period between the 2 CT scans were weakly and positively correlated with the annual change in ESM<sub>CSA</sub>. This result may be caused by the more frequent COPD exacerbations in the PR group compared with the nonrehabilitation group (Table 1).

There are several methods to evaluate muscle mass. Specifically, these include bioelectrical impedance analysis, dual-energy radiography absorptiometry, magnetic resonance imaging (MRI), and B-mode ultrasound. These methods are widely used to quantify both total and local skeletal muscle mass. Most reports of ESM<sub>CSA</sub> are based on CT scans or MRIs.<sup>9,10,27,30,31,40-43</sup> Several studies have reported a moderate correlation between ESM<sub>CSA</sub> and isometric muscle strength using CT<sup>40,43</sup> or MRI.<sup>42</sup> The downside of CT scans is exposure to radiation, while MRIs are costly in terms of time and money. Chest CT scans are often used in Japan to diagnose lung disease, assess changes in emphysematous COPD, diagnose interstitial pneumonia, and for the early detection of lung cancer in the elderly because chest MRI remains inaccessible for the majority of subjects with COPD. Therefore, we used existing CT images to evaluate muscle mass without adding to radiation exposure. Ultrasound imaging may be useful for measuring CSA whenever CT scans are performed infrequently.<sup>44</sup> We could not measure muscle mass in healthy control subjects because of the nature of this retrospective study. Tanimura et al<sup>9</sup> reported ESM<sub>CSA</sub> in subjects without respiratory disease who were nonsmoking controls. ESM<sub>CSA</sub> in control subjects ( $3,920 \pm 698 \text{ mm}^2$ ) was greater than that in the subjects with COPD in this study. Trunk stabilization muscles are categorized as deep or superficial.<sup>45</sup> ESMs are categorized as superficial muscles because they do not directly attach to vertebrae and stabilization is limited to pressurized spinal segments. The deep trunk muscles consist of the transversus abdominis, multifidus, quadratus lumborum, and rotatores muscles, which attach to individual lumbar vertebrae and provide control and rigidity for spinal segments.<sup>45</sup> There are no reports pertaining to the stabilizing role of deep trunk muscles on the health trajectory of patients with COPD, and more research is needed to elucidate this functionality.

There are some limitations of our study. It is possible that it was underpowered, given the relatively small number of subjects. The retrospective study design included subjects with clinical backgrounds that were quite different in the rehabilitation and nonrehabilitation groups. Severe dyspnea symptoms (per mMRC) and severe disease (GOLD III–IV) were more prevalent in the rehabilitation group than in the nonrehabilitation group. The Charlson comorbidity index

was higher in the nonrehabilitation group than the rehabilitation group. Symptomatic subjects with severe disease might have been referred for PR, and comorbidities could have interfered with their attendance at sessions during the PR program. Although these background differences may have affected the results, associated factors were excluded in the multiple regression analysis. The interval between the 2 CT scans also varied, and these differences might have influenced the results. We did not assess muscle areas using multi-slice CT to measure muscle volume. CSA was analyzed via manual shading of a specific muscle area, as done in previous studies.<sup>9,10,27</sup> A standard method for measuring ESM<sub>CSA</sub> has yet to be established. Automated programs to measure ESM<sub>CSA</sub> are necessary to allow more objective and precise analysis. Lastly, there were some missing data, and we were unable to analyze low-attenuation area percentage and D<sub>LCO</sub> in some subjects; these missing data may have affected the study results.

### Conclusions

ESM<sub>CSA</sub> and PM<sub>CSA</sub> declined year by year in subjects with COPD, although it increased in subjects in the pulmonary rehabilitation group, suggesting that a pulmonary rehabilitation program may improve the mass of these muscles.

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