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# **Original Article**

# Association between skeletal muscle mass index and lung function/respiratory muscle strength in older adults requiring long-term care or support

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Abstract. [Purpose] We focused on skeletal muscle mass index, one of the biomarkers of sarcopenia, and investigated the association between skeletal muscle mass index and the parameters of lung function and respiratory muscle strength. [Participants and Methods] After applying the exclusion criteria, we included, in this cross-sectional study, 120 community-dwelling older adults aged ≥65 years who required long-term care/support and underwent ambulatory rehabilitation under the long-term care insurance system in Japan. We measured the skeletal muscle mass index, forced vital capacity, forced expiratory volume in 1 second, peak expiratory flow rate, maximum expiratory pressure, and maximum inspiratory pressure. The data were analyzed using Pearson correlation coefficient and multiple regression analysis. [Results] The skeletal muscle mass index was positively correlated with only maximum expiratory pressure for both male and female participants by Pearson's correlation coefficient. With the skeletal muscle mass index as a dependent variable, only the maximum expiratory pressure was significant for both male and female participants by the multiple regression analysis. [Conclusion] Therefore, the findings of this study suggested that compared with lung function tests, maximum expiratory pressure, which is an indicator of respiratory muscle strength, is related to muscle mass. Maximum expiratory pressure might be the most useful indicator for sarcopenia.

Key words: Maximum expiratory pressure, Sarcopenia, Skeletal muscle mass index

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## **INTRODUCTION**

Various definitions of sarcopenia were announced by several research groups<sup>1-4)</sup>. Sarcopenia must be properly treated to prevent increases in the personal, social, and economic burdens<sup>5)</sup>. Sarcopenia is diagnosed on the basis of decreases in muscle strength, muscle mass, and physical function  $1^{-4}$ . These decreases are age-related, and the prevalence of sarcopenia increases with age<sup>6, 7)</sup>. Respiratory muscle strength also decreases with age<sup>8)</sup>. According to the report by the European Working Group on Sarcopenia in Older People (EWGSOP), the peak expiratory flow rate (PEFR), measured in lung function

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testing, is an indicator of muscle strength that can be analyzed for sarcopenia<sup>1</sup>). However, cutoff values were not described, and subsequent reports of the Asian Working Group for Sarcopenia (AWGS) and EWGSOP2 did not contain information regarding respiratory-related sarcopenia<sup>2–4</sup>).

Kera et al. proposed that PEFR was an effective predictor of sarcopenia with a cutoff value<sup>9, 10)</sup>. Alternatively, the unit of measure for PEFR is liters per second. It represents flow velocity and indicates expiratory muscle in some cases<sup>9, 10)</sup>. In addition, both vital capacity and forced vital capacity (FVC) in typical lung function tests are measured in liters. Because various muscles are involved in breathing, respiratory muscle strength is considered to include the strength of the diaphragm and other respiratory muscles. Consequently, respiratory muscle strength is generally determined as the pressure generated in each part of the lungs and thorax<sup>11)</sup>. The maximum generated pressure is used as an index of respiratory muscle strength. Particularly, the maximum negative pressure generated during expiration is defined as the maximum expiratory pressure ( $PE_{max}$ ), and the maximum negative pressure generated during inspiration is defined as the maximum inspiratory pressure ( $PI_{max}$ ). The American Thoracic Society (ATS) and European Respiratory Society (ERS) have also provided guidelines for respiratory muscle strength assessment<sup>12</sup>). However, only few studies have reported the effects of sarcopenia on respiratory muscle strength in healthy young and older adults<sup>13–15</sup>). According to one report in Brazil, sarcopenia significantly reduced respiratory muscle strength<sup>16</sup>). However, the relationship between sarcopenia and respiratory muscle strength has not been described in an aging population of Japan.

Therefore, we focused on SMI alone, one of the biomarkers of sarcopenia, for basic research. This study aimed to clarify the association between SMI and parameters of lung function and respiratory muscle strength in older adults who were certified as needing long-term care or support based on the measurement of muscle mass using the bioelectrical impedance analysis (BIA) method with older adults in the standing position. We also aimed to explore respiratory parameters related to SMI. This study is a primary step for investigating the association between sarcopenia and respiratory muscle strength.

#### PARTICIPANTS AND METHODS

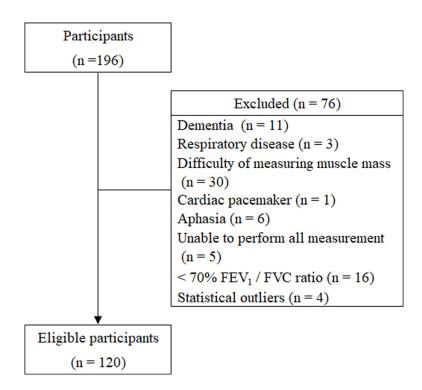
We conducted this cross-sectional study from March 2018 to August 2019. We included 196 older adults aged  $\geq$ 65 years who were certified as needing long-term care or support. They lived in the community and were undergoing ambulatory rehabilitation in the long-term care insurance system at least once a week. Exclusion criteria were a diagnosis of dementia or respiratory disease as the main disease according to a primary doctor, the presence of a cardiac pacemaker, difficulty in measuring body composition during standing, difficulty in measuring lung function and respiratory muscle strength because of aphasia, and inability to perform all measurement testing. In addition, based on the report by Kera et al., participants with <70% of forced expiratory volume in 1 second (FEV<sub>1</sub>)/FVC ratio were excluded by airway obstructions<sup>9, 10</sup>. All participants provided comprehensive written informed consent before the study. This study was approved by the Ethics Review Committee of International University of Health and Welfare (approval number: 17-Io-189-7) and was conducted in accordance with the guidelines present in the Declaration of Helsinki.

A body composition analyzer (InBody 520, InBody, Japan), was used to measure muscle mass by means of multifrequency BIA. During measurement, participants were standing. As a parameter of skeletal muscle mass, SMI was calculated as the appendicular skeletal muscle mass divided by the square of height<sup>17)</sup>. Height was measured in accordance with the protocol of Kubo et al<sup>18)</sup>. An electronic spirometer (Autospiro AS-507, Minato, Japan) and attached unit (AAM377, Minato, Japan) were used to measure lung function and respiratory muscle strength. The parameters of lung function were FVC, FEV<sub>1</sub>, and PEFR. The parameters of respiratory muscle strength were PE<sub>max</sub> and PI<sub>max</sub>. In accordance with the ATS and ERS guidelines for testing lung function, the following three acceptable modes were measured for each participant: FVC (which can measure FVC, FEV<sub>1</sub>, and PEFR); PE<sub>max</sub>; and PI<sub>max</sub><sup>12)</sup>. FVC mode was measured first, followed by PE<sub>max</sub> and PI<sub>max</sub>. The measurements were performed in the sitting position, and the best value was adopted. Physical therapists performed all measurements.

The associations between SMI and parameters of lung function and respiratory muscle strength were investigated with Pearson correlation coefficients and a multiple regression analysis. For multiple regression analysis, SMI was defined as a dependent variable, and all items of lung function and respiratory muscle strength, except  $FEV_1$ , were defined as independent variables after consideration of multicollinearity. The Grubbs–Smirnov test was performed for each measurement, and participant data shown to be outliers were excluded from analysis. Clinical characteristics and data of male and female participants were compared in unpaired t-tests. Most statistical analyses were carried out with SPSS version 25 (IBM Japan, Tokyo, Japan); the Grubbs-Smirnov test was carried out using JSTAT for Windows (Nankodo, Tokyo, Japan). A p value of less than 0.05 was considered statistically significant.

### RESULTS

Figure 1 showed the flow chart of participant selection. A total of 120 eligible older adults (63 males, 57 females) participated in this study. The primary diagnosis of the eligible participants were as follows: 41 older adults with cerebrovascular disease, 14 with spine disease, 14 with fracture, 12 with osteoarthritis, 12 with cancer, 6 with Parkinson disease, 5 with progressive supranuclear palsy, 4 with circulatory disease, 3 with renal failure, 2 with spinocerebellar degeneration, 2 with



**Fig. 1.** Flow chart of participant selection. FEV<sub>1</sub>: forced expiratory volume in 1 second; FVC: forced vital capacity.

| Characteristics                         | Male participants (n=63) | Female participants (n=57) | p value  |  |
|---|--------------------------|----------------------------|----------|--|
| Characteristics                         | $(mean \pm SD)$          | $(mean \pm SD)$            |          |  |
| Age (years)                             | $76.2\pm7.5$             | $80.4\pm8.0$               | 0.004*   |  |
| Height (cm)                             | $162.3\pm5.6$            | $152.0\pm5.3$              | < 0.001* |  |
| Body weight (kg)                        | $60.3\pm7.7$             | $50.1\pm9.8$               | < 0.001* |  |
| BMI (kg/m <sup>2</sup> )                | $22.9\pm2.8$             | $21.7\pm3.9$               | 0.060    |  |
| SMI (kg/m <sup>2</sup> )                | $6.5\pm0.9$              | $5.6\pm0.7$                | < 0.001* |  |
| Lung function                           |                          |                            |          |  |
| FVC (L)                                 | $2.3\pm0.6$              | $1.5\pm0.4$                | < 0.001* |  |
| $FEV_{1}(L)$                            | $1.9\pm0.5$              | $1.3\pm0.3$                | < 0.001* |  |
| PEFR (L/sec)                            | $4.7\pm1.7$              | $3.1 \pm 1.1$              | < 0.001* |  |
| Respiratory muscle strength             |                          |                            |          |  |
| PE <sub>max</sub> (cm H <sub>2</sub> O) | $56.2\pm19.0$            | $39.1\pm11.8$              | < 0.001* |  |
| PI <sub>max</sub> (cm H <sub>2</sub> O) | $39.1\pm16.8$            | $30.6\pm13.1$              | 0.003*   |  |

 Table 1. Clinical characteristics of study participants

\*Unpaired t-test of male participants versus female participants, p<0.05.

SD: standard deviation; BMI: body mass index; SMI: skeletal muscle mass index; FVC: forced vital capacity; FEV<sub>1</sub>: one-second forced expiratory volume; PEFR: peak expiratory flow rate;  $PE_{max}$ : maximum expiratory pressure;  $PI_{max}$ : maximum inspiratory pressure.

depression, 2 with diabetes mellitus, 1 with rheumatoid arthritis, 1 with skin disease, and 1 with liver disease.

Table 1 showed the clinical characteristics of study participants and results of lung function and respiratory muscle strength measurements. Table 2 showed the associations between SMI and the parameters of lung function and respiratory muscle strength. According to Pearson correlation coefficients, SMI was positively correlated with  $PE_{max}$  (r=0.344) in male participants and with  $PE_{max}$  (r=0.393) in female participants. Multiple regression analysis demonstrated that the regression equation was significant for both male and female participants. With the SMI as a dependent variable, only  $PE_{max}$  was significant in male participants ( $\beta$ =0.396) and in female participants ( $\beta$ =0.375), according to the multiple regression analysis.

Table 2. Association between SMI and parameters of lung function and respiratory muscle strength

| Parameter                               | Male participants (n=63) |          |        | Female participants (n=57) |                        |                      |                |                      |
|---|--------------------------|----------|--------|----------------------------|------------------------|----------------------|----------------|----------------------|
|   | $\mathbf{r}^{\dagger}$   | p value† | β‡     | p value <sup>‡</sup>       | $\mathbf{r}^{\dagger}$ | p value <sup>†</sup> | β <sup>‡</sup> | p value <sup>‡</sup> |
| Lung function                           |                          |          |        |                            |                        |                      |                |                      |
| FVC (L)                                 | -0.028                   | 0.827    | -0.216 | 0.178                      | 0.216                  | 0.107                | 0.172          | 0.295                |
| $FEV_{1}(L)$                            | -0.003                   | 0.979    | _      | _                          | 0.142                  | 0.293                | -              | _                    |
| PEFR (L/sec)                            | 0.217                    | 0.088    | 0.245  | 0.136                      | 0.248                  | 0.063                | -0.017         | 0.924                |
| Respiratory muscle s                    | trength                  |          |        |                            |                        |                      |                |                      |
| $PE_{max}$ (cm H <sub>2</sub> O)        | 0.344                    | 0.006*   | 0.396  | 0.009*                     | 0.393                  | 0.003*               | 0.375          | 0.014*               |
| PI <sub>max</sub> (cm H <sub>2</sub> O) | 0.000                    | 1.000    | -0.193 | 0.183                      | 0.196                  | 0.144                | 0.000          | 0.997                |

<sup>†</sup>Association between SMI and parameters of lung function and respiratory muscle strength according to Pearson's test.

<sup>\*</sup>Association between SMI and parameters of lung function and respiratory muscle strength according to multiple regression analysis. p < 0.05.

The FEV<sub>1</sub> was excluded as an independent variable after considering multicollinearity.

SMI: skeletal muscle mass index; FVC: forced vital capacity;  $FEV_1$ : forced expiratory volume in 1 second; PEFR: peak expiratory flow rate;  $PE_{max}$ : maximum expiratory pressure;  $PI_{max}$ : maximum inspiratory pressure.

#### **DISCUSSION**

After applying the exclusion criteria, our study has included 120 eligible older adults who required long-term care or support. In several cases, the ability to stand has declined in older adults requiring long-term care or support. Our study provided useful data because muscle mass was measured using the more accurate BIA method that required standing, not an estimated formula used previously<sup>16</sup>.

Because respiratory muscle strength differs by gender, we examined our findings with regard to gender<sup>8, 19</sup>). According to the report by EWGSOP, PEFR is an indicator of muscle strength in the evaluation of sarcopenia<sup>1</sup>). In this study, Only PE<sub>max</sub> was significantly correlated with SMI according to Pearson correlation analysis and the multiple regression analysis for both male and female participants. In other words, the parameter most clearly related to SMI in lung function and respiratory muscle strength was PE<sub>max</sub>, not PEFR for older adults who required long-term care or support. This result suggested that PE<sub>max</sub> for these older adults, which was defined as an index of respiratory muscle strength, was more related to muscle mass than was PEFR, which was an index of lung function tests. Both PE<sub>max</sub> and PEFR can be indicators of respiratory muscle strength. PE<sub>max</sub> represents the intraoral pressure when "the only maximum expiratory effort" was performed after maximal inspiration. For older adults requiring long-term care/support, PE<sub>max</sub> is much simpler and easier to perform than PEFR, which is measured by repeated inhalation and exhalation. We also assumed that FVC and FEV<sub>1</sub> rather show the overall function of a pulmonary condition via the compliance of the lung-thorax system<sup>20</sup>.

Conversely, although our results showed a significant association between SMI and PE<sub>max</sub>, we found no significant association between SMI and PI<sub>max</sub>. In previous studies, investigators reported associations between SMI and PI<sub>max</sub> in young adults, between SMI and PE<sub>max</sub> in young men, and between SMI and PI<sub>max</sub> in healthy adults<sup>13-15</sup>). Therefore, there has been no consensus about which type of respiratory muscle, expiratory or inspiratory, is related to muscle mass. Resting expiratory function was passively maintained by elastic contraction forces in the lung and chest wall during inspiration, and the diaphragm's main role is in inspiration<sup>21, 22)</sup>. With regard to forced breathing, the activity of the transversus abdominis, obliques, and rectus abdominis muscles was observed during expiration, and the activity of the scalene and sternocleidomastoid muscles was observed during inspiration<sup>21)</sup>. Our study suggested that SMI was associated with PE<sub>max</sub> of respiratory muscle strength during expiration in older adults with a certification of requiring long-term care or support. Therefore, our findings also suggested that aging weakens the respiratory muscles, especially those involved in expiration. The results of several other studies have supported our opinion<sup>23-27</sup>). With regard to changes in respiratory muscles with aging, several investigators reported no or less change in muscle mass and no change in muscle fiber types in diaphragmatic muscle and inspiratory external intercostal muscles<sup>23-26</sup>). In addition, a postmortem study of respiratory muscles in older adults revealed that type II fibers exhibited atrophy in abdominal muscles but not in the diaphragm<sup>27)</sup>. The expiratory muscles might be more affected by aging with long-term care/support as compared with other parameters. However, respiratory muscle strength is considered to include the strength of the diaphragm and other respiratory muscles. Further research is needed to determine the effects of specific muscles.

This study has some limitations. First, this study was a basic research for investigating the association between sarcopenia and  $PE_{max} \& PI_{max}$ . We focused on SMI alone, which is a biomarker of sarcopenia. A previous study has reported the relationship between pulmonary function and physical performance<sup>28</sup>. Second, it was difficult to establish the exclusion criteria for older adults who had various comorbid diseases and a complex medical history. For example, community-dwelling individuals with stroke showed a decrease in the strength of respiratory muscles<sup>29</sup>. The factors associated with the disease could not be excluded in this study. Third, muscle mass and pulmonary function are affected by smoking, and we excluded

participants with <70% FEV<sub>1</sub>/FVC ratio (refer to previous study)<sup>9, 10, 30</sup>). In addition, many older adults were excluded from our study. In particular, 30 participants could not undergo muscle mass measurement in the standing position. However, the AWGS and EWGSOP recommend the BIA method for measuring muscle mass<sup>1-4</sup>). We had to exclude these patients to determine the relationship between sarcopenia and respiratory function. As part of our future study, we will also consider measuring muscle mass by the BIA method in the supine position. In the future, we will investigate the effect of the presence or absence of sarcopenia on PE<sub>max</sub> and PI<sub>max</sub>, including physical performance in cross-sectional and longitudinal studies as well as multicenter studies.

In conclusion, the EWGSOP considered PEFR an indicator of muscle strength for sarcopenia, but we found that  $PE_{max}$  was more related to SMI in community-dwelling older adults undergoing ambulatory rehabilitation in the long-term care insurance system. This result indicated an association between sarcopenia and  $PE_{max}$ .

#### Funding

None.

#### Conflict of interest

The author declares no conflict of interest.

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