Decreased Tongue Strength is Related to Skeletal Muscle Mass in COPD Patients

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Abstract
Dysphagia is frequently observed in patients with chronic obstructive pulmonary disease (COPD). Decreased tongue strength is one of the causes of dysphagia, and it is often observed in patients with sarcopenia. Sarcopenia is also frequently observed in COPD patients. We hypothesized that tongue strength is lower in COPD patients compared to normal subjects. This was a single-center, observational, cross-sectional study. Maximum tongue pressure (MTP) was measured in 27 patients with COPD and 24 age-matched control subjects. We also evaluated handgrip strength, gait speed, and appendicular skeletal muscle mass to define subjects as having sarcopenia. We used bioelectrical impedance analysis to assess body composition. The eating assessment test-10 was used to diagnose dysphagia. MTP was significantly lower in COPD patients than in control subjects (33.8 ± 8.4 vs 38.0 ± 5.3; \( p = 0.032 \)). All measures of muscle and fat free body mass, handgrip strength, and gait speed were also significantly lower in COPD patients compared to control subjects (\( p < 0.01 \)). The prevalence of sarcopenia in COPD patients was higher than that in control subjects (6/27 versus 0/24; \( p = 0.007 \)), but the prevalence of dysphagia was not different between groups (COPD: 5/27, versus control: 1/24; \( p = 0.112 \)). MTP was moderately correlated with skeletal muscle mass index (\( r = 0.56, p = 0.003 \)) and handgrip strength (\( r = 0.43, p = 0.027 \)) in COPD patients. Tongue strength was lower in COPD patients compared to normal subjects, and decreased tongue strength may be correlated with sarcopenia in COPD patients.

Keywords Chronic obstructive pulmonary disease · Tongue strength · Skeletal muscle mass · Handgrip strength · Gait speed

Introduction
Dysphagia is a common complication for patients with chronic obstructive pulmonary disease (COPD), seen in about 85% of COPD patients [1]. Dysphagia in COPD patients is caused by decreased swallowing function due to various causes. Decreased tongue strength strongly affects dysphagia in patients with Parkinson’s disease and cerebrovascular disease. Tongue strength is a part of the swallowing function [2]. The tongue plays a major role in bolus formation, control, and propulsion in swallowing [3]. In the preparation and oral phase of swallowing, a bolus is formed and is placed by the tongue on the occlusal surface of the posterior teeth and buccal mucosa for transport to the pharynx. When the tongue transfers the bolus to the pharyngeal cavity, it must raise the oral pressure to prevent pharyngeal residue. Decreased tongue strength causes pharyngeal residue, and it may lead to dysphagia. Therefore, evaluation of tongue...
strength is necessary in determining swallowing function. Tongue strength will decline in patients not only from the effects of disease such as stroke and amyotrophic lateral sclerosis [4, 5], but also from sarcopenia.

Sarcopenia is characterized by low muscle strength and low muscle mass [6]. In COPD patients, being underweight is associated with higher mortality [7]. Sarcopenia is likely to occur in COPD patients due to the effects of systemic inflammation, oxidative stress, smoking, hypoxemia, chronic inactivity, and malnutrition [8]. It may cause not only whole-body atrophy but also weakness of the tongue. Quadriceps muscle and handgrip strength have been evaluated to assess muscle weakness in COPD patients [9, 10]. However, tongue strength in COPD patients has not been investigated yet. Decreased tongue strength may be a contributing factor to dysphagia in patients with COPD.

The relationship between tongue strength and sarcopenia has been reported in previous studies [11, 12]. One of the ways to assess tongue strength is to measure maximum tongue pressure (MTP). MTP is associated with age, serum albumin concentration, activities of daily living, and the presence of sarcopenia [13]. In patients with sarcopenic dysphagia, atrophy of the swallowing muscles has been observed by the thickness and brightness of tongue muscles using ultrasonography [14]. MTP is also decreased in frail elderly persons [15].

We hypothesized that MTP would be lower in COPD patients compared to normal subjects.

Materials and Methods

Study Subjects

This was a single-center, observational, cross-sectional study. Twenty-seven elderly patients (> 65 years old) with stable COPD were recruited for enrollment in this study. They were chosen from a group of patients who had visited the Department of Respiratory Medicine and Allergology at Kindai University Hospital from December 2019 to May 2020. We also recruited 24 age-matched control subjects who did not have any pulmonary disease. Exclusion criteria included metallic implants and a history of stroke or neuromuscular disease. Subjects who did not have their front teeth were excluded, because they were not able to bite down on the equipment used to measure MTP. According to a preliminary study, the mean MTP in healthy subjects (age ≥ 70) was 31.9 ± 8.9 kPa [16]. In the COPD patients, we assumed 25.5 ± 7.7 kPa for MTP by referring to the data of hospitalized patients [13]. With these values, the required number of cases would be 54 (27 subjects in each group) based on Student’s t-test, which was used to assess the difference between the MTP value of the 2 groups, with a significance level of 5% (both sides) and a study power of 80%. Twenty-seven participants per group were recruited. However, three subjects in the control group were dropped because of erroneous values in their BIA measurements. They were not replaced because the coronavirus had spread in Japan, and we could not recruit anymore subjects. Thus, we had 51 subjects (27 COPD patients and 24 age-matched controls) for the final study.

All subjects included in the study had undergone spirometry (CHEST AC-55V, Chest, Tokyo, Japan) within the last 3 months, according to ATS guidelines [17]. COPD patients were diagnosed using the Global Initiative lung Disease (GOLD) criteria [18].

Protocols were approved by the Committee for Ethics at Kindai University School of Medicine before study enrollment, and all subjects signed informed consents (No. 31-116).

Assessment of Tongue Strength

We measured maximum tongue pressure (MTP) using a balloon-based tongue pressure measurement device (Shown in Fig. 1, JMS tongue pressure measuring device®, JMS, Hiroshima, JAPAN) according to the methods proposed by Takahashi [19]. The probe was inflated at a baseline pressure of 19.6 kilopascal (kPa). To measure MTP, the balloon...
was positioned on the anterior palate with the lips closed. Subjects raised their tongue and compressed the balloon onto the palate with maximal voluntary muscular effort for approximately 7 s. The measurement was performed three times with a 1-min interval rest between trials. The maximum value was recorded as the MTP.

Assessment of Sarcopenia

The Asian Working Group for Sarcopenia (AWGS) 2019 consensus established the criteria for sarcopenia in Asian people [20] (Supplementary Fig. 1). Sarcopenia is diagnosed using appendicular skeletal muscle mass (ASM), handgrip strength, and gait speed. The following cut-off values are used to identify sarcopenia: ASM of < 7.0 kg/m² for men and < 5.7 kg/m² for women, and either a handgrip strength of < 28 kg for men and < 18 kg for women or a gait speed of 1.0 m/s.

For diagnosing cases in a clinical research setting, the Strength, Assistance with walking, Rise from a chair, climb stairs, and Falls (SARC-F) questionnaire is recommended by the AWGS. This questionnaire consists of 5 simple questions and each item scores from 0 to 2 points. A total score of ≥ 4 corresponds to the cut-off for sarcopenia. We evaluated the SARC-F only in the control subjects because subjects with chronic conditions (heart failure, COPD, diabetes mellitus, chronic kidney disease, etc.) can be exempt from this screening tool. The validity of the Japanese version of the SARC-F has been reported in a previous study [21].

Handgrip strength was measured three times for the right hand using a grip strength dynamometer GRIP-D (Takei Scientific Instruments, Niigata, Japan) and mean values were used. To assess gait speed, subjects were asked to walk a timed 6-m course at their usual speed. Time commenced when the subjects started foot movement and stopped when the foot contacted the ground after completely crossing the 6-m mark.

Bioelectrical Impedance Analysis

Body composition was measured using the seca mBCA525 (seca Nihon, Chiba, Japan). The seca mBCA525 is designed for measurements in the supine position, using four pairs of electrodes (eight electrodes in total), positioned on each hand and foot [22]. Supine measurements were taken after lying down for 10 min. Alcohol was prohibited for 24 h prior to the impedance measurements. We adjusted for body size using height squared. Body mass index (BMI), fat free mass index (FFMI), fat mass index (FMI), appendicular skeletal muscle mass (ASM), and skeletal muscle mass index (SMI) were calculated.

Assessment of Swallowing Function

Swallowing function was assessed using the eating assessment test-10 (EAT-10) which indicates the subject’s self-perception of swallowing function [23] (Supplementary table 1). The EAT-10 consists of 10 items. Each item includes a statement describing a scenario that could be a problem for a subject experiencing swallowing difficulty. Subjects scored their symptoms from 0 to 4 (0: no problem, 4: severe problem), with a total score of 3 or higher indicating dysphagia.

Statistical Analysis

Results are shown as the mean ± standard deviation (SD). p Values < 0.05 were considered significant for all analyses. The differences between each measurement among COPD patients and control subjects were compared with a t-test and χ² statistics. Differences in MTP between COPD and control groups and between males and females were analyzed by two-way analysis of variance. Differences between COPD stages (stage I + II, stage III, stage IV) were analyzed by ANOVA with repeated measures. The correlations between MTP and other factors were assessed using a Pearson correlation analysis. Analyses were carried out using SPSS24.0 (Tokyo, Japan).

Results

Subject Characteristics

The characteristics of subjects are summarized in Table 1. Age and gender ratio were not different between groups (p = 0.948, p = 0.856, respectively). Smoking history (pack years) was significantly higher in COPD patients compared to control subjects (p < 0.001). Prevalence of dyslipidemia was higher in COPD patients (p = 0.016). Four of the COPD patients, but none in the control group had chronic cardiovascular disease (p = 0.555).

Comparison of MTP, Prevalence of Sarcopenia, and Dysphagia (Table 2)

MTP was significantly lower in COPD patients than in control subjects (33.6 ± 8.4 versus 38.0 ± 5.3 kPa; p = 0.032) (Fig. 2). There were significant differences between genders (F(1.47) = 4.664, p < 0.036). MTP was lower among female than male COPD patients. The prevalence of sarcopenia was higher in COPD patients compared with control subjects (6/27 versus 0/24; p = 0.007) (Table 2). ASM, FFMI, SMI, handgrip
Table 1  Participant demographic characteristics

|                       | Control subjects (n = 24) | COPD patients (n = 27) | p value |
|-----------------------|---------------------------|------------------------|---------|
| Age (years)           | 77.5 ± 5.0                | 77.6 ± 4.6             | 0.948   |
| Male, n (%)           | 20(83)                    | 23(85)                 | 0.856   |
| Smoking history, n (%)| 13(54)                    | 24(89)                 | 0.014   |
| Smoking history (pack years) | 18.5 ± 24.9          | 68.4 ± 39.9            | < 0.001 |
| FVC (L)               | 3.2 ± 0.7                 | 2.8 ± 0.8              | 0.092   |
| %FVC (%)              | 104.7 ± 18.6              | 90.6 ± 20.6            | 0.010   |
| FEV1 (L)              | 2.3 ± 0.5                 | 1.3 ± 0.6              | < 0.001 |
| %FEV1 (%)             | 97.2 ± 19.2               | 50.4 ± 21.1            | < 0.001 |
| GOLD stage, n (I + II/III/IV) | –                      | 10/10/7               | –       |
| mMRC dyspnea scale (0/1/2/3/4) | –                      | 0/4/17/6/0           | –       |
| Comorbidity, n (%)    |                           |                        |         |
| Hypertension          | 7(29)                     | 13(48)                 | 0.166   |
| Dyslipidemia          | 2(13)                     | 10(42)                 | 0.016   |
| Diabetes mellitus     | 2(8)                      | 5(19)                  | 0.200   |
| Chronic cardiovascular disease | 3(13)                  | 5(19)                  | 0.555   |
| History of aspiration pneumonia, n (%) | 0(0)                  | 0(0)                   | –       |
| LTOT, n (%)           | –                         | 4(15)                  | –       |

Mean ± standard deviation

FVC forced vital capacity, FEV1 forced expiratory volume in one second, mMRC dyspnea scale modified medical research council dyspnea scale, LTOT long term oxygen therapy, GOLD global initiative for chronic obstructive lung disease

Table 2  Measurement values in control subjects and COPD patients

|                       | Control subjects (n = 24) | COPD Patients (n = 27) |
|-----------------------|---------------------------|------------------------|
|                       | All COPD patients (n = 27) | GOLD stage I + II (n = 10) | GOLD stage III (n = 10) | GOLD stage IV (n = 7) |
| MTP (kPa)             | 38.0 ± 5.3                | 33.6 ± 8.4*             | 33.3 ± 11.0             | 34.2 ± 5.5             | 33.1 ± 7.1             |
| Sarcopenia, n (%)     | 0(0)                      | 6(22)**                 | 1(10)                   | 4(40)                   | 2(28)                   |
| SARC-F abnormal (n)   | 0                         | –                       | –                       | –                       | –                       |
| Handgrip strength (kg)| 36.0 ± 8.4                | 29.5 ± 7.5**            | 31.6 ± 7.5              | 28.4 ± 6.2              | 26.5 ± 8.2              |
| Below cut off value, n (%) | 1(4)                   | 10(37)                  | 1(10)                   | 6(60)                   | 3(43)                   |
| Weight (kg)           | 64.7 ± 7.1                | 58.7 ± 12.9*            | 60.5 ± 12.1             | 58.8 ± 11.1             | 56.2 ± 16.1             |
| Height (cm)           | 161.4 ± 6.6               | 163.5 ± 7.8             | 163.0 ± 5.9             | 163.8 ± 8.9             | 163.3 ± 8.4             |
| BMI (kg/m²)           | 24.7 ± 2.2                | 21.8 ± 3.6**            | 22.4 ± 3.3              | 22.2 ± 3.3              | 20.4 ± 3.8              |
| ASM (kg/m²)           | 7.9 ± 0.8                 | 7.0 ± 1.4**             | 7.2 ± 1.2               | 7.2 ± 1.4               | 7.0 ± 1.6               |
| Below cut off value, n (%) | 1(4)                   | 13(48)                  | 5(50)                   | 4(40)                   | 4(57)                   |
| FFMI (kg/m²)          | 17.5 ± 1.7                | 15.4 ± 2.5**            | 16.2 ± 2.1              | 15.7 ± 2.1              | 13.8 ± 2.9              |
| SMI (kg/m²)           | 7.9 ± 1.3                 | 6.4 ± 1.7**             | 7.0 ± 1.5               | 6.6 ± 1.4               | 5.4 ± 2.0               |
| FMI (kg/m²)           | 7.2 ± 2.2                 | 6.4 ± 2.5               | 6.3 ± 1.9               | 6.4 ± 3.3               | 6.6 ± 2.0               |
| Gait speed (m/s)      | 2.1 ± 0.4                 | 1.5 ± 0.4**             | 1.7 ± 0.4               | 1.6 ± 0.3               | 1.3 ± 0.3               |
| Below cut off value, n (%) | 0(0)                   | 2(7)                    | 0(0)                    | 0(0)                    | 2(29)                   |
| EAT-10 abnormal, n (%) | 1(4)                     | 5(19)                   | 1(10)                   | 2(20)                   | 2(28)                   |

Mean ± standard deviation

GOLD global initiative for chronic obstructive lung disease, MTP maximum tongue pressure, BMI body mass index, ASM appendicular skeletal muscle mass, FFMI fat free mass index, FMI Fat mass index, EAT-10 eating assessment test-10

*p value < 0.05 vs control subjects, **p value < 0.01 vs control subjects. There were no significant differences among GOLD stages
strength, and gait speed were also significantly lower in COPD patients \(p=0.004, p=0.001, p=0.001, p=0.006, p<0.001\), respectively). Of the COPD patients, 19% (5/27) were diagnosed with dysphagia, and the prevalence of dysphagia was higher in COPD patients compared to control subjects (1/24). However, the difference was not significant \(p=0.112\). We could not find any significant difference between each GOLD stage \(p\) values are shown in Supplementary table 2).

**Relationship Between MTP and Other Factors in Each Group**

There was a moderate positive correlation between MTP and SMI in COPD patients \(r=0.56, p=0.033\) (Table 3). There was also a moderate positive correlation between MTP and handgrip strength in COPD patients \(r=0.43, p=0.027\). There was no correlation between MTP and age \(p=0.707\). In the control subjects, there was no correlation between EAT-10 and sarcopenia-related factors (all measures of muscle and fat free body mass, handgrip strength, and gait speed).

**Discussion/Conclusion**

In this study, MTP was significantly lower in patients with COPD compared to control subjects, supporting our hypothesis. In addition, the prevalence of sarcopenia was higher in COPD patients, compared to control subjects. As one of the signs of sarcopenia, MTP was lower along with lower SMI and handgrip strength in COPD patients.

The relationship between sarcopenia and dysphagia can be explained using one of two patterns: one in which whole-body sarcopenia is followed by a swallowing disorder, and one in which a swallowing disorder is followed by malnutrition/whole-body sarcopenia [24]. Muscle dysfunction is a major complication for COPD patients [25]. In the UK and the Netherlands, the prevalence of quadriceps weakness in COPD patients was 32%, and it tended to be

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**Table 3** Correlation coefficients for MTP with sarcopenia-related factors and pulmonary functions in each group

|                          | Control subjects | COPD patients |
|--------------------------|------------------|---------------|
|                          | Correlation coefficient \(r\) | \(p\) value   | Correlation coefficient \(r\) | \(p\) value   |
| Age                      | −0.11            | 0.626         | −0.08          | 0.707         |
| FVC (L)                  | −0.41*           | 0.048         | 0.06           | 0.758         |
| %FVC (%)                 | −0.42*           | 0.039         | −0.19          | 0.333         |
| FEV\(_i\) (L)            | −0.37            | 0.073         | 0.13           | 0.489         |
| %FEV (%)                 | −0.34            | 0.105         | −0.16          | 0.937         |
| FEV\(_i\)/FVC (%)        | 0.07             | 0.764         | 0.04           | 0.846         |
| BMI (kg/m\(^2\))         | 0.06             | 0.774         | 0.52**         | 0.006         |
| Handgrip strength (kg)   | −0.24            | 0.259         | 0.43*          | 0.026         |
| ASM (kg/m\(^2\))         | 0.03             | 0.873         | 0.37*          | 0.017         |
| FFMI (kg/m\(^2\))        | 0.05             | 0.811         | 0.50**         | 0.008         |
| SMI (kg/m\(^2\))         | −0.02            | 0.918         | 0.56**         | 0.003         |
| FMI (kg/m\(^2\))         | 0.03             | 0.894         | 0.28           | 0.171         |
| Gait speed (m/s)          | −0.04            | 0.895         | 0.29           | 0.144         |
| EAT-10                   | −0.30            | 0.156         | 0.22           | 0.264         |

\(FVC\) forced vital capacity, \(FEV_i\) forced expiratory volume in one second, \(MTP\) maximum tongue pressure, \(BMI\) body mass index, \(ASM\) appendicular skeletal muscle mass, \(FFMI\) fat free mass index, \(SMI\) skeletal muscle mass index, \(FMI\) fat mass index, \(EAT-10\) eating assessment test-10

\*\(p\) value < 0.05, **\(p\) value < 0.01
observed in the early stages of COPD (GOLD stage I + II) [9]. Decreased skeletal muscle mass is a potential risk factor for dysphagia [26]. This suggests that whole-body atrophy may result in weakness of the swallowing muscles in COPD patients. In addition, MTP values are associated with ASM and handgrip strength but not with age. These results suggest that sarcopenic dysphagia is caused by sarcopenia and whole-body atrophy rather than age-related changes.

Putative triggers of muscle wasting in COPD patients include disuse, hypoxemia, malnutrition, inflammation, and the use of synthetic glucocorticoids [27]. These may be a direct consequence of decreased function and pathological remodeling of the diseased lung, e.g., hypoxemia and pulmonary inflammation, or may concern physiological and behavioral mal-adaptations, e.g., disuse and malnutrition. During disease exacerbations, these factors converge and, together with the use of synthetic glucocorticoids as a common medical intervention, may synergize to accelerate muscle wasting. This could be one of the mechanisms of muscle dysfunction, including that of the tongue, in COPD patients.

In a previous study, the mechanism of dysphagia in COPD patients was thought to be impairment of breathing and swallowing coordination [28]. The abnormal timing of swallows within the respiratory cycle occurs due to dyspnea and breathlessness. Swallowing during inspiration (the I-SW pattern) and swallowing immediately followed by inspiration (the SW-I pattern) were observed in COPD patients. Patients with either the I-SW pattern or the SW-I pattern were associated with a higher frequency of exacerbation [29]. A recent study showed the effectiveness of continuous positive pressure ventilation (CPAP) to decrease SW-I frequency and normalize the timing of swallowing [30]. While this discoordination has been well evaluated, tongue strength in COPD patients had yet to be evaluated. Ours is the first report of decreased tongue strength in COPD patients.

Despite the differences in MTP between groups, there was no difference in dysphagia as measured by the EAT-10 test between groups. However, according to a systematic review of dysphagia in chronic pulmonary disease, many previous studies reported a prevalence of dysphagia in COPD patients [31]. Hiraoka et al. showed that lower MTP (< 20 kPa) is a risk factor for aspiration pneumonia in amyotrophic lateral sclerosis (ALS) patients [5]. In our study, we only recruited patients who were independent in daily living and had no apparent aspiration symptoms. More relevant assessments of swallowing function may be needed, such as swallowing video fluorography or swallowing video endoscopy.

There are several ways to improve tongue strength. Effortful swallowing training (5 days per week for 4 weeks) improved tongue strength in stroke patients with dysphagia [32]. In a randomized controlled trial of tongue-strengthening exercise, anterior and posterior maximal isometric pressure improved after 4–8 weeks of training [33]. In COPD patients, the prevalence of sarcopenia was higher in patients with malnutrition [34]. This suggests that nutrition support may prevent sarcopenia in COPD patients. In fact, a recent study showed that maintaining skeletal muscle mass had a positive impact on tongue strength gained through dysphagia rehabilitation [35]. Having a social network involving neighbors and taking part in leisure activities were associated with higher tongue pressures [36]. Further research is needed to investigate the benefits of lifestyle interventions (increasing physical activity) and nutritional supplements to determine whether these interventions can prevent sarcopenia and atrophy of the tongue muscles or not.

There are some limitations to this study. The main limitation was the small number of subjects. This may be the reason the prevalence of dysphagia was not different between groups. However, the number of the enrolled subjects was enough to show a difference in MTP. There were not enough patients to compare MTP with severity of COPD. Another limitation was a lack of objective evaluation for swallowing. We did not perform objective measures of swallowing such as video fluoroscopy or video endoscopy. EAT-10, which we did use, does not provide any objective measures of swallowing function. Further studies are needed to better define the relationship between swallowing function and tongue strength.

In conclusion, tongue strength was lower in COPD patients compared to normal subjects.

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Declarations

Conflict of interest Dr. Tohda Y. has reported personal fees from Kyorin Pharmaceutical, Co., Ltd., Teijin Pharma Co., Ltd., Kyorin Pharmaceutical Co., Ltd., Meiji Seika Pharma Co., Ltd., Boehringer Ingelheim Co., Ltd., Daiichi Sankyo Co., Ltd., and Astellas, Pearl Therapeutics, Inc., outside the submitted work. The other authors report no conflicts of interest.

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