Table 1. Comparison of demographic characteristics and measurements

	Men				Women				
	All (n = 73)	Higher level SWT (n = 42)	Lower level SWT (n = 31)	*p*-value*	All (n = 76)	Higher level SWT (n = 26)	Lower level SWT (n = 50)	*p*-value*	*p*-value **
General characteristics									
Age, years (SD)†	73.7 (4.6)	72.3 (4.1)	75.6 (4.7)	0.002	73.4 (4.3)	70.2 (3.5)	75.1 (3.7)	<0.001	0.71
BMI, kg/m^2 (SD)†	23.4 (3.1)	24.1 (3.0)	22.6 (3.1)	0.048	23.3 (2.7)	22.6 (2.3)	23.7 (2.8)	0.09	0.81
Smoking-pack-years index (SD)†	29.0 (30.0)	27.2 (33.7)	29.9 (24.6)	0.81	0 (0)	0 (0)	0 (0)	-	<0.001
Motor function									
10-m walk time, s (SD)†	7.3 (1.0)	6.9 (0.7)	7.8 (1.1)	<0.001	7.3 (1.3)	6.9 (0.8)	7.5 (1.5)	0.06	0.81
TUG, s (SD)†	6.4 (1.1)	6.1 (0.9)	7.0 (1.0)	<0.001	6.9 (1.1)	6.4 (0.8)	7.2 (1.1)	0.004	0.008
Handgrip strength, kg	33.4 (5.9)	34.4	32.4 (5.9)	0.09	23.0	24.3 (3.1)	22.3 (3.9)	0.02	<0.001

(SD)†		(5.8)			(3.8)				
Body composition									
SMI, kg/m^2 (SD)†	7.3 (0.7)	7.5 (0.7)	7.0 (0.6)	0.01	5.8 (0.6)	6.0 (0.6)	5.7 (0.5)	0.02	<0.001
Lung function									
FVC, lit. (SD)†	3.2 (0.6)	3.4 (0.5)	3.0 (0.4)	<0.001	2.2 (0.5)	2.5 (0.4)	2.1 (0.5)	<0.001	<0.001
FVC, %-predicted (SD)†	96.2 (13.8)	99.1 (12.7)	92.2 (14.3)	0.03	97.6 (16.0)	104.5 (15.6)	94.0 (15.1)	0.01	0.56
FEV_1, lit. (SD)†	2.3 (0.6)	2.5 (0.5)	2.0 (0.5)	<0.001	1.6 (0.5)	1.9 (0.4)	1.5 (0.4)	<0.001	<0.001
FEV_1, %-predicted (SD)†	88.1 (18.4)	92.5 (17.3)	82.1 (18.4)	0.02	96.9 (21.1)	105.5 (20.2)	92.4 (20.3)	0.01	0.007
FEV_1/FVC, % (SD)†	71.0 (10.5)	72.7 (8.9)	68.8 (12.1)	0.11	72.6 (11.2)	75.5 (11.9)	71.1 (10.6)	0.10	0.39
Cardiovascular function									

Suspected arteriosclerosis, %††	72.6	71.4	74.2	0.79	48.6	34.6	56.0	0.08	0.003
Suspected PAD, % ††	5.5	0	0	-	1.3	0	2.0	0.47	0.56

Note: BMI, body mass index; TUG, Timed Up and Go; SMI, skeletal mass index; FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 s; PAD, peripheral artery disease.

†: t-test, ††: χ^2-test

*: comparison between higher and lower level of SWT

**: comparison between men and women

Table 2. Multivariate logistic regression model with stepwise selection to determine the association with shuttle walking test level

	Odds ratio	95% CI	*p*-value
Men			
10-m walk time (s)	0.24	0.11–0.54	0.001*
FEV_1 (lit.)	12.80	3.05–53.70	0.001*
Women			
Age	0.69	0.57–0.82	< 0.001**

*: $p < 0.05$, **: $p < 0.001$

Note: CI, confidence interval; FEV_1, forced expiratory volume in 1 s.

Title: The physiological characteristics of community-dwelling elderly Japanese with airflow limitation: A cross-sectional study

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Abstract

Background and aims The aim of this study was to investigate the physiological characteristics of community-dwelling elderly subjects, aged ≥65 years, with airflow limitation in the Japanese community.

Methods Subjects were recruited through local press advertisement, and 180 individuals were enrolled. Data on age, body mass index (BMI), gender, smoking history, and past medical history were obtained, as were pulmonary function parameters, skeletal muscle mass index, and physical activity.

Results The final study population comprised 161 participants from whom we obtained valid spirometry results. The mean age of this population was 73.4 ± 4.4 years, and 78 participants (48.4%) were men. The prevalence of airflow limitation was 29.2% (n = 47). Subjects with airflow limitation were significantly older ($P = 0.01$) and had poorer pulmonary function ($P < 0.01$), lower BMI ($P < 0.01$), and lower skeletal muscle mass index ($P = 0.03$) than healthy elderly subjects. Furthermore, skeletal muscle mass index was significantly correlated with the percentage of predicted forced vital capacity ($r = 0.45$, $P < 0.05$) and forced expiratory volume in 1 second ($r = 0.50$, $P < 0.05$) only in men with airflow limitation.

Conclusions We found that the skeletal muscle mass index was significantly reduced in community-dwelling elderly with airflow limitation, and the skeletal muscle mass index was correlated with pulmonary function only in men with airflow limitation.

Keywords: Airflow limitation・Pulmonary function・Skeletal muscle mass index・Community-dwelling elderly・Japanese

Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by airflow limitation [1] that is usually progressive and irreversible [2]. Today, COPD is a global health problem and is predicted to become the fifth most common cause of disability in the world by 2020 [3] and the third largest cause of death by 2030 [4]. The prognosis of COPD is strongly influenced by the severity level of the airflow limitation [5]. The Nippon COPD Epidemiology (NICE) Study reported that Japan has an estimated 5.3 million subjects with airflow limitation [6]. Of them, 5 million (95%) remain undiagnosed within the community, and only some patients received treatment in the hospital. Therefore, early detection of subjects with airflow limitation in the community is very important.

Early detection of cases has the potential to reduce the future burden of COPD for both morbidity and mortality [7]. However, COPD is frequently diagnosed at a relatively late stage of the disease, probably because early symptoms of the disease are subtle and unrecognized due to individual perception and interpretation. Early symptoms of the disease may not be evident, even though spirometry reveals airflow limitation. Therefore, even if there are no subjective clinical symptoms, early detection of community-dwelling elderly subjects with airflow limitation by using spirometry is a major social issue that should be tackled immediately.

To date, many previous studies focused on physiological characteristics have investigated COPD patients. It is known that COPD has a negative influence not only on respiratory function but also on the whole body, being associated with systemic inflammation, cardiovascular disease, osteoporosis, and changes in body composition such as weight loss [8]. Although many studies report on the association between body composition and exercise function in COPD patients [9, 10], skeletal muscle wasting is of particular interest in that because it directly influences exercise performance [11] and is associated with poor health-related quality of life [12]. Ju et al. demonstrated that total-body skeletal muscle mass was significantly decreased in COPD patients compared with controls [13]. In addition, Ischaki et al. demonstrated that lean total skeletal muscle mass is associated with pulmonary function [14]. Although these effects have been well described in COPD patients, no studies have been published on such physiological characteristics related to an adverse prognosis in community-dwelling elderly Japanese, aged ≥65 years, with airflow limitation.

Therefore, the purpose of this study was to investigate physiological characteristics of community-dwelling elderly Japanese with airflow limitation aged ≥65 years.

Materials and methods

Participants

Elderly community-dwelling subjects aged ≥65 years were recruited through local press advertisement, and 180 participants were enrolled. The inclusion criteria were age ≥65 years, living in the community, and the ability to walk independently (or with a cane). The exclusion criteria were cognitive impairment, severe cardiac or musculoskeletal disorders, previously diagnosed pulmonary disease, and hearing impairment. Written informed consent was obtained from each participant in accordance with the guidelines of the Kyoto University Graduate School of Medicine and the Declaration of Human Rights, Helsinki, 1995. This study protocol was approved by the ethical committee of the Kyoto University Graduate School of Medicine.

Measurements

Demographic data

Data on age, body mass index (BMI), gender, smoking history, and past medical history (hypertension, hyperlipidemia, diabetes mellitus, cardiovascular disease, and osteoporosis) were obtained. All subjects completed a self-reported questionnaire on smoking history and past medical history. All data were collected at study onset.

Furthermore, the pack-year index was calculated for each subject by multiplying the number of cigarette packs smoked per day by the number of smoking years [15].

Pulmonary function tests

All subjects underwent spirometric evaluation. Pulmonary function tests were carried out according to the guidelines of the Japanese Respiratory Society [16]. In the recent Global initiative for Chronic Obstructive Lung Disease (GOLD) guideline, all values for forced expiratory volume in 1 second (FEV_1) refer to post-bronchodilator FEV_1, but our values were obtained without a bronchodilator. Forced vital capacity (FVC), FEV_1, and peak flow were measured by spirometry (Spiro Sift SP-370; Fukuda Denshi Co., Ltd, Tokyo, Japan). After that, we calculated FVC% predicted and FEV_1% predicted, corrected by height and age. The formulae for calculating FVC% predicted and FEV_1% predicted were derived from the Japanese criteria [17]. Airflow limitation was defined as a ratio of FEV_1/FVC of <70% [18]. The severity of airflow limitation was based on FEV_1% predicted, in accordance with the GOLD criteria ($FEV_1 \geq 80\%$ predicted, mild; FEV_1 50–79% predicted, moderate; FEV_1 30–49% predicted, severe; $FEV_1 < 30\%$ predicted, very severe) [19].

Skeletal muscle mass index (SMI)

A bioelectrical impedance data acquisition system (Inbody 430; Biospace Co., Ltd, Seoul, Korea) was used to determine bioelectrical impedance. This system applies a constant current of 800 mA at 50 kHz through the body. Participants stood on 2 metallic electrodes and held metallic grip electrodes. Appendicular skeletal muscle mass was determined using segmental body composition and muscle mass, and the value for the appendicular skeletal muscle mass was determined and used for the present analysis. SMI was obtained by dividing the appendicular skeletal muscle mass by the square of height (kg/m^2) [20].

Physical activity

We distributed pedometers and note paper to participants for recording physical activity. Participants were asked to wear the pedometer in the pocket of their dominant leg for 14 consecutive days except when bathing, sleeping, and performing water-based activities. The pedometers had 30-day data storage capacity. The reproducibility and validity of the pedometers in counting walking steps has been previously established in healthy people [21]. The pedometers and note papers were sent to our laboratory by mail after 2 weeks. We calculated averages of daily step counts for 2 weeks.

Statistical analyses

The participants were divided into 2 groups: those with airflow limitation and those who were healthy. We statistically analyzed the differences between the 2 groups using the unpaired *t*-test for age, pulmonary function, body composition, and physical activity, and the χ^2 test for gender, smoking history, and past medical history. The correlation between SMI and pulmonary function was analyzed using Pearson's correlation analysis. Additionally, partial correlation analysis controlling for the variable of age was carried out subsequently to assess the influence of age on SMI and pulmonary function. All statistical analyses were performed with SPSS version 20.0 software (SPSS Inc., Chicago, IL, USA). The level of statistical significance was set at $P < 0.05$ for all analyses.

Results

Prevalence of airflow limitation

Of 180 initially selected community-dwelling elderly Japanese aged ≥65 years, 19 were excluded owing to invalid spirometry results. Thus, the study population comprised 161 community-dwelling elderly. The mean age of this population was 73.4

± 4.4 years, and 78 (48.4%) participants were men. Undiagnosed Airflow limitation existed in 29.2% (n = 47) of the study population. According to the GOLD stage classification, 31.9% (n = 15) of participants were classified as mild, 61.7% (n = 29) as moderate, and 6.4% (n = 3) as severe; no participants were classified as very severe (Table 1). Regarding smoking history, the smoking rate was 39.8% (n = 64) in the entire population and 34.0% (n = 16) in airflow limitation subjects.

Comparison of characteristics between airflow limitation subjects and healthy older subjects

Demographic characteristics for the airflow limitation subjects and healthy elderly subjects are shown in Table 2. Subjects with airflow limitation were older (P = 0.01) and had poorer pulmonary function (FVC% predicted, P = 0.03; FEV_1, FEV_1% predicted, FEV_1/FVC, and peak flow, $P < 0.01$) and lower BMI ($P < 0.01$) than healthy elderly subjects. In addition, the SMI of those with airflow limitation was 6.3 ± 0.9 kg/m^2, whereas that of healthy elderly subjects was 6.6 ± 1.0 kg/m^2; this difference was statistically significant (Figure 1, P = 0.03). Furthermore, physical activity of those with airflow limitation was 6601 ± 2650 steps per day, whereas that of healthy elderly subjects was 7553 ± 3237 steps per day; although the difference in physical activity was not significant, it tended to be lower in those with airflow limitation.

Correlation between SMI and pulmonary function

SMI was significantly positively correlated with FVC% predicted (r = 0.45, P < 0.05) and FEV_1% predicted (r = 0.50, P < 0.05) in men with airflow limitation, but no correlation was found in women with airflow limitation. This significant correlation in men with airflow limitation was apparent after controlling for age using partial correlation analysis (FVC% predicted, r = 0.48; FEV_1% predicted, r = 0.48). By contrast, there was no correlation between SMI and pulmonary function in healthy elderly subjects, as shown in Table 3.

Discussion

This cross-sectional study provides 2 new findings. First, compared with healthy elderly subjects, SMI was significantly decreased in those with airflow limitation. Second, SMI was significantly correlated with pulmonary function in men with airflow limitation.

Airflow limitation was found in 29.2% of our participants. Previous epidemiological studies for 40 years or more in Japan have reported the prevalence of airflow limitation to be approximately 10% [6, 22]. However, Akamatsu et al. reported that the prevalence of airflow limitation exceeded 15% in elderly subjects aged 60–69 years and 28% in those aged >70 years [23]. The difference in prevalence means that the prevalence of airflow limitation increases with aging, and the association between aging and prevalence of airflow limitation has been reported by a previous study [24]. Therefore, our results for subjects aged ≥65 years (mean age was 73.4 ± 4.4 years) are in accordance with the results of a previous study [23], and we believe that our study did not overestimate or underestimate the spirometry measurements. However, a limitation of the process is that the participants might not yield the real picture of airflow limitation, because we excluded subjects with cognitive impairment. Previous study reported that cognitive impairment has been associated with poor pulmonary function [25]. However, we excluded patients with cognitive impairment as they were unable to perform accurately a spirometry measurement because a previous study reported that reproducibility of spirometric measurements was definitely poor in subjects with cognitive impairment [26].

To the best of our knowledge, this is the first study to indicate a reduction in skeletal muscle mass in community-dwelling subjects with airflow limitation. The mechanisms of skeletal muscle wasting are not precisely understood; however, inactivity [27] and systemic inflammation [28] are considered to be major factors in skeletal muscle wasting. We found the difference in physical activity was not significant compared with healthy elderly subjects, but it tended to be lower in subjects with airflow limitation. Pitta et al. reported that daily physical activity values in COPD patients were significantly lower than those in healthy controls [29]. This previous study targeted patients with mild to very severe COPD, but because we targeted airflow limitation subjects with few symptoms and no consultation history in the community, the possibility that there are no significant differences in physical activity in comparison with healthy older subjects is high. However, the trend of reduced physical activity in subjects with airflow limitation is consistent with the results of a previous study in COPD patients [29]. Therefore, there is a possibility that the decrease in physical activity is associated with skeletal muscle wasting. On the other hand, pulmonary function disorders are often associated with a systemic inflammatory state [30]. Although age [31], gender [32], and smoking history [33] have been reported to accelerate systemic inflammation, we found a significant difference only for age between airflow limitation subjects and healthy elderly subjects. Therefore, the reduction in SMI in subjects with airflow limitation may be dependent on systemic inflammation related to older age.

The present study found a significant correlation between SMI and pulmonary function in men with airflow limitation after controlling for age using partial correlation analysis. This relationship might be a consequence of the high resting energy expenditure due to the increased work of breathing [34], inadequate dietary intake, physical inactivity [35], and excessive apoptosis of skeletal muscle due to increased systemic inflammation [36]. However, with the exception of physical activity, our data do not support these hypotheses. To our knowledge, we believe that the recognized gender differences are a reflection of systemic inflammation. Previous studies reported in cross-sectional and longitudinal analyses that systemic inflammation is negatively correlated with both FEV_1 and FVC in men but not in women [32, 37, 38]. That is, it is possible that systemic inflammation contributed to both skeletal muscle wasting and poor pulmonary function in men with airflow limitation. Because the prognosis for elderly people with decreased skeletal muscle mass and pulmonary function is generally adverse, it is important to detect airflow limitation at an early stage in the community.

There are several limitations that warrant mention in this study. First, because the participants were recruited through local press advertisements, there may be a selection bias. The participants may have been highly health conscious; on the other hand, the subjects with health problems might not participate in this study. Second, self-reported questionnaires may not always provide precise data due to recall bias. Third, because we performed only a simple pulmonary function test to detect airflow limitation in the community-dwelling elderly in our study, we were not able to examine pulmonary function in detail. Fourth, because this study was cross-sectional, a cause-effect relationship between SMI and pulmonary function remains unknown. Further investigations, including prospective studies, are required to confirm our discussion.

Conclusions

To the best of our knowledge, this is the first study to investigate the physiological characteristics of community-dwelling elderly Japanese with airflow limitation aged ≥65 years. We found a significant reduction in SMI in subjects with airflow limitation compared with healthy elderly subjects. Furthermore, we found a significant correlation between SMI and pulmonary function in men with airflow limitation, but not in women. Additional studies are needed for the early detection of subjects with airflow limitation and to determine the characteristics of community-dwelling elderly Japanese, aged ≥65 years, with airflow limitation.

Conflict of interest statement

None of the authors have conflicts of interest or financial disclosures.

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