

Prevalence and Impact of Social Frailty in Patients with Chronic Obstructive Pulmonary Disease

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Background: Patients with chronic obstructive pulmonary disease (COPD) are more inclined to have a high level of social vulnerability due to their physical and psychological burden. However, to date, there have been no study on social frailty in patients with COPD. This study aimed to investigate the prevalence, characteristics, and impact of social frailty in patients with COPD.

Methods: Social frailty was assessed using five items in a questionnaire. A patient was diagnosed with social frailty if responses to two or more items were positive. Four hundred and five patients with COPD were assessed for social frailty, dyspnea, and appetite. We also prospectively examined the number of acute exacerbation and unexpected hospitalization for 1 year.

Results: Thirty-six percent of patients with COPD had social frailty. They had reduced appetite and more severe dyspnea [Simplified Nutritional Appetite Questionnaire score: odds ratio (OR) 0.81, 95% confidence interval (CI) 0.69–0.95, $p < 0.01$; modified Medical Research Council score: OR 1.42, 95% CI 1.05–1.93, $P = 0.02$] than patients without social frailty. Social frailty was not a risk factor for moderate acute exacerbation of COPD but a risk factor for severe acute exacerbation and all-cause unexpected hospitalization (severe acute exacerbation: β , standardized regression coefficient: 0.13, 95% CI 0.01–0.25, $P = 0.04$, unexpected hospitalization: β 0.17, 95% CI 0.05–0.29, $P = 0.01$).

Conclusion: The prevalence of social frailty is 36%; however, social frailty has a marked clinical impact in patients with COPD.

Keywords: social frailty, chronic obstructive pulmonary disease, social robustness

Introduction

Frailty is a state of vulnerability, in which homeostasis is lost due to exposure to stressors,¹ resulting in an increased risk of falls, disability, and mortality.² The concept of frailty involves physical, psychological, and social domains.³ In the past, predominantly physical frailty has been studied, but recently, social frailty has begun to attract attention, given that low levels of social activity and participation in social roles adversely affect physical functions.⁴ Similarly, social frailty increases the risk of physical disability and mortality.^{5,6}

Several studies have reported the influence of social factors in patients with chronic obstructive pulmonary disease (COPD). A previous study showed that patients with COPD have low levels of social participation.⁷ In patients with COPD, low social participation and respiratory function are associated with life satisfaction,⁸ social support and self-efficacy with overall functioning,⁹ single marital status with an increased risk of readmission,¹⁰ and physical activity with the level of physical activity of their cohabiting loved ones.¹¹ These studies showed that single patients were more likely to have no one to support them in adhering to medication, ensuring physical activity, and healthy eating habits¹⁰ and that the higher the physical activity of people close to them, the higher the physical activity of patients with COPD.¹¹ Based on these backgrounds, it was expected that social factors would have a large impact on patients with COPD.

Social frailty refers to low social activity, low level of social role, and poor social relationships, and is associated with the risk of malnutrition and mortality among the elderly.^{6,12,13} Social frailty is assessed by combining various factors, such as age, education, marital status, sex, living alone, income, and neighborhood.⁶ The impact of social frailty on some diseases, such as the increased risk of heart failure¹⁴ and osteosarcopenia patients,¹⁵ has attracted attention. However, no study on social frailty in patients with COPD have been conducted, and the prevalence and characteristics of patients with COPD with social frailty are unknown. Patients with COPD often have multifaceted impairments, such as decreased physical activity^{16,17} and psychological burdens, such as anxiety.^{18,19} Therefore, the prevalence of social frailty may be high in patients with COPD. In addition, socially frail patients with COPD are expected to have an increased risk of acute exacerbation of COPD and unexpected hospitalization due to reduced dietary intake, as well as increased threshold for visiting medical institutions.

The aim of this study was to investigate the prevalence, characteristics, and impact of social frailty on acute exacerbation and unexpected hospitalization in patients with COPD.

Materials and Methods

Study Design and Patients

This was a multicenter, prospective, observational study conducted between January 2018 and February 2021. We recruited patients who regularly visited four facilities in Japan. In this study, outpatients were randomly selected by their attending physicians and agreed to participate in the study. COPD was diagnosed by spirometry (post-bronchodilator $FEV_1/FVC < 0.7$) according to the Global Initiative for Chronic Obstructive Lung Disease.²⁰ The inclusion criteria were as follows: age ≥ 40 years and a history of smoking as well as diagnosis of COPD. The physician recorded the patient's objective findings and the patient completed the questionnaire. Adherence with the study was determined based on patient data and medical records. The following exclusion criteria were also applied: acute exacerbation of COPD within 4 weeks, concomitant respiratory diseases other than COPD, concurrent active malignancy, and inability to read and understand the questionnaires. Patients were excluded for the following reasons: not meeting the inclusion criteria (11 patients), not trackable for 1 year (29 patients), missing data on social frailty (1 patient), complications of interstitial pneumonia (3 patients), active non-tuberculous mycobacteria infection (1 patient), and lung cancer (2 patients).

This study was carried out in accordance with the Declaration of Helsinki guidelines and was approved by the ethics committee of Showa University School of Medicine (approval number: 2453) and by an independent ethics committee. All patients provided informed consent.

Definition of Social Frailty and Its Severity

Social frailty was examined using five questions in the baseline survey, which investigated the following: (1) going out less frequently than in the previous year, (2) not sometimes visiting friends, (3) not feeling helpful to friends or family, (4) living alone, and (5) not talking to someone every day.⁶ In accordance with a previous study, we defined social robustness as when none of the five issues were present, social prefrailty as when one issue was present, and social frailty as when two or more issues were present.⁶

Clinical Measurements and Definition of Exacerbation and Hospitalization

Body mass index (BMI) was calculated in kg/m^2 . Dyspnea was evaluated using the modified Medical Research Council (mMRC) dyspnea scale.²¹ The total scores range from 0 to 4, and a high score indicates severe dyspnea. Patient health status was assessed using the COPD Assessment Test (CAT) and high score indicates a poor health condition.²² Appetite was measured using the Simplified Nutritional Appetite Questionnaire (SNAQ).²³ The possible scores range from 4 to 20, and a low score indicates a poor appetite. Mood disorders were assessed using the Hospital Anxiety and Depression Scale (HADS-Anxiety and HADS-Depression).²⁴ The HADS comprises 14 items divided into two subscales, HADS-Anxiety and HADS-Depression, each of which contains seven items and a higher score means a stronger mental load. Low physical performance was defined as the inability to rise from a chair five times without using the arms.²⁵

Participants were followed up for 1 year to determine whether they had exacerbations. Moderate exacerbation of COPD was defined as an exacerbation requiring the administration of antibiotics and/or systemic steroids, but not

hospitalization. Severe exacerbation of COPD was defined as an exacerbation that required hospitalization. Unexpected hospitalization was defined as all-cause hospitalization, per year, excluding scheduled surgery and scheduled hospitalization for examination. The outpatient physician recorded the frequency of exacerbations and unexpected hospitalization based on direct patient interviews, a prescription record book, a diary kept by patients, and a medical record review.

Statistical Analysis

Continuous variables were presented as mean \pm standard deviation. One-way analysis of variance, the Kruskal–Wallis test, and chi-squared tests were used to compare social frailty severity groups (social robust, social prefrailty, and social frailty). The Kruskal–Wallis test was used to analyze the proportion of social frailty severity by age group. Spearman's rank correlation analysis was performed to evaluate the associations between the social frailty score and several clinical factors. Logistic regression analysis was performed to identify clinical factors associated with social frailty. Multivariate linear regression analysis was performed to identify factors associated with the number of moderate and severe COPD acute exacerbation and unexpected hospitalization from baseline to 1 year. We did not use *p*-value to determine variables; rather, we focused on clinical factors to determine the factors to be used in the multivariate analysis.

All statistical tests were two-tailed, and *P*-values < 0.05 were considered to indicate statistical significance. All statistical analyses were performed using JMP Pro for Macintosh version 16 (SAS Institute, Cary, NC, USA).

Results

Participant Characteristics

Patient characteristics are presented in Table 1. Overall, 405 patients with COPD with a mean age of 74.3 ± 8.0 years were enrolled in this study. The mean CAT score and %FEV₁ were 14.1 ± 7.8 and $65.1 \pm 22.4\%$, respectively. The prevalence of social robustness, social prefrailty, and social frailty was 122 (30.1%), 134 (33.1%), and 149 (36.8%), respectively. The more severe the social frailty, the older the patient, the worse the CAT, mMRC, SNAQ, HADS-Anxiety, and HADS-Depression scores, the worse the %FEV₁, the more difficult it was for the patient to get up from a chair, and the more frequent was the severe acute exacerbation and unexpected hospitalization ($P < 0.05$).

Figure 1 shows the percentage of the severity of social frailty according to age group. The prevalence of social frailty or prefrailty was $>60\%$ in all age groups. Although the ratio of the severity of social frailty tended to increase as the age of the group increased, there was no significant difference among groups ($P = 0.08$).

Table 1 Characteristics of Study Participants According to the Social Frailty Group/Level

| | Total | Social Robustness (n=122) | Social Prefrailty (n=134) | Social Frailty (n=149) | P value |
|----------------------------|-----------------|------------------------------|------------------------------|---------------------------|---------|
| Age | 74.3 \pm 8.0 | 72.8 \pm 7.1 | 74.1 \pm 8.6 | 75.6 \pm 8.1 | 0.01 |
| Sex (Male) | 359(88.6%) | 106(86.9%) | 117(87.3%) | 136(91.3%) | 0.44 |
| Pack-year | 50.0 \pm 28.4 | 45.4 \pm 25.3 | 51.4 \pm 24.8 | 52.5 \pm 33.3 | 0.12 |
| CAT | 14.1 \pm 7.8 | 11.5 \pm 7.1 | 13.5 \pm 7.6 | 16.7 \pm 7.8 | <0.01 |
| mMRC | 1.4 \pm 1.0 | 1.1 \pm 1.0 | 1.3 \pm 1.0 | 1.8 \pm 1.0 | <0.01 |
| SNAQ | 14.5 \pm 1.7 | 15.0 \pm 1.6 | 14.6 \pm 1.6 | 13.9 \pm 1.8 | <0.01 |
| HADS-Anxiety | 4.9 \pm 3.5 | 4.2 \pm 3.2 | 4.8 \pm 3.7 | 5.5 \pm 3.6 | 0.01 |
| HADS-Depression | 6.1 \pm 3.5 | 4.6 \pm 3.1 | 6.1 \pm 3.7 | 7.3 \pm 3.3 | <0.01 |
| BMI | 22.8 \pm 4.0 | 22.9 \pm 3.7 | 23.0 \pm 3.9 | 22.5 \pm 4.4 | 0.59 |
| %FEV ₁ | 65.1 \pm 22.4 | 68.6 \pm 22.2 | 67.6 \pm 20.4 | 59.7 \pm 23.5 | <0.01 |
| Getting up from a chair | 265(71.6%) | 81.10% | 72.10% | 63.50% | <0.01 |
| Moderate exacerbation | 0.47 \pm 0.93 | 0.31 \pm 0.64 | 0.52 \pm 0.94 | 0.55 \pm 1.1 | 0.07 |
| Severe exacerbation | 0.16 \pm 0.49 | 0.06 \pm 0.23 | 0.15 \pm 0.42 | 0.26 \pm 0.65 | <0.01 |
| Unexpected hospitalization | 0.22 \pm 0.62 | 0.10 \pm 0.34 | 0.17 \pm 0.45 | 0.37 \pm 0.87 | <0.01 |

Abbreviations: CAT, COPD assessment test; SNAQ, Simplified Nutritional Appetite Questionnaire; mMRC, modified Medical Research Council dyspnea scale; HADS, Hospital Anxiety and Depression Scale; FEV₁, forced expiratory volume in one second.

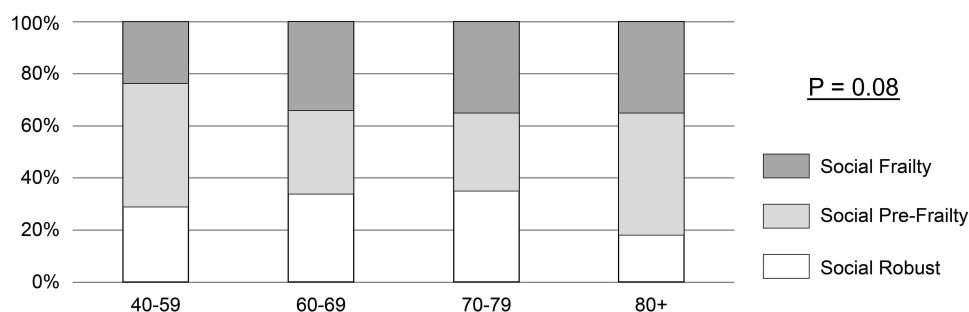


Figure 1 Prevalence of the severity of social frailty by age group. The prevalence of social frailty or prefrailty was more than 60% in all age groups. There were no significant differences among groups ($P = 0.08$).

Figure 2 shows the association between social frailty and clinical factors in patients with COPD. Each of the clinical factors had a weak but significant correlation with social frailty (age: $r = 0.13$, $P = 0.01$; CAT: $r = 0.29$, $P < 0.01$; mMRC: $r = 0.29$, $P < 0.01$; SNAQ: $r = -0.26$, $P < 0.01$; HADS-Anxiety: $r = 0.17$, $P < 0.01$; %FEV₁: $r = -0.15$, $P < 0.01$).

Clinical Characteristics of Patients with Social Frailty

Logistic regression analysis was performed to investigate the characteristics of patients with COPD who had social frailty (Table 2). SNAQ and mMRC were significantly associated with social frailty, independently of age, sex, and other clinical factors (SNAQ score: odds ratio [OR], 0.81 [95% confidence interval (CI): 0.69–0.95], $P < 0.01$; mMRC score: OR, 1.42 [95% CI: 1.05–1.93], $P = 0.02$). Other clinical factors, including age and %FEV₁, were not significantly associated with social frailty according to logistic regression analysis.

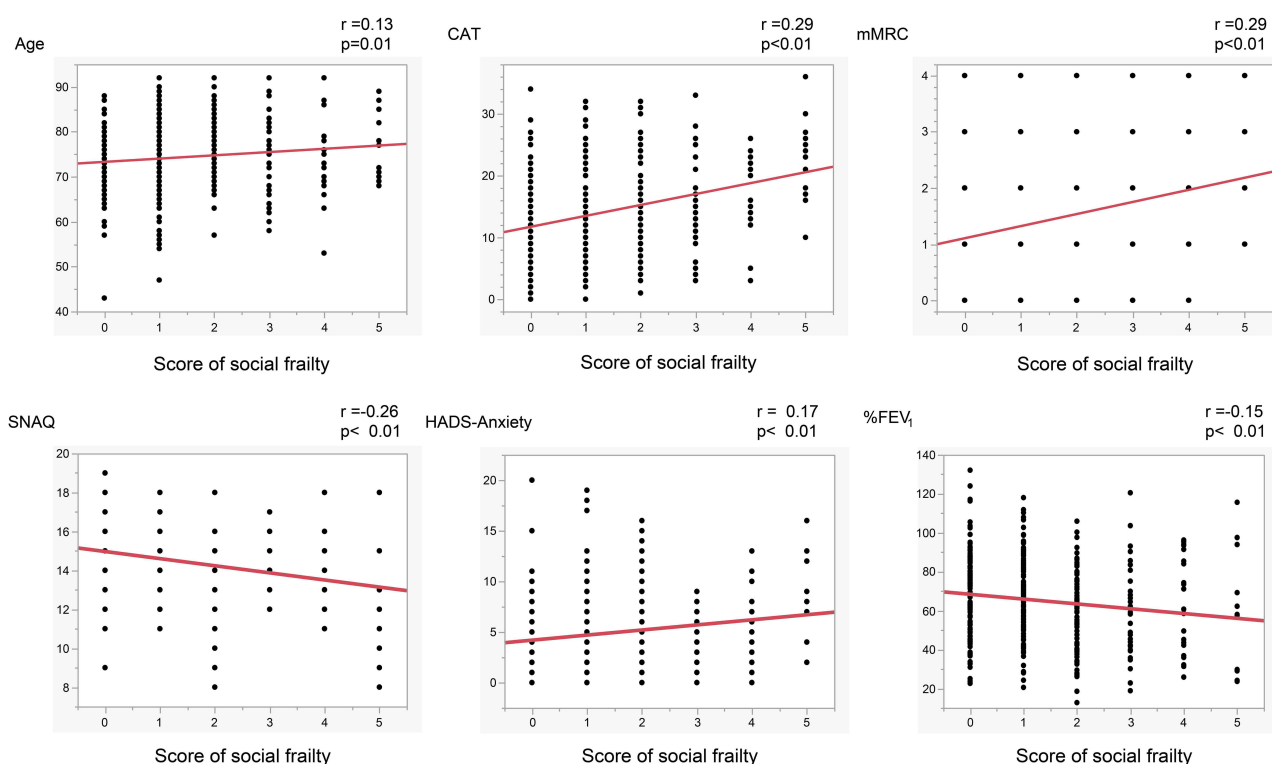


Figure 2 Relationship between social frailty score and clinical factors in patients with chronic obstructive pulmonary disease. Spearman's rank correlation was used to test this relationship. The total score of social frailty was significantly correlated with each clinical factor ($P < 0.05$).

Table 2 Clinical Characteristics of Patients with Social Frailty

| | Univariate Analysis | | | Multivariate Analysis | | |
|--------------------------------|---------------------|-----------|---------|-----------------------|-----------|---------|
| | Odds Ratio | 95% CI | P value | Odds Ratio | 95% CI | P value |
| Age (year) | 1.03 | 1.01–1.06 | 0.01 | 1.02 | 0.98–1.05 | 0.34 |
| Sex (male) | 1.55 | 0.79–3.04 | 0.21 | 1.50 | 0.65–3.47 | 0.33 |
| CAT | 1.07 | 1.04–1.10 | <0.01 | 1.01 | 0.97–1.06 | 0.57 |
| mMRC | 1.71 | 1.39–2.11 | <0.01 | 1.42 | 1.05–1.93 | 0.02 |
| SNAQ | 0.74 | 0.65–0.84 | <0.01 | 0.81 | 0.69–0.95 | <0.01 |
| HADS-Anxiety | 1.08 | 1.02–1.14 | 0.01 | 1.03 | 0.96–1.11 | 0.42 |
| %FEV ₁ (%predicted) | 0.98 | 0.97–0.99 | <0.01 | 1.00 | 0.98–1.01 | 0.44 |
| Unable to get up from a chair | 1.86 | 1.17–2.94 | <0.01 | 1.32 | 0.75–2.31 | 0.34 |

Abbreviations: CI, confidence interval; CAT, COPD assessment test; SNAQ, Simplified Nutritional Appetite Questionnaire; mMRC, modified Medical Research Council dyspnea scale; HADS, Hospital Anxiety and Depression Scale; FEV₁, forced expiratory volume in one second.

Impact of Social Frailty on Acute Exacerbation and Unexpected Hospitalization

Multivariate linear regression analysis showed that the risk factors for moderate acute exacerbation were CAT and %FEV₁ [CAT: β , standardized regression coefficient, 0.24 (95% CI: 0.10 to 0.39), $P < 0.01$; %FEV₁: β , standardized regression coefficient: -0.16 (95% CI: -0.28 to -0.03), $P = 0.01$], while social frailty was not a risk factor (Table 3a). Social frailty was a risk factor for severe acute exacerbation [β , standardized regression coefficient: 0.13 (95% CI: 0.00 to 0.25), $P = 0.04$] (Table 3b). Similarly, social frailty was also a risk factor for unexpected hospitalization [β , standardized regression coefficient: 0.10 (95% CI: 0.03 to 0.18), $P = 0.01$], and unable to get up from a chair was also a risk factor for unexpected hospitalization [β , standardized regression coefficient: 0.10 (95% CI: 0.02 to 0.18), $P = 0.01$]. (Table 3c).

Table 3 Impact of Social Frailty on Acute Exacerbation and Unexpected Hospitalization in Patients with Chronic Obstructive Pulmonary Disease

| (a) | | | |
|-----------------------------------|-----------------------|---|----------------|
| Moderate exacerbation/year | | | |
| Multivariate analysis | Standard error | β, Standardized coefficient | P-value |
| Social frailty | 0.061 | 0.01 (-0.11 to 0.13) | 0.86 |
| CAT | 0.008 | 0.24 (0.10 to 0.39) | <0.01 |
| %FEV ₁ | 0.064 | -0.16 (-0.28 to -0.03) | 0.01 |
| mMRC | 0.075 | 0.11 (-0.04 to 0.26) | 0.15 |
| Age | 0.089 | -0.08 (-0.20 to 0.05) | 0.22 |
| Sex (Male) | 0.089 | 0.03 (-0.14 to 0.21) | 0.73 |
| SNAQ | 0.218 | 0.27 (-0.16 to 0.70) | 0.22 |
| HADS-A | 0.060 | 0.00 (-0.11 to 0.12) | 0.95 |
| Unable to get up from a chair | 0.065 | -0.10 (-0.23 to 0.03) | 0.12 |
| (b) | | | |
| Severe exacerbation/year | | | |
| Multivariate analysis | Standard error | β, Standardized coefficient | P-value |
| Social frailty | 0.063 | 0.13 (0.00 to 0.25) | 0.04 |
| CAT | 0.077 | 0.06 (-0.09 to 0.21) | 0.42 |
| %FEV ₁ | 0.066 | -0.07 (-0.19 to 0.06) | 0.32 |

(Continued)

Table 3 (Continued).

| | | | |
|--|-----------------------|---|----------------|
| mMRC | 0.077 | 0.13 (−0.02 to 0.28) | 0.09 |
| Age | 0.063 | −0.01 (−0.14 to 0.11) | 0.83 |
| Sex (Male) | 0.091 | −0.09 (−0.27 to 0.09) | 0.31 |
| SNAQ | 0.224 | 0.19 (−0.25 to 0.64) | 0.39 |
| HADS-A | 0.062 | −0.01 (−0.13 to 0.11) | 0.86 |
| Unable to get up from a chair | 0.067 | 0.11 (−0.02–0.24) | 0.10 |
| (c) | | | |
| Unexpected hospitalization/year | | | |
| Multivariate analysis | Standard error | β, Standardized coefficient | P-value |
| Social frailty | 0.039 | 0.10 (0.03 to 0.18) | 0.01 |
| CAT | 0.048 | 0.02 (−0.08 to 0.11) | 0.73 |
| %FEV ₁ | 0.040 | 0.03 (−0.05 to 0.11) | 0.51 |
| mMRC | 0.047 | 0.09 (−0.01 to 0.18) | 0.06 |
| Age | 0.039 | −0.03 (−0.10 to 0.05) | 0.47 |
| Sex (Male) | 0.056 | −0.09 (−0.19 to 0.02) | 0.12 |
| SNAQ | 0.137 | 0.01 (−0.25 to 0.28) | 0.92 |
| HADS-A | 0.038 | 0.01 (−0.07 to 0.08) | 0.89 |
| Unable to get up from a chair | 0.041 | 0.10 (0.02 to 0.18) | 0.01 |

Abbreviations: CAT, COPD assessment test; SNAQ, Simplified Nutritional Appetite Questionnaire; mMRC, modified Medical Research Council dyspnea scale; HADS, Hospital Anxiety and Depression Scale; FEV₁, forced expiratory volume in one second.

Discussion

To the best of our knowledge, this is the first study to evaluate the prevalence and characteristics of social frailty in patients with COPD. This study showed the following important findings in patients with COPD: first, the prevalence of social frailty and social prefrailty is 36.8% and 33.1%, respectively; second, social frailty is associated with a reduced appetite and more severe dyspnea; and third, social frailty is a risk factor for severe acute exacerbation and unexpected hospitalization.

Among patients with COPD in this study, 36.8% and 33.1% had social frailty and social prefrailty, respectively. Considering that the prevalence of social frailty was 10.2–14.7% in previous studies of older residents in communities in Japan and Korea,^{6,26,27} which used the same criteria as in this study, patients with COPD seem to have a higher risk of social frailty, in a disease-specific manner. A possible reason for the higher prevalence of social frailty in patients with COPD may be that physical symptoms and mood disorders derived from COPD may reduce social activity, self-affirmation, and the frequency of conversation, leading to social frailty. Previous studies have shown that social vulnerability increases with age;^{26,28} however, in this study, there was no significant relationship between age group and severity of social frailty in the multivariate analysis. This study showed that even non-older patients with COPD may have social frailty, given that the incidence of social frailty was as high as 23.5%, even in the age group of 40–59 years.

This study showed that dyspnea was associated with social frailty, which may be related to the decreasing social activity in patients with COPD. This hypothesis is supported by previous studies suggesting that the presence of dyspnea leads to decreased physical activity,²⁹ and that low physical function limits mobility and social activities.^{30,31} In addition, this study showed that patients with COPD who have social frailty have a reduced appetite. This result is consistent with previous studies that showed that socially isolated older adults may be at a higher risk of dietary inadequacy and poor nutrition.^{32,33} Eating out is expected to provide nutritional intake as well as social connection.³³ Patients with social frailty may have a low appetite because they eat out less frequently due to lack of motivation to go out as well as a lack of friends or partners to visit. The impact of social frailty on patients with COPD is significant, since it was reported that

a loss of appetite, leading to nutritional disorders and weight loss, can lead to a worse prognosis³⁴ and increase the risk of acute exacerbations³⁵ in patients with COPD.

The present study showed that social frailty is a risk factor for severe acute exacerbation and unexpected hospitalization. Acute exacerbation of COPD is important because it induces deterioration of respiratory function³⁶ and increases the risk of mortality and results in high medical costs.³⁷ While previous studies have shown that social frailty is a risk factor for hospitalization and readmission in the general population,^{38,39} no previous study has shown that social frailty is a risk factor for unexpected hospitalization in patients with COPD. Patients with social frailty were more likely to live alone and have less social interaction, making it more difficult for them to obtain social support, and placing them at a higher risk of deterioration and of being hospitalized. In addition, physicians may have admitted such patients with social frailty because they consider it a risk to manage the patient in an outpatient setting. A previous study reported that community-dwelling older people with social frailty have high levels of inflammatory cytokines.⁴⁰ Systemic inflammation is a characteristic finding in patients with COPD and has been reported to exacerbate comorbidities, such as cardiovascular disease, diabetes, and osteoporosis.⁴¹ Therefore, higher levels of inflammatory cytokines may have increased the risk of hospitalization in patients with COPD who are socially frail.

We propose that social frailty should be assessed actively in patients with COPD, as social frailty can be improved through appropriate interventions. In fact, community group interventions, including physical exercise and social participation, prevent the development of functional disabilities in older individuals.^{42,43} It has been reported that various interventions, such as group, individual, and mixed interventions, may be promising tools for addressing social isolation and loneliness.⁴⁴ Recently, it has been reported that digital interventions may be a new method for reducing loneliness in adults.⁴⁵ However, the effectiveness of interventions for patients with COPD who are social frail has not been demonstrated to date, and further studies are therefore needed.

This study had several limitations. First, we did not longitudinally assess social frailty, appetite, and dyspnea; thus, we could not assess their causal relationship accurately. Second, all the study participants were secondary- and tertiary-care patients; thus, the findings of this study, particularly the prevalence of social frailty, may not be applicable to primary-care hospitals. Third, we did not measure the level of physical activity, functional aerobic capacity, and other frailty markers of the participants. Therefore, we were unable to analyze their impact on social frailty. We did not evaluate the patients' economic and geographical factors. However, given that all Japanese citizens are covered by national health insurance and considering the size and location of the participating centers, we did not consider that the patients' economic or geographic circumstances had a significant impact. Fourth, most participants were males and on average, the participants had moderate levels of COPD in our study. Our results may not be the same in people with severe COPD. However, to the best of our knowledge, this is the first study that has investigated social frailty in patients with COPD. In addition, this study has the strength of not being affected by COVID-19, as it used data from patients who participated until February 2020, considering that the Japanese government announced a state of emergency to prevent the spread of COVID-19 in Japan after April 2020.

Conclusions

In this study, 36% of patients with COPD had social frailty. These individuals had reduced appetite, more severe dyspnea, and were at high risk of severe acute exacerbation and unexpected hospitalization. In patients with COPD, social frailty is markedly prevalent and has a strong clinical impact. The results of this study indicate the importance of investigating the long-term impact of social frailty and the need for intervention trials for social frailty in patients with COPD.

Abbreviations

CAT, COPD assessment test; CI, confidence interval; COPD, chronic obstructive pulmonary disease; FEV₁, forced expiratory volume in one second; FVC, forced vital capacity; HADS, Hospital Anxiety and Depression Scale; mMRC, modified Medical Research Council dyspnea scale; OR, odds ratio; SNAQ, Simplified Nutritional Appetite Questionnaire.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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