

Frailty is Associated with Susceptibility to and Severity of Pneumonia in Functionally-independent Community-dwelling Older Adults: A JAGES Multilevel Cross-sectional Study

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Abstract

Pneumonia is a leading cause of mortality among older adults worldwide. Recently, several studies reported that frailty was associated with mortality among older adults hospitalized due to respiratory infectious diseases, including pneumonia. However, it is unknown whether frailty is associated with susceptibility to and severity of pneumonia in functionally-independent community-dwelling older adults. In this study, we examined whether frailty increased the susceptibility to pneumonia and hospitalization in older adults. We used cross-sectional data from the Japan Gerontological Evaluation Study; the data was collected by using mail-based, self-reported questionnaires from 177,991 functionally-independent community-dwelling older adults aged ≥ 65 years. Our results showed that frailty was significantly associated with both occurrence of and hospitalization due to pneumonia after adjustments with covariates; (Prevalence ratio {PR}1.92, 95% confidence interval {95%CI} [1.66 – 2.22] and PR 1.80, 95%CI [1.42 – 2.28], respectively, $p < 0.001$ for the both). Pre-frailty was associated only with the occurrence of pneumonia. Besides, the instrumental activity of daily living, physical strength, nutrition status, oral function, homeboundness, and depression status in frail older adults were associated with either or both occurrence of and hospitalization due to pneumonia. Our results suggest that frailty influenced the susceptibility to and severity of pneumonia in older adults.

Introduction

Pneumonia is a major cause of mortality and morbidity among older adults worldwide ¹. Community-acquired pneumonia (CAP) is a leading cause of morbidity among community-dwelling older adults in many countries and is different from hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP). The overall incidence rates of CAP have been estimates as 1,790–4,000 in Japan, 2015; 630–1,463 in the U.S., 2015, and 1,400 in Europe, 2013 per 100,000 older adults aged ≥ 65 years ^{2–4}. A recent report showed that 6.8 million episodes of clinical pneumonia, including CAP, resulted in hospital admissions of older adults globally in 2015 ⁵.

Frailty is a state of increased vulnerability to stressors, including infectious diseases, which develops as a consequence of age-related decline in multiple physiological and psychological systems, including the central nervous, endocrine, skeletal muscle, and immune systems ^{6,7}. A recent report showed that the pooled prevalence rates of frail older adults in 62 countries were 22–26%, based on the deficit accumulation model ⁸. Several reports have recently shown that frailty was associated with increased severity and mortality of hospitalized older adults due to respiratory infectious diseases. He Witt and colleagues showed that frailty in older adults hospitalized due to COVID-19 was associated with in-hospital mortality ⁹. Lees and colleagues reported that the frailty of hospitalized older adults with influenza and acute respiratory illness was associated with lower odds of recovery ¹⁰. Luo and colleagues recently reported that frailty was associated with the severity of CAP and mortality among hospitalized older adults ¹¹. However, it was unknown whether frailty was related to the susceptibility to and severity of pneumonia among community-dwelling older adults.

Therefore, we examined whether frailty was associated with susceptibility to pneumonia and hospitalization among functionally-independent community-dwelling older adults aged ≥ 65 years. We assessed associations between each physical or psychological condition in frailty and the prevalence and severity of pneumonia.

Methods

Study sample

The present study had a cross-sectional design and uses data from the Japan Gerontological Evaluation Study (JAGES). JAGES was designed to describe the health status and social determinants of people aged 65 years and older, without disabilities, and not eligible for the long-term care insurance (LTCl) in Japan. We used the data "JAGES 2016," which was obtained from self-reported questionnaires mailed to and filled-in by community-dwelling individuals in 39 municipalities in 2016. In the JAGES 2016 wave, self-administered questionnaires were mailed to functionally independent adults aged 65 years or older who did not receive benefits from the LTCl insurance in Japan. The survey was conducted in the municipalities between September 2016 and January 2017. The data included 180,021 individuals who answered the questionnaires with the basic items (response rate was 70.2%). Participants who did not answer questions regarding age or sex were excluded (n=2,030). The data consisted of individuals who were not eligible for LTCl on 1st April 2016. The data consisted of a three-stage hierarchical structure. The individual data were nested into 720 communities based on elementary or junior high school districts, and these communities were further nested into 39 municipalities.

Outcome variables

The occurrence of pneumonia and hospitalization due to it in the past year from September 2016 to January 2017 were the outcome variables. The occurrence of pneumonia was assessed by asking "Did you fall sick in the past year?" and instructing the participants to select an appropriate answer from the following items: "Influenza," "Pneumonia", and "none of them." Hospitalization due to pneumonia was assessed for participants who answered "Influenza" or "pneumonia" in the previous question by asking "If the sickness was due to influenza or pneumonia, were you hospitalized with relation to it?" and instructing the participants to select an answer from the following options: "Not hospitalized," "Hospitalized due to influenza," "Hospitalized due to pneumonia," "Contracted influenza while I was hospitalized for other diseases," and "Developed pneumonia while I was hospitalized for other diseases." Only participants who answered "Hospitalized due to pneumonia" were considered to be hospitalized. The participants who answered "Influenza" in the first question and "Hospitalized due to pneumonia" in the second were included because influenza can cause primary viral or secondary bacterial pneumonia ¹².

Frailty

Frailty was assessed using the Kihon Check List (KCL) ¹³. KCL was developed by the Japanese Ministry of Health, Labor and Welfare to identify older adults requiring LTCl. KCL was included in the self-administered questionnaires of the JAGES 2016 wave. KCL consists of 25 questions classified into the following seven categories: instrumental activity of daily living (IADL), physical strength, nutritional status, oral function, homeboundness, cognitive function, and depressive mood (Supplemental Table 1). The scores from the KCL was well correlated with the validated assessments of physical strength, nutritional state, cognitive function, depressive mood, and the number of frailty phenotypes defined by the Cardiovascular Health Study criteria (CHS) ¹³. Frailty was categorized into three groups based on KCL scores: robust, 0–3; pre-frail, 4–7; and frail, ≥ 8 ; scores were calculated from the KCL questions, which were validated with the pre-frail and frail categories established by the CHS criteria ¹³. KCL variables were generated for each of the seven categories. Each KCL variable was

categorized into three groups, based on answers to questions: 0, not applicable; 1, applicable; and 2 or ≥ 2 applicable.

Covariates

Age was classified into two groups (65–74 years and ≥ 75 years). Educational attainment was categorized into five groups: < 6 years, 6–9 years, 10–12 years, ≥ 13 years, and others. Equalized income was calculated by dividing the normalized household gross income in 2015 by the square root of the number of household members, and was categorized into five groups: < 0.5, 0.50–0.99, 1.00–1.99, 2.00–3.99, and ≥ 4.00 million yen. The household structure was assessed by asking the respondents the question, “Who do you live with?”. They were asked to choose from the following options: “no one,” “spouse,” “son,” “daughter,” “spouse of child,” “grandchild,” “brother or sister,” “father,” “mother,” “father-in-law,” “mother-in-law,” and “other.” The responses were classified into six groups as follows: living alone, living with a spouse, living with children, living with a spouse and children, living in three-generation households (living with/without a spouse, but with one of the sons/daughters/son’s or daughter’s spouse and grandchildren), and the in a household structure other than the above five categories. Marital status was assessed by asking, “What is your marital status?” and participants were instructed to select one from the following five options: “Married,” “Widowed,” “Divorced,” “Never married” and “Other.” Smoking status was assessed by asking, “Do you smoke cigarettes?” and the participants were instructed to select appropriate answers from the following items: “Never smoked,” “Quit smoking ≥ 5 years ago”, “Quit smoking < 5 years ago,” “Smoke sometimes” and “Smoke almost every day.” The population density of the municipality was categorized as follows: metropolitan (density over 4,000 people per km²), urban (density between 1,500 and 4,000 people per km²), semi-urban (density between 1,000 and 1,499 people per km²), and rural (density below 1,000 people per km²)¹⁴. A municipality dummy variable was generated to adjust for differences in municipalities’ policies in preventing frailty¹⁵. The diabetes, respiratory, heart, kidney/prostate gland, hematological, or immune disease status was assessed by asking participants whether they were receiving any treatment or experiencing after-effects of any of the above diseases. Pneumococcal vaccination status was assessed by asking the participants, “Did you get a pneumococcal vaccination in the last five years? They chose from the following options: “No,” “Yes, I got vaccinated using my municipality’s subsidy”, and “Yes, but I did not get vaccinated using my municipality’s subsidy”. The participants who chose the two latter options were categorized as vaccinated.

Statistical analysis

Multilevel Poisson regression analyses with random intercepts were performed to assess associations between frailty and pneumonia/hospitalization after adjusting for all the covariates. The data were structured in three levels: the individuals were nested within their elementary or junior high school districts and the districts were further nested within the municipalities. The covariates consist of all the covariates at individual-level and the municipality dummy variable used to adjust for differences in municipalities’ policies in older adult’s health including preventing frailty and pneumonia at municipality-level^{15,16}. The individual-level covariates were: age group, sex, educational attainment, equalized income, household structure, marital status, smoking status, municipality population density, diabetes, respiratory disease, heart disease, kidney/prostate gland disease, hematological/immune disease, and pneumococcal vaccination. The prevalence ratios (PRs) and 95% confidence

intervals (95% CIs) were calculated after adjusting for all covariates. We used Stata version 14.2 (StataCorp., College Station, TX, USA) for all analyses, with a 2-tailed significance level set at 5%.

Ethical consideration

The process of obtaining informed consent in the present study was as follows: the questionnaire was sent by mail with the explanation of the study; the participants read the written explanation about the purpose of study and replied. Hence, we considered that informed consent was provided by those who replied and sent back the questionnaire. The JAGES protocol in 2016 was approved by the ethics committee of National Center for Geriatrics and Gerontology (No. 992) and the ethics committee of Chiba University (No. 2493). We followed the STROBE Statement to report our observational study. This study was performed in accordance with the principles of the Declaration of Helsinki. Informed consent was obtained from all participants.

Results

The relationship between prevalence rates of pneumonia and hospitalization with frailty and other characteristics of older adults

Table 1 compares the prevalence rates of pneumonia in the past year with the characteristics of community-dwelling older adults. Frail and pre-frail older adults were 3- and 1.5-times, respectively, more likely to contract pneumonia than non-frail adults. Older adults, with ≥ 1 applicable question in KCL related to IADL, physical strength, nutrition status, oral function, homeboundness, cognitive function, and depression status, were likely to contract pneumonia than those with a score = 0 (none of the questions were applicable). Older adults aged ≥ 75 years, who were male, had lower education/income, who lived in three-generation households, had "other" marital status, who had quit smoking < 5 years ago, and who lived in rural or semi-urban areas were more likely to contract pneumonia than those in other categories. Older adults with diabetes, respiratory, heart, kidney/prostate gland, and hematological/immune diseases, and those who received pneumococcal vaccination were more likely to contract pneumonia more than those without any disease.

Table 1
Prevalence rates of pneumonia in comparison with the characteristics of older adults

Variable	Category	Number	PR (%)	Variables	Category	Number	PR (%)
Frailty	Non-frail	46103	1.0	Household structure (Living alone or with family)	Alone	17960	1.6
	Pre-frail	74226	1.5		With spouse	76735	1.7
	Frail	27826	3.0		With children	13484	1.7
IADL	0*	93053	1.4		With spouse and children	25782	1.6
	1	48447	1.7		In a three-generation household	20935	1.9
	≥ 2	30470	2.3		Others	25095	1.6
Physical strength	0	81729	1.3	Marital status	Married	127198	1.7
	1	50748	1.7		Widowed	35437	1.6
	≥ 2	38648	2.4		Divorced	7995	1.7
Nutrition status	0	141534	1.4		Never married	5272	1.3
	1	31089	2.7		Others	1328	3.1
	2	2885	5.7	Smoking status	Never smoked	106724	1.3
Oral function	0	93575	1.2		Quit smoking ≥ 5 years ago	44794	2.3
	1	50797	1.8		Quit smoking < 5 years ago	5800	4.0
	≥ 2	30043	2.8		Smoking sometimes	2821	2.0
Homeboundness	0	143613	1.4		Smoking almost every day	16230	1.2
	1	29376	2.6	Municipality Population density	Metropolitan	58881	1.7
	2	3972	4.1		Urban	48294	1.5
			Semi-urban		18071	1.8	
Cognitive function	0	115270	1.5		Rural	54745	1.8
	1	44923	1.9				

*Numbers in IADL, physical strength, nutrition status, oral function, homebound, cognitive function, depressive mode are the numbers of the applicable KCL questions for the older adults.

PR, prevalence rate; IADL, instrumental activity of daily living; KCL, Kihon checklist.

Variable	Category	Number	PR (%)	Variables	Category	Number	PR (%)
Depression status	≥ 2	15224	2.6	Diabetes	No	148495	1.6
	0	99421	1.2		Yes	22991	2.1
	1	28866	1.8	Respiratory disease	No	162577	1.1
	≥ 2	37415	2.6		Yes	8909	12.9
Age groups	65–74	101025	1.4	Heart disease	No	154312	1.6
	≥ 75	78966	2.1		Yes	17174	3.0
Sex	Male	82257	2.1	Kidney/Prostate gland disease	No	158970	1.6
	Female	97734	1.3		Yes	12516	2.6
Educational attainment	> 6	1723	2.8	Hematological/Immune disease	No	169260	1.7
	6–9	57731	1.8		Yes	2226	4.0
	10–12	72100	1.6	Pneumococcal vaccination	No	94509	1.1
	≥ 13	45388	1.5		Yes	72274	2.5
	The other	1117	2.1				
Equivalentized income, million yen	< 0.5	6996	1.8				
	0.50–0.99	18547	1.7				
	1.00–1.99	47711	1.6				
	2.00–3.99	43949	1.6				
	≥ 4.00	19882	1.5				
*Numbers in IADL, physical strength, nutrition status, oral function, homebound, cognitive function, depressive mode are the numbers of the applicable KCL questions for the older adults.							
PR, prevalence rate; IADL, instrumental activity of daily living; KCL, Kihon checklist.							

Table 2 compares the prevalence rates of hospitalization due to pneumonia with the characteristics of older adults. Frail and pre-frail older adults were 3.3- and 1.6-times, respectively, more likely to be hospitalized than non-frail adults. Older adults, with ≥ 1 applicable question in KCL from all the seven categories were more likely to be hospitalized than those with a score = 0 (none of the questions were applicable). Older adults aged ≥ 75, who were male, had lower education/income, who lived in three-generation households, had “other” marital status, who had quit smoking < 5 years ago, and who lived in rural areas were more likely to be hospitalized than those in other categories. Older adults with diabetes, respiratory, heart, kidney/prostate gland, and hematological/immune diseases and who received pneumococcal vaccination were more likely to be hospitalized than those without any disease.

Table 2

Prevalence rates of hospitalization due to pneumonia in comparison with the characteristics of older adults

Variable	Category	Number	PR (%)	Variables	Category	Number	PR (%)	
Frailty	Non-frail	1993	7.7	Household structure (Living alone or with family)	Alone	784	14.9	
	Pre-frail	3580	12.7		With spouse	3833	14.8	
	Frail	1692	25.1		With children	579	13.6	
IADL	0*	4483	11.4		With spouse and children	1220	14.8	
	1	2352	15.3		In a three-generation household	1126	16.6	
	≥ 2	1516	23.6		Others	1140	16.4	
Physical strength	0	3701	11.1	Marital status	Married	6399	14.9	
	1	2475	13.1		Widowed	1497	16.1	
	≥ 2	2125	23.6		Divorced	397	13.9	
Nutrition status	0	6498	12.2		Never married	217	11.1	
	1	1777	22.0		Others	68	29.4	
	2	223	38.6		Smoking status	Never smoked	4748	11.3
Oral function	0	3934	11.9	Quit smoking ≥ 5 years ago		2546	19.5	
	1	2584	14.9	Quit smoking < 5 years ago		384	36.2	
	≥ 2	1881	21.4	Smoking sometimes	155	19.4		
Homeboundness	0	6733	12.2		Smoking almost every day	687	10.8	
	1	1569	22.8		Population density	Metropolitan	2840	14.1
	2	249	41.4			Urban	2263	14.5
Cognitive function	0	5320	13.7	Semi-urban		926	14.9	
	1	2284	16.0	Rural	2653	17.1		
	≥ 2	883	21.2	Diabetes	No	7200	14.8	
Depression status	0	4458	11.1		Yes	1178	19.2	

*Numbers in IADL, physical strength, nutrition status, oral function, homebound, cognitive function, depressive mode indicate how many of the KCL questions were applicable to older adults.

PR, prevalence rate; IADL, instrumental activity of daily living; KCL, Kihon checklist.

Variable	Category	Number	PR (%)	Variables	Category	Number	PR (%)
	1	1453	14.3	Respiratory disease	No	6989	10.1
	≥ 2	2155	22.7		Yes	1389	42.1
Age groups	65–74	5020	10.4	Heart disease	No	7293	14.1
	≥ 75	3662	21.8		Yes	1085	24.3
Sex	Male	4402	19.3	Kidney/Prostate gland disease	No	7608	14.7
	Female	4280	11.0		Yes	770	22.5
Educational attainment	> 6	76	32.9	Hematological/Immune disease	No	8213	15.3
	6–9	2678	20.4		Yes	165	22.4
	10–12	3492	13.1	Pneumococcal vaccination	No	4296	10.5
	≥ 13	2296	11.8		Yes	4181	19.1
	The other	67	11.9				
Equivalentized income, million yen	< 0.5	357	15.1				
	0.50–0.99	876	13.6				
	1.00–1.99	2294	14.5				
	2.00–3.99	2146	14.9				
	≥ 4.00	930	13.9				
*Numbers in IADL, physical strength, nutrition status, oral function, homebound, cognitive function, depressive mode indicate how many of the KCL questions were applicable to older adults.							
PR, prevalence rate; IADL, instrumental activity of daily living; KCL, Kihon checklist.							

Frailty was associated with susceptibility to and severity of pneumonia among community-dwelling older adults.

Table 3 shows PR and 95% CI of the association between frailty and the occurrence of pneumonia in the past year or hospitalization due to pneumonia among the community-dwelling older adults. After adjusting with all the covariates, frailty in older adults was significantly associated with both occurrence of and hospitalization due to pneumonia compared to non-frailty (PR 1.92 [95% CI 1.66–2.22] and PR 1.80 [95% CI 1.42–2.28], respectively, $p < 0.001$ for the both). Pre-frailty was also significantly associated with the occurrence of pneumonia but not with hospitalization, compared to non-frailty (PR 1.30 [95% CI 1.14–1.48, $p < 0.001$] and PR 1.23 [95% CI 0.98–1.53], respectively).

Table 3

Prevalence ratios (PR) and 95% confidence intervals (95% CIs) between the occurrence of or hospitalization due to pneumonia and frailty among the community-dwelling older adults

	Pneumonia		The hospitalization	
	PR	95% CI	PR	95% CI
Non-frail	1.00	Reference	1.00	Reference
Pre-frail	1.30***	1.14 – 1.48	1.23	0.98 – 1.53
Frail	1.92***	1.66 – 2.22	1.80***	1.42 – 2.28

The PRs and 95% CI were adjusted for all the covariates in the multilevel Poisson regression with random intercepts. *** $p < 0.001$

Associations between each of the KCL categories and pneumonia/hospitalization among community-dwelling older adults

Table 4 shows PRs and 95% CIs of associations between each of the KCL categories and the occurrence of or hospitalization due to pneumonia in the past year. After adjusting with all the other KCL categories and covariates, the lower and lowest IADL (≥ 1 and ≥ 2 KCL questions were applicable) were negatively associated with the occurrence of pneumonia (PR 0.90, 95% CI [0.84–0.97], $p < 0.01$ and PR 0.79, 95% CI [0.72–0.86], $p < 0.001$, respectively) and the lowest was associated with hospitalization in older adults (PR 1.24, 95% CI [1.01–1.53], $p < 0.05$). The lowest physical strength was associated with both occurrence of and hospitalization due to pneumonia in older adults (PR 1.12, 95% CI [1.03–1.22] and PR 1.32, 95% CI [1.07–1.64]), respectively, $p < 0.01$ for the both). The lower nutrition status was associated with both occurrence of and hospitalization due to pneumonia (PR 1.09, 95% CI [1.004–1.14], $p < 0.05$ and PR 1.54, 95% CI [1.30–1.82], $p < 0.001$, respectively), and the lowest was associated only with hospitalization in older adults (PR 1.71, 95% CI [1.25 – 2.34], $p < 0.01$). The lower and lowest oral function were associated with the occurrence of pneumonia in older adults (PR 1.18, 95% CI [1.10 – 1.27] and PR 1.27, 95% CI [1.17 – 1.39], respectively, $p < 0.001$ for the both). The worst case (≥ 2 KCL questions were applicable) of homeboundness was associated with hospitalization in older adults (PR 1.60, 95% CI [1.11 – 2.12], $p < 0.05$). The worse and worst cases of depression were associated with the occurrence of pneumonia in older adults (PR 1.10, 95% CI [1.006 – 1.19], $p < 0.05$ and PR 1.13, 95% CI [1.04 – 1.23], $p < 0.01$, respectively).

Table 4

Prevalence ratios (PR) and 95% confidence intervals (95% CIs) of associations between the occurrence of/hospitalization due to pneumonia and each of the KCL categories in community-dwelling older adults

	Occurrence of pneumonia		Hospitalization due to pneumonia	
	PR	95% CI	PR	95% CI
IADL				
0	1.00	Reference	1.00	Reference
1	0.90**	0.84–0.97	1.11	0.93–1.34
≥ 2	0.79***	0.72–0.86	1.24*	1.01–1.53
Physical strength				
0	1.00	Reference	1.00	Reference
1	1.03	0.96–1.10	1.07	0.88–1.29
≥ 2	1.12**	1.03–1.22	1.32**	1.07–1.64
Nutrition status				
0	1.00	Reference	1.00	Reference
1	1.09*	1.004–1.17	1.54***	1.30–1.82
2	0.94	0.73–1.21	1.71**	1.25–2.34
Oral function				
0	1.00	Reference	1.00	Reference
1	1.18***	1.10 – 1.27	1.01	0.84 – 1.21
≥ 2	1.27***	1.17 – 1.39	0.85	0.69 – 1.05
Homeboundness				
0	1.00	Reference	1.00	Reference
1	0.97	0.89–1.06	1.09	0.90–1.33
2	0.86	0.67–1.09	1.60*	1.11–2.12
Cognitive function				
0	1.00	Reference	1.00	Reference
1	1.06	0.99–1.14	0.97	0.82–1.16
≥ 2	1.12	0.99–1.25	0.92	0.72–1.18
Depression status				

The KCL and other variables were inputs for the multilevel Poisson regression with random intercepts. Numbers in KCL scores represent how many questions were applicable to older adults.

*p < 0.05, **p < 0.01, ***p < 0.001

IADL, instrumental activity of daily living; KCL, Kihon checklist.

	Occurrence of pneumonia		Hospitalization due to pneumonia	
0	1.00	Reference	1.00	Reference
1	1.10*	1.006–1.19	1.01	0.81–1.25
≥ 2	1.13**	1.04–1.23	1.05	0.87–1.28
The KCL and other variables were inputs for the multilevel Poisson regression with random intercepts. Numbers in KCL scores represent how many questions were applicable to older adults.				
*p < 0.05, **p < 0.01, ***p < 0.001				
IADL, instrumental activity of daily living; KCL, Kihon checklist.				

Discussion

We examined whether frailty was associated with the occurrence of and hospitalization due to pneumonia compared to non-frailty in community-dwelling older adults. Our analysis showed that frailty was significantly associated with both occurrence of and hospitalization due to pneumonia after adjusting for all covariates (Table 3). Besides, IADL, physical strength, nutrition status, oral function, homeboundness, and depression status were associated with either or both of them (Table 4). Our results also suggested that frailty was associated with both susceptibility to and severity of pneumonia, and the six physical or psychological conditions in frailty were associated with either or both of them in community-dwelling older adults.

Several reports have recently shown that frailty was related to mortality in older adults hospitalized due to respiratory infectious diseases^{9–11}. However, it is unknown whether frailty is associated with susceptibility to and severity of pneumonia in community-dwelling older adults. Our results showed that frailty was associated with both occurrence of and hospitalization due to pneumonia in community-dwelling older adults, suggesting that frailty was associated with susceptibility to and severity of pneumonia in these adults (Table 3). Therefore, our results indicate the possibility that frailty may be one of the risk factors related to CAP and hospitalization in community-dwelling older adults. The pneumonia cases were likely CAP because HAP and VAP were excluded by asking corresponding questions to the participants (see “*Outcome variables*” in Methods). Our results also suggest that frailty may be an important indicator in the prevention of pneumonia among community-dwelling older adults, not only be an indicator of the mortality in older adults hospitalized for pneumonia as recently reported¹¹.

Our results showed that low IADL was negatively associated with pneumonia after adjusting for all other KCL categories and covariates (Table 4). However, a negative association between low IADL and pneumonia has not been reported so far. Several reports have shown that community-dwelling older adults with low IADL are less social than those with normal IADL^{17–19}. Social participation was reported to be associated with influenza among community-dwelling older adults²⁰. Taken together, low IADL may present fewer opportunities for infection with respiratory infectious pathogens. However, our results showed that the lowest IADL was associated with hospitalization among older adults (Table 4). Reichard and colleagues reported that adults with low IADL delayed or forewent receiving healthcare services twice more often than those with normal IADL, even if they were insured²¹. Older adults with the lowest IADL may have done the same when compared to those with normal IADL;

they might have delayed visiting the physician even if they had perceived subjective symptoms of pneumonia and hence, the symptoms may have worsened and become more severe leading to hospitalization.

The decline in immune function, so-called “immune senescence”, occurs in frail older adults; this is associated with the malfunction of the cellular and humoral immune systems^{6,22}. Several research groups have reported that antibodies against influenza were more prevalent in physically active older adults than in sedentary individuals after vaccination; exercise enhanced the production of immunoglobulin A (IgA) secreted by the salivary gland in adults aged ≥ 65 ²³⁻²⁵. IgA is important for mucosal immunity as frontline protection against infections. Our results showed that the lowest physical strength was associated with both occurrence of and hospitalization due to pneumonia (Table 4). Older adults with the lowest physical strength may be more susceptible to infections by pneumonia-causing pathogens due to decreased immunity, including the poor secretion of IgA; this may enable pathogens to invade the upper and lower respiratory tracts causing pneumonia and subsequent hospitalization.

Beard and the colleagues reported that iron deficiency was common among homebound older adults and it was associated with the impairment of cellular and innate immunities²⁶. However, the relationship between older adults’ homebound status and the prevalence of pneumonia has not been investigated before. Our results showed that the worst case of homeboundness was associated with hospitalization (Table 4). Impairment of immunity may increase the severity of pneumonia and subsequent hospitalization among homebound older adults.

Several reports have already shown that poor nutrition is associated with CAP and hospitalization²⁷⁻²⁹. The decline in oral function, including poor swallowing and cough reflex, causes dysphagia, which induces aspiration pneumonia in frail older adults^{4,30-33}. Geriatric depression is associated with the malfunction of the immune system and increased susceptibility to infection³⁴⁻³⁶. Our results showed that the nutrition status, oral function, and depression status were associated with either or both occurrence of and hospitalization due to pneumonia (Table 4). The concordance between our results and the reported studies on the associations between poor conditions and infectious diseases, including pneumonia, suggests that frailty is associated with susceptibility to pneumonia or hospitalization.

Our study has some limitations. First, this study has a cross-sectional design. Therefore, the possibility of pneumonia causing frailty cannot be completely excluded. However, the prevalence rate of pneumonia was 3.0% among all frail older adults (Table 1). Second, the occurrence of and hospitalization due to pneumonia were self-reported by the participants and not collected from medical records from the physicians in-charge. However, it is unlikely that they arbitrarily diagnosed themselves with pneumonia or non-medical professionals did so and they trusted it because most Japanese citizens have good medical access due to the national health coverage³⁷. Third, we did not categorize the medical records based on the type of pneumonia, for example, CAP, HAP, or VAP. However, we expect most cases to be CAP because we excluded cases of nosocomial pneumonia with a question (see Methods). Besides, all the participants were functionally-independent community-dwelling older adults, not eligible for Japan’s LTCL.

Conclusion

It was unknown whether frailty was associated with the susceptibility to and severity of pneumonia among community-dwelling older adults, although recent reports have shown that it is related to mortality due to respiratory infectious diseases in hospitalized older adults. We examined whether frailty was associated with the

occurrence of and hospitalization due to pneumonia in functionally-independent community-dwelling older adults. Our results showed that frailty was significantly associated with both occurrence of and hospitalization due to pneumonia after adjusting for all covariates. Our results showed that the IADL, physical strength, nutrition status, oral function, homeboundness, and depression status in frail older adults were significantly associated with either or both. Our results suggested that frailty was associated with susceptibility to and severity of pneumonia, which is a leading cause of mortality and morbidity among community-dwelling older adults worldwide. This study showed frailty as a risk factor for increased susceptibility to and severity of pneumonia among community-dwelling older adults. It is necessary to assess whether frailty is also significantly associated with CAP diagnosed by medical doctors and the causal relationship between frailty and pneumonia should be confirmed in longitudinal studies in the future.

Declarations

Data availability

All data needed to evaluate the conclusions in the paper are presented in the paper and/or the Supplementary Material. The JAGES data used in this study will be made available upon request—the authors require the applicant to submit an analysis proposal that will be reviewed by an internal JAGES committee to avoid duplication. Confidentiality concerns prevent us from depositing our data in a public repository. Proposals submitted by outside investigators will be discussed during the monthly investigators' meeting to ensure that there is no overlap with ongoing analyses. If approval to access the data is granted, the JAGES researchers will request the outside investigator to financially support the data manager for the time he/she requires to prepare the data for outside use.

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Author contributions

All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by KS and YS. The first draft of the manuscript was written by KS and YS. JA and KK prepared the subsequent versions of the manuscript. All authors have read and approved the final manuscript.

Conflict of Interest

The authors declare that they have no conflict of interest.

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