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Original Study

Combined Prevalence of Frailty and Mild Cognitive Impairment in a Population of Elderly Japanese People

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A B S T R A C T

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Objective: Preventive strategies for frailty and mild cognitive impairment (MCI) are important for avoiding future functional decline and dementia in older adults. The purpose of this study was to use a population-based survey to ascertain the single and combined prevalence of frailty and MCI and to identify the relationships between frailty and MCI in older Japanese adults.

Design: Cross-sectional study.

Setting: General community.

Participants: A total of 5104 older adults (aged 65 years or older, mean age 71 years) who were enrolled in the Obu Study of Health Promotion for the Elderly (OSHPE).

Measurements: Each participant underwent detailed physical and cognitive testing to assess frailty and MCI. We considered the frailty phenotype to be characterized by limitations in 3 or more of the following 5 domains: mobility, strength, endurance, physical activity, and nutrition. Screening for MCI included a standardized personal interview, the Mini-Mental State Examination, and the National Center for Geriatrics and Gerontology-Functional Assessment Tool (NCGG-FAT), which included 8 tasks used to assess logical memory (immediate and delayed recognition), word list memory (immediate and delayed recall), attention and executive function (tablet version of Trail Making Test-part A and B), processing speed (tablet version of digit symbol substitution test), and visuospatial skill (figure selection).

Results: The overall prevalence of frailty, MCI, and frailty and MCI combined was 11.3%, 18.8%, and 2.7%, respectively. We found significant relationships between frailty and MCI (the odds ratio adjusted for age, sex, and education was 2.0 [95% confidence interval 1.5–2.5]).

Conclusions: Using the OSHPE criteria, we found more participants with MCI than with frailty. The prevalence of frailty and MCI combined was 2.7% in our population. Future investigation is necessary to determine whether this population is at increased risk for disability or mortality.

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The rate of frailty and mild cognitive impairment (MCI), which increases with age, is a major risk factor for dependency, institutionalization, and mortality.^{1,2,3,4} Individuals with disabilities

have greater health care needs compared with those without.⁵ The elderly population is highly heterogeneous, such that elderly people in the same age range may have a widely varied risk of disability. To prevent disability, population-based intervention programs should be targeted at those in the population with an increased risk of frailty and MCI.

Many studies have worked within research and clinical settings to identify target populations with frailty and MCI. For instance, the Interventions on Frailty Working Group assessed various methods for screening, recruiting, evaluating, and retaining frail elderly individuals in clinical trials.⁶ They reported that most researchers focused on the following domains when identifying physical frailty: mobility,

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such as lower-extremity performance and gait abnormalities; muscle weakness; poor exercise tolerance; unstable balance; and factors related to body composition, such as weight loss, malnutrition, and muscle loss.⁶ Participants with MCI in a community cohort were described by a group of investigators from the Mayo Clinic in 1999, who then produced a series of diagnostic criteria.⁷ A conference of international MCI experts then revised these criteria,⁸ and the National Institute on Aging joined the Alzheimer's Association to revise the diagnostic criteria for the symptomatic predementia phase of Alzheimer disease (AD). They outlined the following factors for the identification of MCI: concern regarding a change in cognition, impairment in one or more cognitive domains, preservation of independence in functional abilities, and absence of dementia.⁹

Using the frailty criteria developed by the Cardiovascular Health Study (CHS), the overall prevalence of frailty in community-dwelling adults aged 65 or older in the United States has been found to range from 7% to 12%. In the CHS, the prevalence of frailty increased with age from 3.9% in the 65 to 74 age group to 25.0% in the 85+ age group, and was greater in women than in men (8% vs 5%).¹⁰ Using the MCI criteria in the CHS cognition study, the overall prevalence of MCI was found to be 18.8%, and the prevalence increased with age from 18.8% in participants younger than 75 years to 28.9% in those older than 85 years.¹¹

Several cross-sectional studies have reported an association between physical frailty and cognitive function.^{6,10,12,13} In addition, longitudinal studies have revealed that a higher level of physical frailty is associated with an increased risk of incident AD¹⁴ and MCI.¹⁵ These studies suggest that in some older adults, physical frailty is associated with the development of MCI. Older adults who show signs of both physical frailty and MCI may be more likely to exhibit functional decline than those with either frailty or MCI. However, the combined prevalence of frailty and MCI and the relationships between frailty and MCI in the Japanese population has not been clearly established. Thus, the purpose of this study was to ascertain the combined prevalence of frailty and MCI and to identify the relationships among frailty, MCI, and demographics including age, sex, and education in the Japanese population, using a community-based survey.

Methods

Participants

Our national study assessed 5104 individuals 65 years and older (mean age 71 years) who were enrolled in the Obu Study of Health Promotion for the Elderly (OSHPE). Each individual was recruited from Obu, Japan, which is a residential suburb of Nagoya. Inclusion criteria required each participant to be 65 years or older at the time of examination (2011 or 2012), and to reside in Obu city. Based on previous reports, we excluded participants with a history of Parkinson disease, stroke, or Mini-Mental State scores less than 18, as these conditions could produce characteristics of frailty.^{3,10,16} We also excluded participants who had participated in similar studies, those with severe disabilities, and those with missing data values regarding determinants for frailty and MCI. In the present study, we examined the prevalence of frailty in 4745 participants, MCI in 5025 participants, and the combined prevalence of frailty and MCI in 4681 participants. Informed consent was obtained from all participants before their inclusion in the study, and the Ethics Committee of the National Center for Gerontology and Geriatrics approved the study protocol.

Measurements

The assessments were conducted by well-trained staff who had nursing, allied health, or similar qualifications. Before

commencement of the study, all staff received training from the authors in the correct protocols for administering the assessment measures.

Operationalization of the Frailty Phenotype in OSHPE

We considered the frailty phenotype to be characterized by limitations in 3 or more of the following 5 domains: mobility, strength, endurance, physical activity, and nutrition. Mobility was measured in seconds using a stopwatch. Participants were asked to walk on a flat and straight surface at a comfortable walking speed. Two markers were used to indicate the start and end of a 2.4-meter walk path, with a 2-meter section to be traversed before passing the start marker so that participants were walking at a comfortable pace by the time they reached the timed path. Participants were asked to continue walking for an additional 2 meters past the end of the path to ensure a consistent walking pace while on the timed path. A low level of mobility was established according to a cutoff (<1.0 m/s). Grip strength was measured in kilograms using a Smedley-type handheld dynamometer (GRIP-D; Takei Ltd., Niigata, Japan). Low grip strength was established according to a sex-specific cutoff (male: <26 kg, female: <17 kg). Endurance was assessed via a self-report of exhaustion, which included questions from the Geriatric Depression Scale,¹⁷ such as: "Do you feel full of energy?" If participants answered "no" to this question, we classified them as low endurance. We evaluated the role of physical activity by asking the following questions about time spent engaged in sports and exercise: (1) "Do you engage in moderate levels of physical exercise or sports aimed at health?" and (2) "Do you engage in low levels of physical exercise aimed at health?" If participants answered "no" to both of these questions, we considered them to be physically inactive. Nutritional status was established according to self-reports of weight loss in response to the following question: "In the past 2 years, have you lost more than 5% of your body weight irrespective of intent to lose weight?" Patients with impairments in at least 3 of the 5 domains were considered to be frail.

Operationalization of the MCI in OSHPE

We defined MCI based on previous studies,^{18,19,20} using the following criteria: subjective memory complaints, cognitive impairment (indicated by an age-adjusted score at least 1.5 SDs below the reference threshold of any of the tests, all of which are commonly used for detailed neuropsychological assessments); no evidence of functional dependency (no need for supervision or external help in performing activities in daily life); and exclusion from the clinical criteria for dementia. Screening for MCI included a standardized personal interview for collection of sociodemographic, lifestyle, medical history, and functional status (activities of daily living) data, along with cognitive screening that was conducted using the Mini-Mental State Examination (MMSE)²¹ and the National Center for Geriatrics and Gerontology-Functional Assessment Tool (NCGG-FAT).²² Individuals with 23 or fewer points on the MMSE were considered to have a general cognitive impairment.²³ The NCGG-FAT consists of 8 tasks used to assess logical memory (immediate and delayed recognition), word list memory (immediate and delayed recall), attention and executive function (tablet version of Trail Making Test-part A and B), processing speed (tablet version of Digit Symbol Substitution Test), and visuospatial skill (figure selection). The participants were given 20 to 30 minutes to complete the battery, which consisted of the previously mentioned 8 tasks. High test-retest reliability and moderate to high validity were confirmed in community-dwelling older adults for all task components of the NCGG-FAT.²² All tests used in this study had previously established

standardized thresholds for the definition of impairment in the corresponding domain (score <1.5 SDs below the age-specific mean) for population-based OSHPE cohort consisting of older adults.

Statistical Analysis

We compared age-, sex-, and education-specific prevalence, as well as the combined prevalence rates of frailty and MCI using χ^2 tests. The prevalence of frailty and MCI were explored in 4745 and 5025 participants, respectively. In calculating the combined prevalence, we found that 4681 participants did not meet the exclusion criteria for frailty or MCI. A multivariate logistic regression model was used to determine the odds ratios of MCI or frailty with respect to age category, sex, and education level. Participants with low general cognitive function were excluded from the multivariate analysis. As a result, the multivariate analysis included data from 3497 participants. All data management and statistical computations were performed using the IBM SPSS Statistics 19.0 software package (SPSS Inc., Chicago, IL).

Results

The OSHPE identified 538 (11.3%) elderly participants who had symptoms of frailty and 945 (18.8%) who had MCI (Table 1). Figures 1 and 2 show our findings regarding the prevalence of frailty and MCI, respectively. We found that the prevalence of frailty increased with advancing age. Of the 538 participants who were classified as frail, 192 (34.9%) were 80 years and older. The prevalence of frailty was higher in women than in men ($P < .05$), and a lower level of education was significantly associated with prevalence of frailty ($P < .01$). Participants who reported 9 or fewer years of education had a 16.4% rate of frailty, whereas in those who reported at least 13 years of education, this rate was 7.7% (Table 1 and Figure 1).

The OSHPE found young-old, 65 to 74 years, participants to have a higher rate of MCI than old-old, 75 years and older, participants. Educational level was significantly associated with MCI ($P < .01$). Participants who reported 9 or fewer years of education had a 23.4% rate of MCI, whereas this rate was reduced to 14.1% in participants who reported at least 13 years of education (Table 1 and Figure 2). The OSHPE found no significant sex-specific differences in the prevalence of MCI.

Table 1 shows the distribution of the combined prevalence of frailty and MCI by age, sex, and educational level. The OSHPE revealed 126 (2.7%) participants with a combined incidence of frailty and MCI. Combined prevalence increased with age, with the highest rate found in the age group containing participants who were

80 years and older (6.9%). Participants with a low educational level had a higher rate of MCI combined with frailty (4.4% for 9 or fewer years) than those with higher education (1.3% for 13 years and more). No clear pattern emerged for any sex-specific differences in the prevalence of combined frailty and MCI (Table 1).

Our multivariate analysis found 3497 participants from the OSHPE cohort who did not meet the exclusion criteria for frailty and MCI and who maintained objective cognitive function. We found several significant relationships between frailty and MCI (odds ratio [OR] = 2.0, 95% confidence interval [95% CI] 1.5–2.5). In terms of the relationship between frailty and sociodemographics, participants aged 65 to 69 years were less likely to be frail than older participants (OR = 2.7, 95% CI 1.9–3.8, for the group 75 to 79 years of age, and OR = 6.9, 95% CI 4.9–9.7, for the group 80 years and older). There were no significant associations observed between frailty and sex. Participants with 9 or fewer years of education had a higher OR (1.4) than participants with at least 13 years of education (Table 2).

In terms of the relationship between MCI and sociodemographics, female participants had a significantly lower OR (0.8, 95% CI 0.7–1.0) than male participants. There was an evident relationship between MCI and educational level. In comparison with participants with at least 13 years of education, participants with a lower level of education were more likely to have MCI (OR = 1.5, 95% CI 1.2–1.8, for those with 10–12 years of education, and OR = 3.2, 95% CI 2.5–4.0, for those with 9 or fewer years of education) (Table 2).

Discussion

This study presents original data regarding vulnerability for physical and cognitive decline in a sample of 5104 elderly community dwellers in Japan. To our knowledge, this is the first study about frailty and MCI in this region of the world. Japan has a rapidly aging population in comparison with North, Central, and South America, as well as Europe. An examination of the differences in levels of frailty and MCI between countries may be useful in developing health care policies, especially in countries where the population is expected to rapidly age in the near future.

Growing evidence has indicated that there is a connection between frailty and cognitive impairment. Several studies have reported a longitudinal association between frailty and rate of MCI in elderly community-dwelling individuals. Boyle et al¹⁵ reported, in an assessment that used 12 years of annual follow-up data, that physical frailty was associated with a high risk of MCI, such that each 1-unit (grip strength, timed walk, body composition, and fatigue) increase in physical frailty was associated with a 63% increase in the risk of MCI. Auyeung et al²⁴ identified that physical frailty, as indicated by

Table 1
Number of Participants and Prevalence of Frailty and Mild Cognitive Impairment (MCI)

	Frailty (n = 4745)			MCI (n = 5025)			Combined (n = 4681)
	Without Frailty	With Frailty	Prevalence	Without MCI	With MCI	Prevalence	Prevalence
All participants	4207	538	11.3%	4080	945	18.8%	2.7%
Age, y			$P < .01$			$P < .02$	
65–69	1794	106	5.6%	1583	390	19.80%	1.6%
70–74	1344	105	7.2%	1221	307	20.10%	2.2%
75–79	711	135	16.0%	771	145	15.80%	3.4%
≥80	358	192	34.9%	505	103	16.90%	6.9%
Sex			$P < .05$			$P < .05$	
Females	2157	302	12.3%	2073	489	19.10%	3.0%
Males	2050	236	10.3%	2007	456	18.50%	2.4%
Educational level, y			$P < .01$			$P < .01$	
≤9	1420	279	16.4%	1414	431	23.40%	4.4%
10–12	1812	179	9.0%	1712	357	17.30%	2.0%
≥13	963	80	7.7%	943	155	14.10%	1.3%

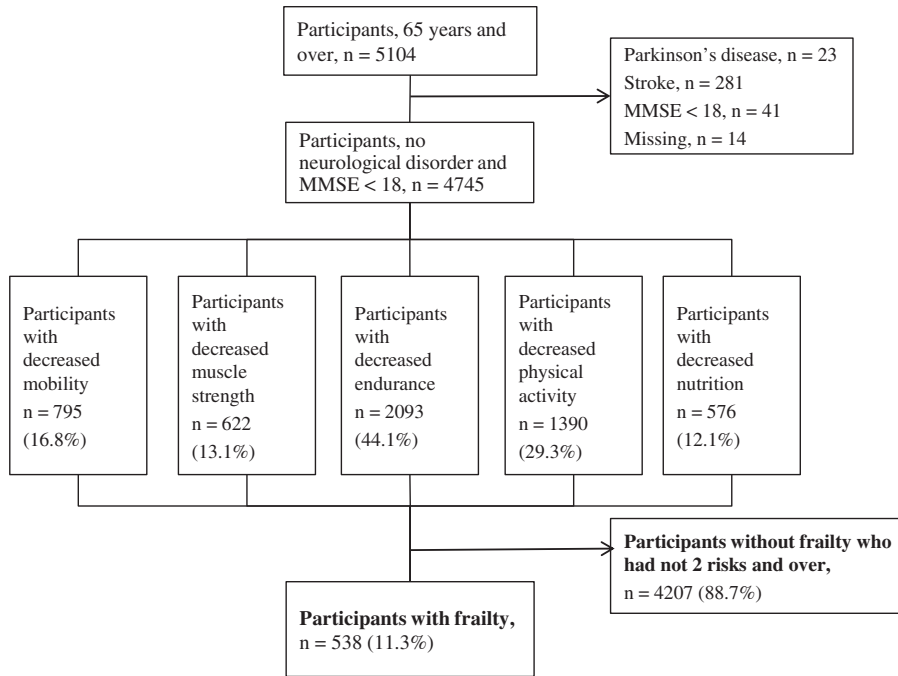


Fig. 1. Participants' flow to find frail older adults.

low body weight, weaker grip strength, slower performance in the chair-stand test, and shorter step-length in men and weaker grip strength in women, was associated with a decline in MMSE score over a 4-year period. Similarly, low cognitive function was independently

associated with an increased risk of frailty in older adults. Raji et al. reported that nonfrail participants with a poor MMSE score (<21) at baseline had a 9% probability per year of becoming frail over a 10-year period, compared to individuals with normal cognition (MMSE

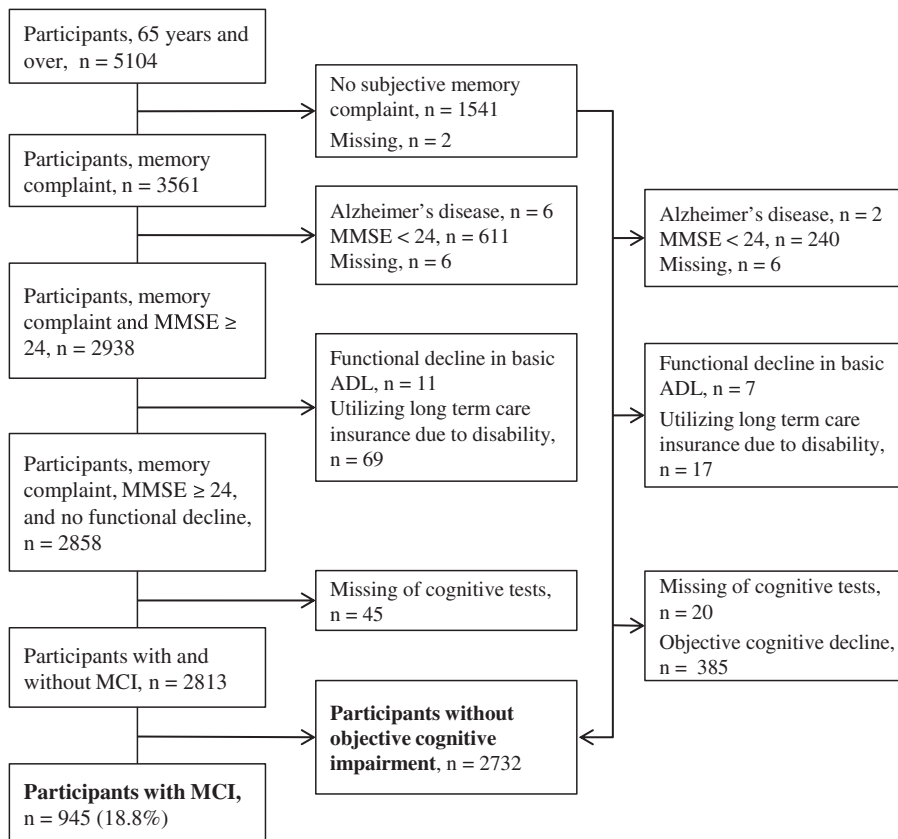


Fig. 2. Participants' flow to find MCI older adults.

Table 2
Relationships Between Frailty, Mild Cognitive Impairment (MCI), and Sociodemographics

	Frailty		MCI	
	Odds Ratio (95% Confidence Interval)	P	Odds Ratio (95% Confidence Interval)	P
MCI	2.0 (1.5–2.5)	<.01		
Frailty			2.0 (1.5–2.5)	<.01
Age, y				
P for trend		<.01		>.05
65–69	1		1	
70–74	1.2 (0.9–1.7)	.30	1.0 (0.8–1.2)	.95
75–79	2.7 (1.9–3.8)	<.01	0.7 (0.6–0.9)	.01
≥80	6.9 (4.9–9.7)	<.01	0.9 (0.7–1.2)	.54
Sex				
Males	1		1	
Females	1.1 (0.9–1.4)	.45	0.8 (0.7–1.0)	.04
Educational level, y				
P for trend		.02		<.01
≥13	1		1	
10–12	1.0 (0.7–1.4)	.85	1.5 (1.2–1.8)	<.01
≤9	1.4 (1.0–2.0)	<.05	3.2 (2.5–4.0)	<.01

21+).²⁵ Although the criteria for determining frailty and MCI vary slightly between studies, our results were in accordance with previous findings, and thus add support to the association between frailty and MCI.

The prevalence of frailty was 11.3% in our participant group, a rate slightly higher than that of previous studies that also used the CHS frailty criteria. In the American Cardiovascular Health Study, the prevalence of frailty among 5317 community-dwelling men and women aged 65 years and older was 6.9%, and frailty was associated with older age, male gender, being African American, having lower education and income, poorer health, and higher rates of comorbid chronic disease and disability.¹⁰ The French Three-City Study demonstrated a frailty prevalence of 7% among 6078 community-dwelling men and women aged 65 years and older, and frailty was associated with older age, female gender, lower education, lower income, a poorer self-reported health status, and more chronic disease in addition to incident disability.²⁶ The Hertfordshire Cohort Study (HCS), UK, reported that the prevalence of frailty, as defined by CHS frailty criteria, among 638 community-dwelling participants aged 64 to 74 years was 8.5% for women and 4.1% for men.²⁷ The principal difference in the frailty criteria used by the CHS and OSHPE is the cutoff point for walking speed: in the CHS it is set at 0.65 m/s (height ≤173 cm) and in the OSHPE it is 1.0 m/s. This difference may be one explanation for the higher prevalence observed in studies using the OSHPE. The Survey of Health, Aging, and Retirement in Europe (SHARE) studied 16,584 men and women aged 50 years and older, and found that the prevalence of frailty in the nondisabled population aged 65 years and over ranged from 3.9% to 21.0%. The SHARE study demonstrated a higher prevalence of frailty in southern (9.3% to 21.0%) compared with northern Europe (<9.0%).²⁸ The SHARE study defined slowness using the following 2 questions regarding mobility: “Because of a health problem, do you have difficulty [expected to last more than 3 months] walking 100 meters” and “... climbing 1 flight of stairs without resting.” Gait velocity has consistently been reported to differentiate between participants with and without functional decline, as frail elderly individuals walk significantly slower than their nonfrail peers.^{29,30} Thus, gait velocity has been found to be a strong predictor of adverse events, such as disability,^{31–37} mortality,^{32,33,38,39} hospitalization,^{32,33,35,40} and falls.^{40,41} The cutoff point for walking speed in the present study was 1.0 m/s, which appears to be a critical point for predicting future functional decline in community-dwelling elderly individuals.^{32,33,35,36,37} These results suggest that walking speed may be the

most useful measurement for determining frailty and predicting future functional decline in older adults.^{42,43}

It is likely that the reported prevalence of MCI varies between studies as a result of different diagnostic criteria, as well as different sampling and assessment procedures. Despite some methodological differences, most previous studies report prevalence figures for MCI or for cognitive impairment without dementia ranging from 11% to 23%. The Women’s Cognitive Impairment Study used global and domain-specific cognitive measures and found the prevalence of MCI or cognitive impairment without dementia to be 23.2% in a sample of 1299 participants aged 85 years and older.¹⁹ The Mayo Clinic Study of Aging diagnosed 329 of 1969 study participants (16.7%) with MCI or cognitive impairment without dementia using the Clinical Dementia Rating Scale, a neurologic evaluation, and neuropsychological testing to assess 4 cognitive domains: memory, executive function, language, and visuospatial skills.⁴⁴ A study from Leipzig, Germany, that used a 55-point composite instrument found the overall prevalence of MCI or cognitive impairment without dementia to be 19.3% in participants aged 75 years and older.⁴⁵ The Cardiovascular Health Study found the overall rate of MCI or cognitive impairment without dementia to be 19% in participants aged 75 years and older.¹¹ In the Aging, Demographics, and Memory Study, an estimated 5.4 million people (22.2% of the total population of the country) in the United States aged 71 years or older were found to have cognitive impairment without dementia.⁴⁶ In a Japanese study, MCI was diagnosed in 271 of 1433 study participants (18.9%).⁴⁷ In the above-mentioned study, a diagnosis of MCI was contingent on cognitive performance 1.0^{44,45,47} or 1.5 SDs^{11,19,46} below at least one test measure. In the present study, we found the prevalence of MCI to be 18.8%, which is similar to previous studies that used multiple cognitive tests to detect MCI.

In the present study, we found the combined prevalence of frailty and MCI to be 2.7% among 4681 community-dwelling elderly participants. Our analyses of the relationships among frailty, MCI, and sociodemographics revealed a significant relationship between frailty and MCI (OR 2.0). These results suggest that frailty may coincide with MCI in older adults who exhibit vulnerability factors for both conditions. Many researchers believe that the definition of frailty should include mental health as well as physical functioning. The Frailty Operative Definition-Consensus Conference Project reported that experts agreed on the importance of a more comprehensive definition of frailty that should include assessment of physical performance, including gait speed and mobility, nutritional status, mental health, and cognition.⁴⁸ The results of the present study were in line with the new concept of frailty, which included cognition. Individuals with a co-occurrence of frailty and MCI may face a higher risk of incidence disability than healthy older adults or older adults with either frailty or MCI. The French Three-City Study established that frail persons with a cognitive impairment are significantly more likely to develop disabilities in activities of daily living (ADL) and instrumental ADL disabilities.⁴⁹ Moreover, the Hispanic Established Populations for the Epidemiologic Study of the Elderly demonstrated that frailty and cognitive impairment affect mortality differently when they occur independently compared with when they are present together. For instance, individuals with cognitive impairment and frailty had higher mortality compared with individuals with either frailty or cognitive decline.⁵⁰ Further longitudinal study is needed to clarify the ways in which frailty and MCI might affect vulnerability among older adults.

Our multivariate analysis indicated that the participants with the highest risk of developing frailty were 80 years and older or had received fewer than 9 years of education. Many studies have reported relationships among frailty, age, and education. For instance, the Women’s Health Initiative Observational Study found

that age is significantly correlated with incident frailty. In contrast, the previously mentioned study found no clear relationship between MCI and age. The MCI criteria in the OSHPE is based on cognitive score (ie, <1.5 SDs below the age-specific mean of healthy peers). Our inability to find a relationship between MCI and age may have been because of our use of age-specific criteria.

Our logistic model revealed that participants with the highest risk of MCI were predominantly male and had received 9 or fewer years of education. The Mayo Clinic Study of Aging reported that the prevalence OR for MCI in men was 1.54 (95% CI 1.21–1.96; adjusted for age, and education). Several other studies have reported a higher rate of MCI in older adults who received fewer years of education.^{19,20,44,51} In one study, this result remained essentially unchanged after adjusting for several demographic and clinical variables, as well as the Apolipoprotein E genotype, suggesting that this association is not due to comorbid conditions or to a differential rate of MCI in men compared with women.⁴⁴ Our results support these previous discoveries while adding the finding that ethnic differences do not explain the higher prevalence of MCI in men than in women. There is a clear relationship between educational level and prevalence of MCI. Indeed, our results suggest that educational level is more closely associated with MCI risk than age in the OSHPE criteria.

One strength of the present study is the size of the cohort assessed in a specific community. Our findings are backed by comprehensive geriatric assessments intended to identify frailty and cognitive impairments. To our knowledge, this is the first study to demonstrate the combined prevalence of frailty and MCI in a large sample of older adults. We identified MCI using the NCGG-FAT, which is useful for multidimensional cognitive screening in population-based samples to assess the risk of cognitive decline. In a hospital setting, psychologists, neurologists, and other specialists are available to perform psychological tests. It can be difficult to assemble specialists in Japan for assessments in a community setting. The NCGG-FAT is easily administered using a tablet PC with the instructions shown on the display. Therefore, it is not necessary for those collecting the data to have a thorough knowledge of neurocognitive measures, and the identity of the person administering the questionnaire will not strongly affect the results.

An important limitation of our study is that participants were not recruited randomly to complete the OSHPE. This may lead to an underestimation of the prevalence of frailty and MCI, as the participants were relatively healthy elderly persons who were able to access the health checkup from their homes. Second, for some participants, we were not able to contact an informant, such as family member, to verify medical records, lifestyle information, and asymptomatic aberrant behavior.

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