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COGNITIVE FRAILTY IS ASSOCIATED WITH FALL-RELATED FRACTURE AMONG OLDER PEOPLE

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Abstract: *Objective:* Cognitive frailty refers to cognitive impairment and physical frailty. Both cognitive impairment and physical frailty include risks of falling. The purpose of the study is to examine cognitive frailty and falling with/without a fracture. *Design:* Cross-sectional observation study. *Setting:* General communities in Japan. *Participants:* Data of 10,202 older adults aged ≥ 65 years were collected. *Measurements:* Physical frailty was characterized as slow walking speed and/or muscle weakness. Assessment of cognitive function included word lists memory, attention, executive function, and processing speed. Cognitive impairment refers to one or more cognitive decline indicated by at least 1.5 standard deviations below the threshold after adjusting for age and education. We operationally defined cognitive frailty as having both cognitive impairment and physical frailty. Participants were interviewed about their falling, history of fall-related fractures, and several potentially confounding factors such as demographic characteristics. *Results:* Multinomial logistic regression analysis revealed that functional decline in all groups, as compared to the robust group, was significantly associated with falling without fractures, after adjusting for the covariates; cognitive impairment group (P = .017), physical frailty group (P = .002), and cognitive frailty group (P < .001). Only the cognitive frailty group had a significant association with fall-related fracture after adjusting for the covariates (OR 1.92, 95% CI: 1.20–3.08, P = .007). *Conclusion:* Cognitive frailty is associated with not only falling but also fall-related fractures. Cognitive frailty may have a greater risk for fall-related fractures than cognitive impairment or physical frailty alone. Future research should examine causal the relationship between fall-related fractures and cognitive frailty.

Key words: Fall-related fracture, cognitive frailty, older people.

Introduction

Fractures among older people have a negative impact not only in terms of their activity in daily life (1) and mortality (2-4), but also financially. In fact, medical expenses for older people with fractures run into 1,777 million US dollars in Japan (5). Moreover, Northeastern Ohio trauma study III reported that 87% of all fractures among older people are due to falling (6). According to these studies, the incidence of falling, especially those resulting in fractures, should be prevented for older people for their successful aging.

Falling, as with many geriatric syndromes, most often results not from a single disease process but from the accumulated effect of multiple factors (7). Among them, cognitive impairment was associated with an increased risk of falling (8, 9), suggesting that they often engage in risky activities, which increases their rate of falling (10). Physical frailty is also a risk for falling among older people and a systematic review showed that older people with frailty were extremely prone to falling by 1.8 times compared to the healthy elderly (11). Moreover, in even a 24-week short-term prospective study, the status of physical frailty was found to be a significant predictor of incidence of future falling among community-dwelling elderly adults (12).

Recently, the working group proposed the operational definition of "cognitive frailty" characterized by the simultaneous presence of both physical frailty and cognitive impairment(13). With respect to falling with/without a consequent fracture, older people with cognitive frailty were considered to have high risk due to the combined risk of cognitive impairment and physical frailty. However, the association between cognitive frailty and falling with/without fracture remains unclear. This association could be the catalyst for developing an intervention to prevent falls in the elderly.

Methods

Participants

The present cross-sectional observational study involved 10,885 community-dwelling older adults registered in the National Center for Geriatrics and Gerontology – Study of Geriatric Syndromes (14). Our inclusion criteria were that all participants resided in Aichi, Japan and were 65 years or older at the time of examination. Exclusion criteria was as follows; 1) the need for support or care as decided by the Japanese Public Long-Term Care Insurance System, 2) having

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a disability in basic activities of daily living, 3) incapacity of undergoing assessments of physical function, 4) with a history of Parkinson's disease, stroke, depression, or dementia, and 5) with general cognitive impairment (Mini-Mental State Examination (MMSE) (15) scores were less than 21). Then, Six hundred eighty three of the initial 10,885 participants were excluded, and 10,202 elderly people (mean age 73.6 ± 5.5 years, 65–96 years; 4,948 men, 5,254 women) were analyzed in the present study. Informed consent was obtained from all participants prior to their inclusion in the study, and the Ethics Committee of the National Center for Geriatrics and Gerontology approved the study protocol.

Operationalization of cognitive frailty

First, physical assessments were conducted by measuring walking speed and grip strength. Walking speed 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 indicated the start and end of a 2.4 m walk path, with a 2 m section to be traversed before/after passing the start marker such 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 m past the end of the path to ensure a consistent walking pace while on the timed path. Deficit in walking speed was determined based on a cutoff (< 1.0 m/s) (16, 17). Grip strength was measured in kilograms using a Smedley-type handheld dynamometer (GRIP-D; Takei Ltd., Niigata, Japan). Deficit in grip strength was determined based on a sex-specific cutoff (< 26 kg for men and < 18 kg for women) (18). Participants with one or more physical deficit were included in the physical frailty group.

Second, cognitive assessment was conducted using the National Center for Geriatrics and Gerontology-Functional Assessment Tool (NCGG-FAT) (19). The NCGG-FAT consists of four domains including memory (word list memory-I and word list memory-II), attention (an tablet version of the Trail Making Test (TMT) part A), executive function (an tablet version of the TMT part B), and processing speed (a tablet version of the Symbol Digit Substitution Test (SDST)). It takes about 20 minutes to complete all the tests in NCGG-FAT, and NCGG-FAT have possessed high test-retest reliability and moderate to high validity in community-dwelling older adults (19). From the date of a population-based cohort study, the standardized thresholds of cognitive impairment have set as test score <1.5 SDs below the age and education-specific means in each test (word list memory, TMT part A and B, SDST). We considered cognitive impairment to be characterized under standardized thresholds in one or more of the NCGG-FAT tests.

The participants were categorized into these four groups: 1) robust older individuals who had neither physical frailty nor cognitive impairment (robust group), 2) non-physically frail older adults with cognitive impairment (cognitive impairment group), 3) physically frail older adults without cognitive impairment (physical frailty group), and 4) physically frail older adults with cognitive impairment (cognitive frailty group) (13).

Falling and fall-related fracture

Information about fall history was collected in a face-to-face interview. A fall was defined as "an unexpected event in which the person comes to rest on the ground, floor, or lower level" (20). The question "Do you have a history of a fall within the past year?" was used for categorizing "fallers" and "non-fallers." We asked further questions to fallers: "Did you have a fracture anywhere in the body when you fell down?" Then, we categorized the participants into three groups: 1) non-fallers, 2) fallers without fracture, and 3) fallers with fracture.

Sociodemographic variables and covariates

Using face-to-face interviews, we examined participants' sociodemographic characteristics (age, gender, and education level) and medical history (number of medications and chronic diseases (stroke, heart disease, and diabetes)). The examined covariates were as follows: body mass index (BMI), depressive symptoms, and risk of osteoporosis. As the psychological examination, the Geriatric Depression Scale (GDS) whose higher scores had more depressive symptoms was conducted (21). With respect to general cognitive function, we used the MMSE (15). Bone status was assessed using speed of sound (SOS) measured using a quantitative ultrasound device (Canon Life Care Solutions Inc., CM-200, Osaka, Japan) at the calcaneus of the dominant foot while the participants were barefoot and seated.. Bone status was shown as the percent of Young Adult Mean of the SOS (%YAM), and SOS levels of less than -2.5SD (lower than 70%) of %YAM were defined as having the risk for osteoporosis in the present study (22).

Statistical analysis

Analysis of variance and chi square test were used to investigate difference between the cognitive frailty groups. Multinomial logistic regression analysis was used to examine the association between cognitive frailty and fall-related fractures, with cognitive frailty as the independent variable. Adjusted odds ratios (OR) and 95% confidential intervals (CIs) were calculated. GDS scores were categorized using cutoffs drawn from previous studies (GDS: 5/6 (21)). All analysis was performed using SPSS v.20 (IBM Corp., Chicago, IL, USA). The findings at $p<0.05$ were considered significant.

Results

Prevalence of cognitive frailty among Japanese elderly and comparing variables between groups

Table 1 presents demographic characteristics and scale scores of each group. Mean scores on the following variables varied significantly between groups: age, sex, education, number of medications, all chronic diseases (stroke, heart disease, and diabetes), GDS, and risk of osteoporosis (lower than 70%YAM of SOS) (all $P < .001$). BMI was not significantly related to cognitive frailty status ($P = .698$).

Table 1
Characteristics in each cognitive frailty group

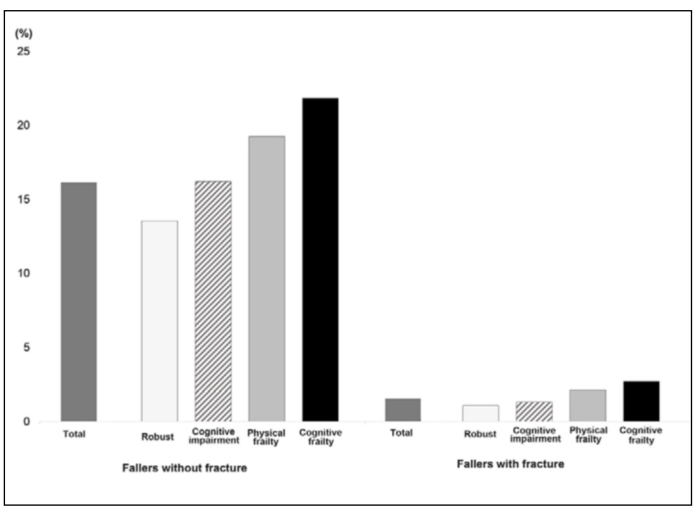
	Total N = 10202	Robust N = 5350 (52.4%)	Cognitive impairment N = 1363 (13.4%)	Physical frailty N = 2266 (22.2%)	Cognitive Frailty N = 1223 (12.0%)	P value
Age, years ± SD	73.7 ± 5.5	72.2 ± 4.8	72.4 ± 4.8	76.2 ± 5.8	76.9 ± 5.8	< .001
Sex, male (%)	4948 (48.6)	2693 (50.4)	710 (52.1)	995 (44.0)	550 (45.0)	< .001
Education, years ± SD	11.8 ± 2.6	12.1 ± 2.6	11.6 ± 2.5	11.5 ± 2.8	10.9 ± 2.7	< .001
BMI, kg/m2 ± SD	23.2 ± 3.1	23.3 ± 3.0	23.2 ± 3.1	23.2 ± 3.3	23.2 ± 3.4	.698
Medication, number ± SD	2.8 ± 2.7	2.3 ± 2.4	2.5 ± 2.4	3.6 ± 3.0	3.6 ± 3.0	< .001
Chronic disease						
Stroke, with (%)	604 (6.0)	230 (4.4)	92 (6.8)	154 (6.9)	128 (10.5)	< .001
Heart disease, with (%)	1800 (17.7)	869 (16.3)	206 (15.2)	477 (21.1)	248 (20.3)	< .001
Diabetes, with (%)	1341 (13.2)	575 (10.8)	179 (13.2)	369 (16.3)	218 (17.9)	< .001
GDS, score ± SD	2.9 ± 2.7	2.5 ± 2.4	2.9 ± 2.7	3.4 ± 2.9	4.0 ± 3.1	< .001
Risk of osteoporosis, lower than 70%YAM (%)	4154 (40.8)	1890 (35.4)	498 (36.6)	1121 (49.5)	645 (52.8)	< .001

Pearson's chi-square test was used for proportions and analysis of variance for continuous measures; SD; standard deviation, BMI; body mass index, GDS; geriatric depression scale, YAM; young adult mean

Fallers with and without fracture history compared with cognitive frailty status

The number of fallers with and without fracture is shown in Figure 1. It was found that functional decline in only the cognitive frailty group had a significant association with falling with fracture after adjusting for the covariates (OR 1.92, 95% CI: 1.20–3.08, P = .007).

Figure 1
Prevalence of falling with or without fracture



Bar graphs indicate the percentage of faller with or without fracture.

Cognitive frailty and fall-related fracture

In multinomial logistic regression analysis (Table 2), functional decline in all groups (physical frailty, cognitive impairment, and cognitive frailty) was significantly associated with falling without fracture after adjusting for the covariates.

Discussion

The rates of falling with/without fracture were different between groups and older people with cognitive frailty had a higher rate of both falling with and without fracture (Figure 1). Cognitive frailty is associated with not only falling, but also fall-related fractures. However, participants with cognitive impairment or physical frailty alone were also associated with falling but not with fall-related fractures.

In multinomial regression analysis, compared with the robust group, functional decline in groups (cognitive impairment, physical frailty, and cognitive frailty) was associated with falling without fracture. This result was consistent with previous studies that found that deficits in physical and/or cognitive functioning had negative impact on the rates of falling among older people. In fact, diminished scores in executive function and attention were associated with future fall risk (23). Furthermore, multiple falls and increased fall risks were associated with the presence of deficits in executive and visuo-spatial functioning (8, 24). The components of physical frailty (weakness (25) or slowness (26)) were also strongly associated with the risk of falling.

Only the cognitive frailty group showed associations with falling with fracture. Cognitively impaired older people often engage in risky activities (e.g., stepping over the edge of a bathtub even in the absence of a grab bar, or not holding on to any support while stepping) increasing their fall rate (10). Those with physical frailty (weakness, impaired balance, and abnormal gait) are at an increased risk of falling (27) (28). Given that older people with cognitive frailty had both cognitive impairment and physical frailty (11), they were considered to perform risky activities that might result in falling, without adequate physical function to safely avoid injuries after the fall. In addition, there was another explanation

Table 2
Relation between cognitive frailty status and fall-related fracture using multinomial logistic regression model

		Fallers without fracture vs. Non-fallers			Fallers with fracture vs. Non-fallers		
		Odds Ratios	**95% confidential intervals**	**P value**	**Odds Ratios**	**95% confidential intervals**	**P value**
Cognitive frailty status							
	Cognitive frailty	1.46	(1.23 - 1.73)	< .001	1.92	(1.20 - 3.08)	.007
	Physical frailty	1.25	(1.08 - 1.44)	.002	1.49	(0.99 - 2.27)	.059
	Cognitive impairment	1.23	(1.04 - 1.45)	.017	1.24	(0.72 - 2.12)	.434
	Robust		Reference			Reference	
Age		1.03	(1.01 - 1.04)	< .001	1.03	(0.99 - 1.06)	.100
Sex							
	Male	0.74	(0.66 - 0.83)	< .001	0.55	(0.39 - 0.79)	.001
	Female		Reference			Reference	
BMI		1.03	(1.01 - 1.05)	.002	1.04	(0.99 - 1.09)	.135
Education		1.04	(1.02 - 1.06)	< .001	0.99	(0.93 - 1.06)	.874
Medication		1.02	(1.00 - 1.05)	.032	1.07	(1.01 - 1.13)	.026
Chronic diseases							
	Stroke	1.32	(1.07 - 1.62)	.010	0.75	(0.36 - 1.56)	.440
	Heart disease	1.12	(0.97 - 1.30)	.111	0.89	(0.57 - 1.37)	.590
	Diabetes	1.22	(1.04 - 1.42)	.014	1.23	(0.78-1.94)	.368
Risk of osteoporosis							
	lower than 70% YAM	1.00	(0.89 - 1.12)	.998	1.77	(1.25 - 2.49)	.001
	70% YAM and higher		Reference			Reference	
GDS cut-off point(5/6)							
	6 and higher	1.74	(1.52 - 2.00)	< .001	1.61	(1.09 - 2.38)	.016
	5 and lower		Reference			Reference	

GDS; geriatric depression scale, YAM; young adult mean

for the association between cognitive frailty and falling with fracture. Although the present study was cross-sectional in design, the status of cognitive frailty may result from falling with fracture as a "post-fall syndrome" (29). In other words, older people who experienced fall-related fractures may be admitted into the hospital and be confined to bed temporally. Hospitalization among older people accelerated not only cognitive impairment (30), but also disability (31), which occurs following physical frailty. Cognitive frailty and fall-related fractures were considered to have a bi-directional association. Thus, we should investigate the casual association between cognitive frailty and falling with fracture in future studies.

This study has the following limitations. First, a cross-sectional design was used; therefore, the findings do not illustrate any causal relationships between the examined variables. Second, participants were not randomly recruited (participants were relatively healthy elderly persons who were able to undergo health checkups from their homes). This may have caused the underestimation of cognitive frailty and prevalence of falling. Third, falling was related to many factors (i.e. fear of falling, arthritis) that we did not measure. Future studies on the association between falling and cognitive frailty should consider these covariates. Finally, we investigated the falling event of the participants using questionnaire, thus there may be a recall bias, although the participants with general cognitive decline (MMSE score < 21) were excluded in the present study.

In summary, cognitive frailty is associated with falling among community-dwelling older people. Especially, cognitive frailty is associated with fall-related fractures in contrast to cognitive impairment or physical frailty alone. Future research should prospectively examine causal relationship between fall-related fractures and cognitive frailty.

Conflicts of interest: None

Author contributions: Tsutsumimoto planned the study, wrote the first draft of the manuscript, and coordinated the review and editing process leading to the final manuscript. Doi and Makizako participated in the design of the study and wrote the paper. Nakakubo, Hotta, and Makino corrected data and contributed to the editorial process and review of the manuscript. Shimada and Suzuki supervised the study, suggested many ideas that have been pursued in this research, and participated in the planning, editorial, and review processes that led to the final manuscript.

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Ethical Standards: Ethical standards for epidemiological study were adhered to according to guidelines from the Ministry of Health, Labour and Welfare, Japan.

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