

Research Article

Frailty, With or Without Cognitive Impairment, Is a Strong Predictor of Recurrent Falls in a US Population-Representative Sample of Older Adults

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Abstract

Background: Physical frailty and cognitive impairment have been separately associated with falls. The purpose of the study is to examine the associations of physical frailty and cognitive impairment separately and jointly with incident recurrent falls among older adults.

Methods: The analysis included 6000 older adults in community or non-nursing home residential care settings who were at least 65 years old and participated in the National Health and Aging Trends Study. Frailty was assessed using the physical frailty phenotype; cognitive impairment was defined by bottom quintile of the clock-drawing test or immediate and delayed 10-word recall, or self/proxy-report of diagnosis of dementia, or AD8 score at least 2. The marginal means/rates models were used to analyze the associations of frailty and cognitive impairment with recurrent falls over 6 years of follow-up between 2011 and 2017.

Results: Of the 6000 older adults, 1787 (29.8%) had cognitive impairment only, 334 (5.6%) had frailty only, 615 (10.3%) had both, and 3264 (54.4%) had neither. After adjusting for age, sex, race, education, living alone, obesity, disease burden, and mobility disability, those with frailty (with or without cognitive impairment) at baseline had higher rates of recurrent falls than those without cognitive impairment and frailty (frailty only: rate ratio [RR] = 1.31, 95% confidence interval [CI] = 1.18–1.44; both: RR = 1.28, 95% CI = 1.17–1.40). The association was marginally significant for those with cognitive impairment only (RR = 1.07, 95% CI = 1.00–1.13).

Conclusions: Frailty and cognitive impairment were independently associated with recurrent falls in noninstitutionalized older adults. There was a lack of synergistic effect between frailty and cognitive impairment.

Keywords: Cognitive impairment, Falls, Frailty, Older adults

Falls are among the most common and serious threats to independence experienced by older adults. Approximately 30% of community-dwelling adults aged 65 years and older experience at least one fall in a 1-year period (1). Falls are associated with considerable morbidity and mortality in older adults (2–4). Those individuals who experience recurrent falls constitute a sizable and particularly high-risk subset of older adults who experience falls.

They are more likely to sustain serious injuries and have a distinct set of risk factors when compared with older adults who experience only a single fall (5). Hence, identifying risk factors for recurrent falls and implementing effective preventive interventions are of significant public health importance.

Many factors contribute to falls including demographic, environmental, and health-related characteristics (6). Frailty, a common

geriatric syndrome (7,8), has been identified as a risk factor for falls (9–11). In addition, increasing epidemiological and clinical evidence finds that physical frailty is associated with and often coexistent with cognitive impairment in older adults (12,13), which in theory would further increase susceptibility to falling (14–16). A meta-analysis of 27 studies found that community-dwelling older adults with global cognitive impairment had more than twice the increased risk of falls of cognitively intact individuals (17). Taking into account the association between frailty and cognitive impairment, it is critical to understand their separate and joint effects on falls incidence in order to better tailor falls interventions for maximal impact.

To the best of our knowledge, there was only one study by Martin et al. which found that the association between poorer cognitive function and falls risk was amplified by the presence of physiological factors such as greater body sway, less ambulatory physical activity, slower reaction time and gait speed, weaker muscle strength, and poorer visual contrast (18). Recently, a multicenter study of 6204 older adults found that coexistent gait and cognitive impairment had a multiplicative association with falls risk (19). To the best of our knowledge, only one study reported associations of frailty and cognitive impairment separately and jointly with falls prevalence (20); however, the temporal relationships between falls and frailty and/or cognitive impairment could not be determined due to the cross-sectional design. Additionally, insufficient research has attempted to estimate the associations of frailty and cognitive impairment with the risk of recurrent falls. Using data from a nationally representative sample of US older adults, we aimed to evaluate (a) cross-sectional associations of frailty and cognitive impairment with history of falls at study baseline (2011) and (b) separate and joint effects of frailty and cognitive impairment on the risk of incident recurrent falls during a 6-year follow-up (2011–2017).

Method

Data Source and Sample

The National Health and Aging Trends Study (NHATS) is a study of disability trends and dynamics in US adults aged 65 and older from a nationally representative sample of Medicare beneficiaries (21). The original NHATS cohort was established in 2011 and conducted by the Johns Hopkins University Bloomberg School of Public Health in collaboration with the University of Michigan. Study design and data collection and management procedures have been described previously (22). Study participants were interviewed beginning in 2011 and annually thereafter, and details on health, economic, and social consequences of aging and disability were collected. Informed consent was obtained from each participant prior to data collection. The study was approved by the Johns Hopkins Bloomberg School of Public Health Institutional Review Board.

At baseline, 8245 participants completed the interview, with a response rate of 71%. Inclusion criteria for the present analysis were participants aged 65 years or older residing in community or non-nursing home residential care settings in 2011, with information available on frailty, cognitive status, and history of falls at baseline, and having at least 1-year follow-up. We excluded the 636 older adults in nursing homes, leaving 7609 older adults in community or non-nursing home residential care settings. We further excluded 112 individuals with insufficient data on frailty

at baseline. An additional 1497 individuals were excluded due to missing follow-up data on falls. Finally, 6000 individuals were included in our analyses. The individuals with missing data on falls were significantly older, with lower education level, higher prevalence of underweight and depression, probable dementia, and poorer mobility function.

Study Outcome

Information on falls was collected at baseline (2011) and annually during the 6-year follow-up (2012–2017), based on participants' response to the question: "In the past 12 months, have you (or has the sample person [in the case of proxy interview]) fallen down?" A fall was defined as any fall, slip, or trip in which the participant lost balance and landed on the floor or ground or at a lower level. Given that the exact number of falls was not asked during the interview, "recurrent falls" were defined as the occurrence of one or more falls in the prior year by self-report at 2 or more interviews during the 6-year follow-up.

Operationalization of Frailty

Frailty was assessed using the approach developed by Bandeen-Roche et al. (23), a modified version of the 5-item Cardiovascular Health Study frailty phenotype (8), with a total score ranging from 0 to 5. The 5 binary-coded items included (a) shrinking: present for those who self-reported unintentionally losing weight of 10 or more pounds in the previous year or body mass index (BMI) less than 18.5 kg/m²; (b) exhaustion: present for those who self-reported having low energy or being easily exhausted, enough to limit their activities; (c) weakness: present for those in the lowest 20th percentile within 8 sex-by-BMI categories of the maximum grip strength of dominant hand over 2 trials; (d) slow walking speed: present for those in the lowest 20th percentile of the weighted population distribution within 4 sex-by-height categories of the first of 2 usual-pace 4-m walking trials; and (e) low physical activity: present for those self-reported not having walked for exercise or engaged in vigorous activities, recently. The total score was used to categorize participants as not-frail (score = 0–2) or frail (score = 3–5).

Operationalization of Cognitive Impairment

Cognitive impairment was identified by either cognitive performance testing or by self/proxy-report. Participants met criteria for "cognitive impairment" if at least one of the 3 criteria were met: (a) scored in the bottom quintile in at least one of the 2 cognitive domains: executive functioning (scoring <3 on a clock-drawing test scored on a 0–5 scale) and memory (scoring ≤5 on a summed score of immediate and delayed 10-word recall batteries); (b) a report by the NHATS participants or a proxy respondent that a physician told the sample person that he/she had dementia or Alzheimer's disease (AD); or (c) a score of 2 or higher on the AD8 Dementia Screening Interview, an 8-item instrument administered to proxy respondents not reporting a diagnosis, which assesses memory, temporal orientation, judgment, and function (24).

In NHATS, probable dementia was defined as meeting any one of the 3 criteria: (a) self- or proxy-report of physician's diagnosis of dementia or AD, (b) a score of at least 2 on the AD8 administered to proxy-respondents not reporting a diagnosis, or (c) test performance scores more than 1.5 SD below the mean in at least 2 of 3 domains: memory (immediate and delayed 10-word recall), executive function (clock-drawing test), and orientation (date, month, year, and day of the week; naming the President and Vice President) (25).

Other Covariates

To address potential confounding, we controlled for several sociodemographic, health, and functional characteristics at baseline. Sociodemographic variables included age grouped in 5-year increments from 65 to 90 and 90 and older; race categorized as White non-Hispanic, Black non-Hispanic, Hispanic, and other; education categorized into 8th grade or less, 9th–12th grade (no diploma), and high school graduate or higher; and living arrangement coded as living alone or not by self-report.

The following health conditions were recorded: (a) obesity if BMI at least 30 kg/m²; (b) comorbidity burden was measured by the number of diagnosed diseases including heart disease, hypertension, arthritis, osteoporosis, diabetes mellitus, lung disease, stroke, non-skin cancer, and hip fracture history. Number of comorbidities was categorized into 0, 1, and at least 2. (c) Mobility disability was coded based on items that asked about going outside, getting around inside, and getting out of bed as 0 for no disability (no device use, reduction in activities, difficulty, or assistance with any activity), 1 for moderate disability (device use or reduction in 1 or more activities but no difficulty or assistance), and 2 for severe disability (difficulty by oneself or help from another person to perform activities, or, rarely, not doing the particular activity). (d) Depression was measured via the 2-item Patient Health Questionnaire (PHQ-2) (26,27). The participants were classified as having depression if the PHQ-2 was 3 or higher.

Statistical Analysis

Frailty and cognitive impairment status were used to classify participants into 4 groups: (a) neither frail nor cognitively impaired (termed “neither,” henceforth), (b) not-frail and cognitively impaired (termed “cognitive only,” henceforth), (c) frail and cognitively intact (termed “frailty only,” henceforth), and (d) frail and cognitively impaired (termed “both,” henceforth). Chi-square tests were used to test the differences of the baseline demographic, health, and mobility disability characteristics across the 4 groups. NHATS survey weights and sampling design variables were used to adjust for the complex sampling design.

We performed cross-sectional and longitudinal analyses of the associations of frailty and cognitive impairment with prevalent and incident falls using logistic regression and marginal means/rates model, respectively. We estimated odds ratios (ORs) or rate ratios (RRs) of the association and their 95% confidence intervals (CIs). The marginal means/rates model used longitudinal data, treating falls, one or more occurring within the year prior to the interview at each of 6 annual follow-ups as a recurrent event over time. By treating all recurrent events of the same participant as a single counting process, the marginal means/rates model has the advantage of being flexible and parsimonious (28).

To adjust for possible confounding, models were fit sequentially with an expanding pool of covariates. Model 1 included the sociodemographic variables including age, sex, race, education, and living alone. Model 2 additionally included obesity, comorbidity burden, and mobility disability.

In addition, we conducted two sensitivity analyses. First, we reran all models by excluding individuals with probable dementia at baseline to approximate the condition of cognitive frailty by the International Academy Nutrition and Aging (IANA) and the International Association of Gerontology and Geriatrics (IAGG) (29), defined as the concurrent presence of physical frailty and cognitive impairment in the absence of clinical diagnosis of dementia. Second, we excluded the individuals with depression (PHQ-2 score

≥3) who might exhibit signs and symptoms mimicking those of frailty (30,31), such as exhaustion (31).

All analyses were conducted using Stata 15.1 software (Stata Corp, College Station, TX), and a *p* value of less than .05 was considered statistically significant.

Results

Baseline Characteristics of Study Participants

Of the 6000 older adults included in the study 1787 (30%) had cognitive only, 334 (6%) had frailty only, 615 (10%) had both, and 3264 (54%) had neither. Baseline characteristics by frailty and cognitive impairment categories are given in Table 1. Compared with the neither group, those with frailty only, cognitive only, and both were older, had a lower education level, poorer mobility function, and greater prevalence of depressive symptoms at baseline. Compared with the neither group, those with frailty only and both had a greater prevalence of comorbidities. The comorbidity burden was similar between the cognitive only and neither groups. Overall, 1849 (30.1%) experienced at least one fall during the past 12 months at baseline. Fifty-nine percent of those in both groups had a fall in the year before baseline, compared to 48% in the frailty only, 32% in the cognitive only, and 25% among the neither (Table 1).

Cross-sectional Relationships Between Frailty and Cognitive Impairment and History of Falls at Baseline

The cross-sectional associations between frailty, cognitive impairment, and history of falls at baseline are given in Table 2. In Model 1, after adjusting for the sociodemographic covariates, compared to the neither group, individuals with both experienced the greatest odds for falls (OR = 4.34, 95% CI = 3.56–5.30, *p* < .001), with frailty only and cognitive only being associated with 2.58-fold (95% CI = 2.04–3.26, *p* < .001) and 1.36-fold higher odds of falls (95% CI = 1.18–1.56, *p* < .001). In Model 2, after additional adjustment for obesity, comorbidity, and mobility disability, the associations remained significant with OR of 2.48 (95% CI = 1.98–3.11, *p* < .001) for both, 1.53 for frailty only (95% CI = 1.19–1.97, *p* = .001), and 1.22 for cognitive only (95% CI = 1.05–1.41, *p* = .009). The interaction between frailty (yes/no) and cognitive impairment (yes/no) as a product term in the model was not statistically significant (*p* = .077).

Longitudinal Relationships Between Frailty and Cognitive Impairment and Recurrent Falls

Table 3 presents the results of the marginal means/rates model of the relationships between frailty and cognitive impairment at baseline and recurrent falls over 6 years of follow-up. In Model 1, after adjusting for sociodemographic covariates (age, sex, race, education, and living alone), frailty and cognitive impairment separately and jointly were significantly associated with higher rates of recurrent falls than was neither (cognitive only: RR = 1.10, 95% CI = 1.03–1.17, *p* = .003; frailty only: RR = 1.58, 95% CI = 1.44–1.73, *p* < .001; both: RR = 1.60, 95% CI = 1.48–1.73, *p* < .001). The associations remained significant after additional adjustment for obesity, comorbidity, and mobility disability (RR = 1.07, 95% CI = 1.00–1.13 for cognitive only, *p* = .042; RR = 1.31, 95% CI = 1.18–1.44 for frailty only, *p* < .001; RR = 1.28, 95% CI = 1.17–1.40 for both, *p* < .001; Table 3, Model 2). In addition, compared to those with cognitive only, participants with both had significantly higher risk for

Table 1. Participant Characteristics by Frailty and Cognitive Impairment Status at Baseline in the National Health Aging Trends Study, 2011 (*n* = 6000)

Characteristic	Overall, <i>n</i> = 6000	Cognitively Intact and Not Frail, <i>n</i> = 3264 (54.4%)	Cognitively Impaired Only, <i>n</i> = 1787 (29.8%)	Frail Only, <i>n</i> = 334 (5.6%)	Cognitively Impaired and Frail, <i>n</i> = 615 (10.3%)	<i>p</i>
Age (years), <i>n</i> (%)						
65–69	1144 (28.7)	837 (35.8)	200 (16.8)	60 (23.2)	47 (13.4)	<.001
70–74	1258 (25.0)	825 (27.6)	304 (22.0)	66 (24.2)	63 (13.5)	
75–79	1216 (19.2)	701 (18.7)	355 (21.0)	66 (19.9)	94 (17.0)	
80–84	1193 (14.6)	553 (11.6)	418 (19.3)	71 (16.8)	151 (21.5)	
85–89	721 (8.6)	247 (4.9)	277 (13.1)	45 (11.3)	152 (23.0)	
≥90	468 (3.9)	101 (1.4)	233 (7.8)	26 (4.6)	108 (11.7)	
Sex, <i>n</i> (%)						
Female	3499 (56.4)	1849 (55.1)	1022 (55.1)	230 (69.6)	398 (62.4)	<.001
Male	2501 (43.6)	1415 (44.9)	765 (44.9)	104 (30.4)	217 (37.6)	
Race/ethnicity, <i>n</i> (%)						
White non-Hispanic	4166 (81.9)	2549 (87.6)	1076 (73.2)	211 (76.1)	330 (68.3)	<.001
Black non-Hispanic	1310 (8.1)	520 (5.7)	507 (11.9)	87 (11.8)	196 (13.5)	
Hispanic	348 (6.5)	118 (4.1)	135 (9.8)	30 (10.3)	65 (13.5)	
Other	176 (3.4)	77 (2.7)	69 (5.1)	6 (1.7)	24 (4.7)	
Education, <i>n</i> (%)						
8th grade or less	732 (9.6)	171 (4.4)	336 (17.1)	39 (10.0)	186 (27.1)	<.001
9th–12th grade (no diploma)	829 (11.0)	330 (8.2)	313 (14.6)	55 (15.5)	131 (19.1)	
High school graduate or higher	4422 (79.4)	2761 (87.3)	1130 (68.3)	239 (74.5)	292 (53.8)	
Living alone, <i>n</i> (%)						
Living alone	1987 (30.2)	970 (26.7)	705 (37.5)	119 (35.4)	193 (31.7)	<.001
Obese, <i>n</i> (%)						
Obese	1607 (28.6)	938 (29.6)	401 (25.1)	122 (36.1)	146 (26.3)	.003
Depression, <i>n</i> (%)						
Depression	902 (13.7)	296 (8.6)	264 (14.4)	101 (31.8)	241 (41.6)	<.001
Falls history, <i>n</i> (%)						
Falls history	1849 (30.1)	806 (24.5)	533 (31.5)	151 (48.3)	359 (59.2)	<.001
Probable dementia, <i>n</i> (%)						
Probable dementia	699 (8.7)	0 (0.0)	416 (21.9)	0 (0.0)	283 (42.5)	<.001
Number of comorbidities, <i>n</i> (%)						
0	534 (10.3)	335 (11.8)	174 (10.1)	6 (1.7)	19 (3.6)	<.001
1	1107 (20.2)	653 (21.6)	370 (22.0)	26 (7.9)	58 (10.2)	
≥2	4304 (69.6)	2255 (66.5)	1224 (67.9)	297 (90.4)	528 (86.2)	
Mobility disability, <i>n</i> (%)						
No disability	3658 (68.0)	2525 (81.0)	996 (61.1)	69 (24.1)	68 (12.7)	<.001
Moderate disability	1060 (15.3)	477 (12.7)	388 (19.5)	87 (23.4)	108 (17.3)	
Severe disability	1282 (16.7)	262 (6.3)	403 (19.4)	178 (52.5)	439 (70.0)	
Years of follow-up, median (interquartile range)						
Years of follow-up	4.1 (2.1)	4.4 (2.0)	3.8 (2.0)	3.9 (2.1)	3.1 (1.9)	<.001

Notes: Analyses of weighted data from the National Health and Aging Trends Study; raw numbers and weighted percentages (%) were presented, except for the years of follow-up, where median and interquartile range were provided. Chi-square test for categorical variables between the 4 groups.

recurrent falls (RR = 1.19, 95% CI = 1.09–1.30). The risk for recurrent falls was similar between the frailty only and both groups (RR = 0.98, 95% CI = 0.88–1.09). A formal test of interaction between frailty (yes/no) and cognitive impairment (yes/no) yielded a *p* value of .156.

Sensitivity Analyses

After excluding those with probable dementia or depression at baseline, the results from both the cross-sectional and the longitudinal analyses were largely unchanged, showing significant associations of frailty only and both with history of falls and incident recurrent falls. However, cognitive only was no longer significantly associated with the risk of recurrent falls due to the smaller sample size (Supplementary Tables S1–S4).

Discussion

To the best of our knowledge, this is the first study to evaluate the associations of frailty and cognitive impairment with the risk of recurrent falls in a nationally representative sample of US

community-dwelling older adults. In this study, we found that physical frailty, with or without cognitive impairment, was a strong predictor of recurrent falls; and the association was independent of disease burden, obesity, and mobility limitation. It is also notable that having cognitive impairment only (ie, without frailty) was only marginally associated with recurrent falls.

Regarding the relationship between frailty and cognitive impairment, recent consensus papers advocated for expanding the definition of frailty to include cognition (32,33). Motivated by findings that adding cognitive impairment to models that already included physical frailty increased accuracy in identifying those at high risk for adverse health outcomes such as disability and mortality (12,34,35), some have argued that optimal risk assessment should supplement measures of physical frailty with measures of cognitive function. For the purpose of risk prediction, our study supports that recommendation, finding that frailty and cognitive impairment were independently associated with the history of falls, consistent with previous studies that identified frailty (10,36,37) and cognitive impairment (14,38,39) as independent risk factors. In addition, we

Table 2. Logistic Regression Models of the Cross-Sectional Relationships Between Frailty, Cognitive Impairment, and a History of Falls: the National Health Aging Trends Study, 2011 ($n = 6000$)

	Model 1*			Model 2†		
	Odds Ratio	95% CI	<i>p</i>	Odds Ratio	95% CI	<i>p</i>
Frailty and cognitive impairment condition						
Cognitively intact and not frail ($n = 3264$)	1.0		—	1.0		—
Cognitively impaired only ($n = 1787$)	1.36	1.18–1.56	<.001	1.22	1.05–1.41	.009
Frail only ($n = 334$)	2.58	2.04–3.26	<.001	1.53	1.19–1.97	.001
Cognitively impaired and frail ($n = 615$)	4.34	3.56–5.30	<.001	2.48	1.98–3.11	<.001

Note: CI = confidence interval.

*Model 1: adjusted for age, sex, race, education, and living alone.

†Model 2: adjusted for age, sex, race, education, living alone, obesity, comorbidity, and mobility disability.

Table 3. Adjusted Marginal Means/Rates Model for Assessing the Longitudinal Relationships Between Frailty, Cognitive Impairment, and Recurrent Falls During the 6-Year Follow-up in the National Health Aging Trends Study (2012–2017)

	Model 1*		Model 2†	
	Rate Ratio (95% CI)	<i>p</i>	Rate Ratio (95% CI)	<i>p</i>
Frailty and cognitive impairment status				
Cognitively intact and not frail ($n = 3264$)	Reference	—	Reference	—
Cognitively impaired only ($n = 1787$)	1.10 (1.03–1.17)	.003	1.07 (1.00–1.13)	.042
Frail only ($n = 334$)	1.58 (1.44–1.73)	<.001	1.31 (1.18–1.44)	<.001
Cognitively impaired and frail ($n = 615$)	1.60 (1.48–1.73)	<.001	1.28 (1.17–1.40)	<.001

Note: CI = confidence interval.

*Model 1: adjusted for age, sex, race, education, and living alone.

†Model 2: adjusted for age, sex, race, education, living alone, obesity, comorbidity, and mobility disability.

found that having both frailty and cognitive impairment was most strongly associated with the history of falls, even after adjusting for potential confounders. Specifically, older adults who were both frail and cognitively impaired had a more than 2-fold greater prevalence of falls. These findings are consistent with the previous work (20), showing that the presence of both cognitive impairment and physical frailty was significantly associated with a history of falls. It is also worth noting that the associations in our study remained essentially unchanged after excluding participants with probable dementia, effectively transforming the group with both frailty and cognitive impairment into the subset meeting the definition of cognitive frailty.

In the analysis of recurrent falls, we found that having both frailty and cognitive impairment was associated with a significantly greater risk of recurrent falls relative to those exhibiting cognitive impairment alone. Plausibly the group with frailty and cognitive impairment may represent a more advanced stage of cognitive decline, consistent with the fact that the prevalence of probable dementia in this group was almost twice than that of cognitive impairment only in this cohort. Interestingly, the difference remained unchanged after excluding dementia cases at baseline, therefore refuting the hypothesized difference in the severity of cognitive impairment. Coupled with the fact that the risk of recurrent falls was similar between “both” and “frailty only,” it may be that frailty is a more important predictor of fall risk than cognitive impairment. It is also possible that the risk associated with “both” was underestimated due to the greater rate of study attrition evidenced by the shorter median length of follow-up (Table 1).

While there have been many studies on risk factors for falls and recurrent falls; the results have been mixed. Older age, prior history

of falls, functional impairment, use of a walking aid or assistive device, and cognitive impairment have been identified as key contributors to falls in older adults (40). Moreover, a recent meta-analysis of 22 studies identified 4 domains of risk factors (ie, balance and mobility, medication, psychological, and sensory and neuromuscular risk factors) that are predictive of recurrent falls in older adults (40). Risk factors belonging to these domains such as muscle weakness, poor balance, and slow gait have been associated with both physical frailty and cognitive impairment (41,42). These results suggest that geriatric syndromes such as frailty and cognitive impairment may represent common pathways that mediate the relationships between individual risk factors and recurrent falls. In addition, the complex interplay between physical frailty and cognitive impairment has led some to hypothesize that physical frailty and cognitive impairment may interact to present a synergistic risk for falls. For example, cognitive impairment and the resulting decline in cognitive reserve may have made it difficult to compensate for physical frailty, leading to the weakening of the mechanisms that are protective against falling (18). Unlike the previous study (20), our study did not find evidence of a strong synergistic effect, suggesting that the co-occurrence of physical frailty and cognitive impairment identifies a subset of older adults that may be characteristically different from those with physical frailty alone or cognitive impairment alone as shown in recent studies (43,44). Future research should explore the heterogeneity in the pathophysiology of separate versus joint physical frailty and cognitive impairment and its relationship with falls.

The major strengths of this study are a large sample that is nationally representative of noninstitutionalized older adults in the United States, which enhances the generalizability of the findings. In addition, our study moved beyond the cross-sectional associations to study the

longitudinal effects of frailty and cognitive impairment on future recurrent falls, which helped to better discern their temporal relationships. From a statistical modeling perspective, we chose the marginal means/rates model over Poisson or negative binomial models so that information on the timing of recurrent events, that is, falls, could be taken into account while relaxing the strong parametric assumptions associated with the latter (45,46). Some limitations should be noted in our approach. First, cognitive impairment was ascertained based on self or proxy-report and cognition performance limited to 2 specific domains: executive function and verbal memory, therefore raising the possibility of misclassification bias. However, the use of more in-depth neurocognitive assessment batteries would be cost-prohibitive in large-scale population surveys such as NHATS where speed and ease of assessment are essential. Second, data from NHATS did not allow us to determine the severity or the exact number of falls. While the total number of falls might have been underestimated, we believe the definition of recurrent falls used in this study to be more indicative of a more serious health hazard. Third, recall bias, particularly among participants with cognitive impairment, and missing data on falls due to competing mortality could potentially bias the associations toward null, therefore making our findings conservative. Finally, compared to the analytic sample, those who were excluded due to missing data on falls were older and were more likely to be from racial and ethnic minority groups, underweight, frail, disabled, and have depressive symptoms (Supplementary Table S5), which could result in underestimation of the predictive power of frailty and cognitive impairment.

In conclusion, this study offered evidence for a predictive association between frailty and recurrent falls in noninstitutionalized older adults, and the association remained significant with or without cognitive impairment. On the other hand, there was a weak and marginally significant association between cognitive impairment and falls risk in the absence of physical frailty. While the lack of a synergistic effect between frailty and cognitive impairment argues for treating frailty and cognitive impairment separately in order to mitigate the risk of recurrent falls, our findings raised the question of whether falls risk assessment should prioritize physical frailty over cognitive impairment. The answer to this question would require a better understanding of the temporal relationships between physical frailty and cognitive impairment and the possibility of multiple etiological pathways being differentially associated with falls risk.

Supplementary Material

Supplementary data are available at *The Journals of Gerontology, Series A: Biological Sciences and Medical Sciences* online.

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Conflict of Interest

None declared.

Disclosures

None.

Author Contributions

M.-L.G. participated in concept design, data analysis, interpretation, drafting, critical revision, and approval of the article. Q.-L.X. participated in concept

design, interpretation, critical revision, and approval of the article. E.M.S. participated in interpretation, critical revision, and approval of the article. B.-R.D. participated in critical revision and approval of the article. J.D.K. participated in interpretation, critical revision, and approval of the article.

References

- World Health Organization. Falls. <https://www.who.int/news-room/fact-sheets/detail/falls>
- Tinetti ME, Kumar C. The patient who falls: "It's always a trade-off". *JAMA*. 2010;303:258–266. doi:10.1001/jama.2009.2024
- Bergen G, Stevens MR, Burns ER. Falls and fall injuries among adults aged ≥ 65 years—United States, 2014. *MMWR Morb Mortal Wkly Rep*. 2016;65(37):993–998. doi:10.15585/mmwr.mm6537a2
- Katz R, Shah P. The patient who falls: challenges for families, clinicians, and communities. *JAMA*. 2010;303:273–274. doi:10.1001/jama.2009.2016
- Nevitt MC, Cummings SR, Kidd S, Black D. Risk factors for recurrent nonsyncopal falls. A prospective study. *JAMA*. 1989;261:2663–2668. doi:10.1001/jama.1989.03420180087036
- Tinetti ME, Speechley M, Ginter SF. Risk factors for falls among elderly persons living in the community. *N Engl J Med*. 1988;319:1701–1707. doi:10.1056/NEJM198812293192604
- Xue QL. The frailty syndrome: definition and natural history. *Clin Geriatr Med*. 2011;27:1–15. doi:10.1016/j.cger.2010.08.009
- Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci*. 2001;56:M146–M156. doi:10.1093/gerona/56.3.m146
- Cheng MH, Chang SF. Frailty as a risk factor for falls among community dwelling people: evidence from a meta-analysis. *J Nurs Scholarsh*. 2017;49:529–536. doi:10.1111/jnu.12322
- Samper-Ternent R, Karmarkar A, Graham J, Reistetter T, Ottenbacher K. Frailty as a predictor of falls in older Mexican Americans. *J Aging Health*. 2012;24:641–653. doi:10.1177/0898264311428490
- O'Connell MD, Tajar A, O'Neill TW, et al. Frailty is associated with impaired quality of life and falls in middle-aged and older European men. *J Frailty Aging*. 2013;2:77–83. doi:10.14283/jfa.2013.12
- Feng L, Zin Nyunt MS, Gao Q, Feng L, Yap KB, Ng TP. Cognitive frailty and adverse health outcomes: findings from the Singapore Longitudinal Ageing Studies (SLAS). *J Am Med Dir Assoc*. 2017;18:252–258. doi:10.1016/j.jamda.2016.09.015
- Fougere B, Daumas M, Lilamand M, et al. Association between frailty and cognitive impairment: cross-sectional data from Toulouse frailty day hospital. *J Am Med Dir Assoc*. 2017;18(11):990.e1–990.e5. doi:10.1016/j.jamda.2017.06.024
- Allali G, Launay CP, Blumen HM, et al. Falls, cognitive impairment, and gait performance: results from the GOOD initiative. *J Am Med Dir Assoc*. 2017;18:335–340. doi:10.1016/j.jamda.2016.10.008
- Segev-Jacobovskii O, Herman T, Yogeve-Seligmann G, Mirelman A, Giladi N, Hausdorff JM. The interplay between gait, falls and cognition: can cognitive therapy reduce fall risk? *Expert Rev Neurother*. 2011;11:1057–1075. doi:10.1586/ern.11.69
- Holtzer R, Friedman R, Lipton RB, Katz M, Xue X, Verghese J. The relationship between specific cognitive functions and falls in aging. *Neuropsychology*. 2007;21:540–548. doi:10.1037/0894-4105.21.5.540
- Muir SW, Gopaul K, Montero Odasso MM. The role of cognitive impairment in fall risk among older adults: a systematic review and meta-analysis. *Age Ageing*. 2012;41:299–308. doi:10.1093/ageing/afs012
- Martin KL, Blizzard L, Srikanth VK, et al. Cognitive function modifies the effect of physiological function on the risk of multiple falls—a population-based study. *J Gerontol A Biol Sci Med Sci*. 2013;68:1091–1097. doi:10.1093/gerona/glt010
- Callisaya ML, Ayers E, Barzilai N, et al. Motoric cognitive risk syndrome and falls risk: a multi-center study. *J Alzheimers Dis*. 2016;53:1043–1052. doi:10.3233/JAD-160230
- Tsutsumimoto K, Doi T, Makizako H, et al. Cognitive frailty is associated with fall-related fracture among older people. *J Nutr Health Aging*. 2018;22:1216–1220. doi:10.1007/s12603-018-1131-4

21. Kasper JD, Freedman VA. *National Health and Aging Trends Study User Guide: Rounds 1, 2, 3 & 4 Final Release*. Johns Hopkins University School of Public Health; 2015.
22. Kasper JD, Freedman VA. 2020. National Health and Aging Trends Study user guide: rounds 1-9 final release. Baltimore: Johns Hopkins University School of Public Health. www.NHATS.org
23. Bandeen-Roche K, Seplaki CL, Huang J, et al. Frailty in older adults: a nationally representative profile in the United States. *J Gerontol A Biol Sci Med Sci*. 2015;70:1427–1434. doi:10.1093/gerona/glv133
24. Galvin JE, Roe CM, Powlishta KK, et al. The AD8: a brief informant interview to detect dementia. *Neurology*. 2005;65:559–564. doi:10.1212/01.wnl.0000172958.95282.2a
25. Kasper JD, Freedman VA, Spillman BC. Classification of persons by dementia status in the National Health and Aging Trends Study. Technical Paper #5. Updated 2013. Accessed October 30, 2018. www.nhats.org
26. Löwe B, Wahl I, Rose M, et al. A 4-item measure of depression and anxiety: validation and standardization of the Patient Health Questionnaire-4 (PHQ-4) in the general population. *J Affect Disord*. 2010;122:86–95. doi:10.1016/j.jad.2009.06.019
27. Kroenke K, Spitzer RL, Williams JB. The Patient Health Questionnaire-2: validity of a two-item depression screener. *Med Care*. 2003;41:1284–1292. doi:10.1097/01.MLR.0000093487.78664.3C
28. Li QH, Lagakos SW. Comparisons of test statistics arising from marginal analyses of multivariate survival data. *Lifetime Data Anal*. 2004;10:389–405. doi:10.1007/s10985-004-4774-x
29. Kelaiditi E, Cesari M, Canevelli M, et al. Cognitive frailty: rational and definition from an (I.A.N.A./I.A.G.G.) international consensus group. *J Nutr Health Aging*. 2013;17:726–734. doi:10.1007/s12603-013-0367-2
30. Lohman M, Dumenci L, Mezuk B. Depression and frailty in late life: evidence for a common vulnerability. *J Gerontol B Psychol Sci Soc Sci*. 2016;71:630–640. doi:10.1093/geronb/gbu180
31. Lohman M, Dumenci L, Mezuk B. Sex differences in the construct overlap of frailty and depression: evidence from the Health and Retirement Study. *J Am Geriatr Soc*. 2014;62:500–505. doi:10.1111/jgs.12689
32. Gobbens RJ, Luijkx KG, Wijnen-Sponselee MT, Schols JM. Towards an integral conceptual model of frailty. *J Nutr Health Aging*. 2010;14:175–181. doi:10.1007/s12603-010-0045-6
33. Rodríguez-Mañás L, Féart C, Mann G, et al. Searching for an operational definition of frailty: a Delphi method based consensus statement. The frailty operative definition-consensus conference project. *J Gerontol A Biol Sci Med Sci*. 2013;68:62–67. doi:10.1093/gerona/gls119
34. Aliberti MJR, Cenzer IS, Smith AK, Lee SJ, Yaffe K, Covinsky KE. Assessing risk for adverse outcomes in older adults: the need to include both physical frailty and cognition. *J Am Geriatr Soc*. 2019;67:477–483. doi:10.1111/jgs.15683
35. Hao Q, Dong B, Yang M, Dong B, Wei Y. Frailty and cognitive impairment in predicting mortality among oldest-old people. *Front Aging Neurosci*. 2018;10:295. doi:10.3389/fnagi.2018.00295
36. Kojima G, Kendrick D, Skelton DA, Morris RW, Gawler S, Iliffe S. Frailty predicts short-term incidence of future falls among British community-dwelling older people: a prospective cohort study nested within a randomised controlled trial. *BMC Geriatr*. 2015;15:155. doi:10.1186/s12877-015-0152-7
37. Schultz M, Rosted E, Sanders S. Frailty is associated with a history with more falls in elderly hospitalised patients. *Dan Med J*. 2015;62:A5058.
38. Whitney J, Close JC, Jackson SH, Lord SR. Understanding risk of falls in people with cognitive impairment living in residential care. *J Am Med Dir Assoc*. 2012;13:535–540. doi:10.1016/j.jamda.2012.03.009
39. van Doorn C, Gruber-Baldini AL, Zimmerman S, et al. Dementia as a risk factor for falls and fall injuries among nursing home residents. *J Am Geriatr Soc*. 2003;51:1213–1218. doi:10.1046/j.1532-5415.2003.51404.x
40. Jehu DA, Davis JC, Falck RS, et al. Risk factors for recurrent falls in older adults: a systematic review with meta-analysis. *Maturitas*. 2021;144:23–28. doi:10.1016/j.maturitas.2020.10.021
41. Davis DH, Rockwood MR, Mitnitski AB, Rockwood K. Impairments in mobility and balance in relation to frailty. *Arch Gerontol Geriatr*. 2011;53:79–83. doi:10.1016/j.archger.2010.06.013
42. Lichter DG, Benedict RHB, Hershey LA. Importance of balance-gait disorder as a risk factor for cognitive impairment, dementia and related non-motor symptoms in Parkinson's disease. *J Parkinsons Dis*. 2018;8:539–552. doi:10.3233/JPD-181375
43. Chu NM, Bandeen-Roche K, Tian J, et al. Hierarchical development of frailty and cognitive impairment: clues into etiological pathways. *J Gerontol A Biol Sci Med Sci*. 2019;74:1761–1770. doi:10.1093/gerona/glz134
44. Ge ML, Carlson MC, Bandeen-Roche K, et al. U.S. National profile of older adults with cognitive impairment alone, physical frailty alone, and both. *J Am Geriatr Soc*. 2020;68:2822–2830. doi:10.1111/jgs.16769
45. Gill DP, Zou GY, Jones GR, Speechley M. Comparison of regression models for the analysis of fall risk factors in older veterans. *Ann Epidemiol*. 2009;19:523–530. doi:10.1016/j.annepidem.2009.03.012
46. Amorim LD, Cai J. Modelling recurrent events: a tutorial for analysis in epidemiology. *Int J Epidemiol*. 2015;44:324–333. doi:10.1093/ije/dyu222