Cumulative effects of cognitive impairment and frailty on functional decline, falls and hospitalization: a four-year follow-up study with older adults

OBJECTIVE: Evaluate the cumulative effects of cognitive impairment and frailty on functional decline, falls and hospitalization in older adults over a four-year period. **METHOD:** Four hundred five older adults (60-95 years; mean age: 70.62 ± 7.12 years), 57% female. The frailty evaluation was performed using the clinical criteria of the Cardiovascular Health Study (CHS): weight loss, fatigue, weakness, slowness and low physical activity. Cognitive impairment was defined by cutoff scores of the Mini Mental State Examination (MMSE) based on schooling. Follow-up – functional decline was assessed using the Lawton&Brody scale of instrumental activities of daily living (IADL). An investigation was also performed of the occurrence of falls and admissions to the hospital in the previous twelve months. **RESULTS**: Cognitive impairment was associated with admissions to the hospital and declines in the IADL category of using a telephone. Frailty was associated with admissions to hospital. Cumulative effects were observed for hospitalization and the decline in using the telephone and shopping. Frailty and cognitive impairment increased the risk of being admitted to hospital by 557% and increased the risk of a decline in using the phone by 262% and shopping by 208%. No conditions were associated to risk of falls. **CONCLUSION:** The combination of the MMSE and the CHS criteria was adequate for measuring the cumulative effects of cognitive impairment and frailty. Shared physiological mechanisms may explain the relation between cognitive impairment and frailty, but further investigations are needed in Brazil and other low/middle-income countries.

Keywords: Frailty. Cognition. Risk factors. Falls. Activity of Daily Living. Hospitalization.

Introduction

The Brazilian Institute of Geography and Statistics, which is the government agency responsible for the analysis of demographic data, estimates that the population aged 60 years or older will surpass 64 million people by the year 2050. Considering the rapid increase in life expectancy in the country, an individual born in the year 2017 is expected to live to the age of 76 years, which is an increase of thirteen months and eleven days compared to a person born in 2016.[1]

The longevity achieved by the human race in recent centuries translates to an increase in years of living, but it is uncertain whether these additional years will be lived with quality. Vulnerability in old age is a multidimensional issue. The decline in biological functions over time is expected and this decline interacts with sociocultural processes, with low schooling and income favoring the emergence of vulnerability.[2,3] A vulnerable individual is less likely to cope with stressful events,[4] which can lead to adverse health outcomes, such as functional decline,[5] and the aggravation of preexisting conditions, such as cognitive decline and physical frailty.[6]

A slight decrease in cognitive function is expected during the aging process. However, cognitive impairment regards a poorer performance in terms of memory, judgment, language and attention than that expected for one's age and educational level.[7,8] Neurodegeneration, vascular and metabolic problems, chronic stress, depressive symptoms and anxiety can contribute to a poorer mental performance in the old age[9] and cognitive reserves (plasticity) may be insufficient to neutralize or minimize the effects of stressors, leading to the impairment of cognitive function.

In both research and the clinical practice of health care, frailty is a frequent clinical condition in the older population. One of the main theories considers frailty to be a clinical syndrome defined as a multiple-cause condition.[10] The Cardiovascular Health Study (CHS) offered one of the first definitions of frailty as a geriatric syndrome assessed using five clinical criteria: unintentional weight loss, fatigue (exhaustion), muscle weakness, slow gait/slowness and low level of physical activity.[11]

Both cognitive impairment and frailty have been described as independent risk factors for adverse outcomes, such as vulnerability, functional dependence and death.[10,12]

The main adverse outcomes expected in cognitively impaired and/or frail older adults are a reduction in functional capacity, the occurrence of falls and a greater likelihood of being admitted to high-complexity healthcare services, such as hospitals and emergency/urgent care units. Such outcomes constitute a burden to healthcare services as well as the affected older adult, his/her family and his/her caregiver. Thus, a gerontological/geriatric assessment can serve as a warning so that steps can be taken for the prevention of these outcomes.

As stated above, a small decline in cognitive function is normal, but functional decline or the loss of functioning in comparison to previous functioning is worrisome. Approximately 10% of community-dwelling older adults need assistance for the performance of basic activities living (BADLs), which involve self-care, and approximately 30% either require supervision or are unable to perform more complex tasks, which are known as instrumental activities of daily living (IADLs),[13] such as administering medications, managing finances and performing housework. In a study conducted in southern Brazil with a sample of 1593 older adults, the increase in age, low schooling, morbidities and the need for hospitalization were identified as factors associated with low functioning.[13] The loss of functioning in older adults is the main reason for the need for new family arrangements and the designation of a caregiver.[14]

The occurrence of falls in the geriatric population is considered a major public health challenge. Approximately 30% of older adults experience a fall event at least once a year, the consequences of which may be fractures, muscle injuries, neurological damage and death.[15,16] Other outcomes of falls include functional decline, a fear of falling, a reduction in social activities and the loss of autonomy.[16]

In low/middle-income countries, few longitudinal investigations have evaluated the cumulative effects of cognitive impairment and frailty on functional decline, the occurrence of falls and hospitalizations among older adults. A study of this type can generate important knowledge that assists in the prevention of such outcomes. Therefore, the aim of the present study was to analyze the cumulative effects of cognitive impairment and physical frailty on the risk of functional decline, the occurrence of falls and recent hospitalizations among the Brazilian older adults in a four-year period. We also investigated whether cognitive impairment and the concomitant occurrence of frailty have a greater effect on the occurrence of adverse outcomes or whether the effects are similar when analyzed individually.

Methods

Design

A longitudinal study with four-year follow-up was conducted by the Health and Ageing Group of the Federal University of São Carlos, Brazil.

Participants

We evaluated community-dwelling cohabitants older adults registered with primary care centers in the city of São Carlos, state of São Paulo, Brazil. São Carlos is located in the southeastern region of the country and has an estimated population of 221,950 residents, among whom 13% were aged 60 years or older according to the 2010 census.[17]

The baseline study was conducted in 2014. The participant selection process is described elsewhere,[9,18,19] but a brief description is given here. Community-dwelling older adults (age ≥60 years, as defined by the World Health Organization for developing countries) registered with 18 primary care centers (n = 1188) in rural and urban areas of São Carlos were contacted in person and invited to participate in the survey. Individuals with hearing, visual or language limitations that could constitute barriers to the data collection process were excluded. The response rate was 59.1% (total: 702 individuals).

The follow-up data collection began in April 2018. Among the 702 participants of the baseline study, 37 participants had changed address and could not be contacted for the 2018 wave. Two hundred forty-five participants were lost to the follow-up (were not located at home after three attempts [n = 125] or had died [n = 120]). Fifteen were excluded due incomplete data on cognitive level, educational background and frailty. Thus, the longitudinal study involved data on 405 individuals (57.7% of the baseline sample).

This study received approval from the Human Research Ethics Committee of the Federal University of São Carlos (certificate number: 1.123.813/2015) and all participants signed a statement of informed consent. At-home interviews were conducted by trained professionals in the fields of gerontology and nursing.

Baseline assessments

- *Demographic characteristics:* sex (male, female), age group (continuous variable), schooling (continuous variable), retirement (yes, no), place of residence (rural or urban area) and ethnicity (black/brown, white or other).

- *IADLs*: Functioning was assessed using the Lawton and Brody Scale for the determination of the degree of dependence on instrumental activities, such as performing housework, managing finances, using a telephone, administering

medications, traveling, shopping and preparing meals. The total score ranges from seven (complete dependence) to 21 (complete independence), with intermediate scores (8 to 20 points) indicative of partial dependence.[20,21]

- *Cognitive impairment*: Cognitive screening was performed using the Mini Mental State Examination (MMSE), the score of which ranges from 0 to 30.[22] The cutoff points were adjusted for different levels of schooling: < 26 for those with nine or more years of schooling, < 24 for those with five to eight years of schooling, < 22 for those with one to four years of schooling and < 17 for illiterate individuals.[23]

- *Frailty syndrome and criteria:* The five CHS clinical criteria for frailty were considered: unintentional weight loss in the previous year (self-declared) were assessed with the question "Have you lost any weight in the last 12 months without dieting?" Affirmative answers of weight loss greater than 4.5 kg or 5% of body weight were considered positive for this criteria. Fatigue in the previous week (self-declared) was assessed with two questions from the Center for Epidemiological Studies–Depression (CES-D) (a) "How often in the last week did you feel that everything demanded great effort?" and (b) "How often in the last week did you feel you could not carry on with your activities?" Answers of "always" or "most of the time" for either question were considered positive for this criteria.Muscle weakness was assessed by the mean of three consecutive measures of grip strength on dominant side in kilogram-force using a Jamar hydraulic dynamometer (model SH5001; SAEHAN®, Lafayette, IL, USA). Strength categorized in the lowest quintile after controlling for sex and body mass index (BMI) was considered positive for this criteria. Slowness was assessed by the mean of three consecutive measures of the time to walk 4.6m. Two meters were added to the beginning and end of the track to allow for acceleration and deceleration. Mean speed categorized in the lowest quintile after controlling for sex and height was considered positive for this criteria. ,Decreased physical activity level compared to the previous year (self-declared) was assessed with the question, "Do you believe you practice less physical activities when compared with 12 months ago?". Based on Fried's phenotype, individuals with three to five criteria were considered frail, those with one or two criteria were considered pre-frail and those negative for all five criteria were considered robust/non-frail.[11]

Follow-up assessments

- *IADL*: Described above.

- *Occurrence of falls:* Self-declared based on the answer to the following questions: 'Have you suffered a fall from your own height anywhere in the last 12 months? If so, how many times?'

- *Admission to hospital or complex healthcare service*: Self-declared based on the answer to the following questions: 'Did you need to be hospitalized or admitted to a complex healthcare service for at least 24 hours in the last 12 months? If so, how many times and what was the total number of days you were hospitalized?'

Statistical analysis

The Statistical Package for Social Sciences (SPSS software, version 21.0) was used for the data analysis. Descriptive statistics were performed to characterize the sample. Frequency (n), percentage (%), mean and standard deviation (±) values were calculated for the description of the participants at baseline (Table 1) and the prevalence of the outcomes assessed at follow-up (Table 2).

Single multinomial regression models were run to analyze the effects (odds ratio[OR] and respective 95% confidence intervals [CI]) of cognitive impairment (independent variable; Figure 1) and frailty (independent variable; Figure 2) on the outcomes hospitalization, falls and decline in IADLs (dependent variables).

A third multinomial regression model tested the cumulative effect of cognitive impairment occurring concomitantly with frailty on these outcomes (Figure 3). The reference group for this model was composed of robust (non-frail) participants with intact cognition. Age (continuous), education (continuous), BMI in kg/m^2 (continuous) and sex (reference: male) were the controlling variables in all models. Effects with a two-sided p-value ≤ 0.05 were considered statistically significant.

Results

From 282 participants lost on the follow-up, n=120 were death confirmed. We analyzed characteristics on n=156 lost on follow-up with complete baseline data. The mean age was 69.87 years and 61.5% had between 60-69 years old. Formal schooling time was 3.92 years and 91% were living a marital-like status. Regarding ethnicity, 30.8% self-declared black/brown and 67.3% self-declared white. Regarding cognitive

status, 25% scored lower than cutoff, 34,6% were characterized as frail and 8.3% presented both conditions together.

Women accounted little more than half of the sample (Table 1). Mean age was 71.59 ± 6.71 years among the men and 69.90 ± 7.35 years among the women (t = 2.33; p = 0.018). No significant difference was found in mean schooling between men (3.78 ± 3.52 years) and women (3.36 ± 3.23 years) and both sexes had similar MMSE scores (men: 22.55 ± 4.96; women: 21.48 ± 4.98). The prevalence of cognitive impairment, frailty and the two conditions concomitantly was respectively 29.3%, 17.2% and 8.6% among the men and 35.5%, 26% and 12.6% among the women.

Table 1. Description of participants at baseline. São Carlos, Brazil, 2014. (n = 405)

Profile	**n (%) or mean ± SD**
Male	174 (43.0)
Female	231 (57.0)
Age, *baseline*	70.62 ± 7.12
60-69	204 (50.4)
70-79	152 (37.5)
80+	49 (12.1)
Marital status	
Married or stable partner	363 (89.6)
Without partner	42 (10.7)
Schooling	3.54 ± 3.54
Illiterate	91 (22.5)
1-4 years	233 (57.5)
5-8 years	46 (11.4)
9+ years	35 (8.6)
Ethnicity	
Black/Brown	126 (31.1)
White	277 (68.4)
Others	2 (0.5)
MMSE, points	21.84 ± 4.99
Cognitive decline (below cutoff)	133 (32.8)
Frailty (3-5 criteria)	90 (22.2)

Cumulative cognitive impairment and frailty	44 (10.9)

±SD: standard-deviation. MMSE: Mini Mental State Examination

Ninety-eight participants (24.2%) were classified as independent in 2014 and this percentage dropped to nearly half (12.8%) in 2018. An increase in partial dependence was also found (24.6% in 2014 and 82.5% in 2018). In contrast, the complete dependence rate dropped from 41.2% in 2014 to 4.7% in 2018.

Table 2 shows the outcomes evaluated in the four-year follow-up. Regarding IADLs, the most prevalent decline (no longer independent or aggravation of pre-existing dependency) was found for traveling, followed by managing finances and shopping. For men, the mean IADL score was 16.02 ± 3.47 in 2014 and 14.96 ± 3.88 in 2018 (mean difference: 1.06; p <0.000). For women, the mean IADL score was 18.26 ± 3.57 in 2014 and 16.87 ± 4.05 in 2018 (mean difference: 1.39; p <0.000).

Table 2. Prevalence of outcomes assessed at follow-up. São Carlos, 2018. (n = 405)

Follow-up assessments	n (%)	95% CI of prevalence (%)
Functional decline (IADLs)		
Using telephone	54 (13.3)	10-17
Travelling	159 (39.3)	34-44
Shopping	85 (21.0)	17-25
Preparing meals	49 (12.1)	9-15
Housework	84 (20.7)	17-25
Administering medications	60 (14.8)	11-18
Managing finances	90 (22.2)	18-26
Falls		
Occurrence of fall in previous year	103 (25.4)	21-30
Number of falls (mean ± SD)	1.28 (0.65)	
Hospitalization in previous year		
Admission to hospital	118 (29.1)	25-34
Number of hospitalizations (mean ± SD)	1.29(0.76)	
Hospitalization stay in days (mean ± SD)	3.40 (3.90)	

CI: confidence interval. IADL decline: functional decline in instrumental activity of daily living between 2014-2018,

The occurrence of falls in the previous year was only assessed in 2018. Fewer men reported falls than women (19.5% vs. 30.3%). In contrast, self-reported admissions to hospital were higher among men than women (33.9% vs 25.5%).

As shown in Figure 1, cognitive impairment at baseline was associated with future functional declines in using a telephone (OR = 3.01). . Participants with cognitive impairment also had a 95% greater risk of being admitted to hospital in comparison to those with intact cognition.

Figure 1. Forest plot indicating odds ratios for cognitive impairment as factor associated with listed outcomes over four-year follow-up adjusted for sex, age, education and BMI.

As shown in Figure 2, being frail at baseline was associated with a greater risk of hospitalization than cognitive impairment. Frail participants were 2.19-fold more likely to be admitted to hospital than non-frail participants.

Figure 2. Forest plot indicating odds ratios for frailty as factor associated with listed outcomes over four-year follow-up adjusted for sex, age, education and BMI

The cumulative effect of cognitive impairment and frailty was evident in the occurrence of hospitalizations, with a 557% higher risk compared to non-frail, cognitively healthy participants.. Moreover, concomitant cognitive impairment and

frailty was associated with a decline in using a telephone (OR = 3.62) and with a decline in shopping (OR = 3.08). No cumulative effects were found regarding the occurrence of falls (Figure 3).

Figure 3. Forest plot indicating odds ratios for cumulative concomitant cognitive impairment and frailty as factor associated with listed outcomes over four-year follow-up adjusted for sex, age, education and BMI

In cognitively impaired individuals, the mean number of hospitalizations was 1.23 ± 0.50 and mean hospital stay was 3.58 ± 4.37 days. In frail individuals, the mean number of hospitalizations was 1.16 ± 0.43 and mean hospital stay was 3.42 ± 3.83 days. Among those with concomitant cognitive impairment and frailty, the mean number of hospitalizations was similar to that found for those with either cognitive impairment or frailty alone (1.21 ± 0.504), but mean hospital stay was longer (3.75 ± 4.63). In the reference group (non-frail individuals with intact cognition), the mean number of hospitalizations was 1.50 ± 1.24 and mean hospital stay was 3.58 ± 6.05 days.

Discussion

Studies involving the Brazilian population of older adults report that women account for the majority of the samples,[6,24] which is likely due to the greater longevity of women compared to men, leading to a larger contingent of women aged 60 years or older.[25] This phenomenon is directly reflected in scientific studies involving samples recruited from the community. The similar number of men and women in the present study is due to the uniqueness of the recruitment of the sample, which was composed of older adults that reside in the same home, many of whom were conjugal partners. The mean age of the participants was close to 70 years, with the men slightly older than the women. This result is in agreement with data described in previous studies conducted in Brazil.[2,13,26]

Approximately 30% of the participants exhibited cognitive impairment. The same rate is reported in a Chinese study involving 480 participants using the same

instrument for cognitive screening (MMSE) with cutoff points adjusted for education, in which women had a greater probability of cognitive impairment.[27] This rate is high in comparison to previous Brazilian population-based studies, in which the prevalence ranges from 8 to 14%.[28,29] The divergence may be due to the profile of older adults in different samples as well as the measures and cutoff points employed. In the present study, the majority of participants had less than five years of schooling and the full version of MMSE was used. Another point to consider is the differences in cutoff points used in different studies based on schooling and age.[30]

Regarding the prevalence of frailty, studies conducted in low/middle-income countries report similar results, with rates of 12.2% in Colombia,[31] 4.9% in Taiwan[32] and 10% in a study involving data from different low/middle-income countries.[33] The divergence may be explained by the different manners of assessing frailty.

The concomitant cognitive impairment and frailty was present in 10.9¨% participants of this study The association between both conditions were reported by other Brazilian studies.[34,35]

In the present study, one-quarter of the participants were completely independent regarding the performance of IADLs in 2014 and this proportion dropped to half after four years. This was observed because the completely independent and completely dependent groups (the extremes categories) lose number of participants to the partially dependent group (middle category). It is expected that independent participants starts needing support for some IADL over the time. Recovering abilities in performing IADL or the changes of aspect of the care can be reasons for completely dependent participants in 2014 being categorized as partially dependent in 2018. [36]

Functional loss in terms of IADLs ranged from 12 to 40%, with the most evident declines related to travelling, managing finances and shopping. The data from 2014 are in agreement with results described by Nunes et al.,[13] who found that nearly 30% of older adults required supervision or were unable to perform IADLs. A study involving octogenarians found overall functional decline in 20% of the participants during eight months of follow-up.[37]

The occurrence of falls (assessed at follow-up) was reported by 19.5% of the men and 30.3% of the women. A study conducted in the United Kingdom involving

4301 men and women between 50 and 75 years of age reports similar data, with falls more prevalent among women (29.1%) than men (23.5%).

Hospitalizations were only investigated in 2018 and men were admitted more often than women (33.9% vs. 25.5%). Regarding hospital admissions, the study found 1.2 times of hospitalization and 3.5 days of hospital stay.

Cognitive impairment increased the chance of being admitted to hospital in the previous year. A previous study found that the main clinical conditions associated with hospitalizations were cardiovascular disease and diabetes.[38] A systematic review of the literature confirms these associations but also reports the possible mediation of depression, stress and the use of medications.[39] The study also highlighted the complexity of this relation, as cognitive decline may emerge or become aggravated following the occurrence of a hospitalization.

The association between cognitive impairment and the loss of functioning is well-documented in the literature. Each daily activity has a specific level of complexity and requires specific cognitive skills. In the present study, cognitive impairment was associated with functional decline in using the telephone. A previous longitudinal study confirms these results, stating that initiating a telephone call and maintaining an appropriate telephone connection becomes an increasingly difficult task with the progression of cognitive decline.[40]

Frailty alone was associated with hospitalization, which is in agreement with both classic and recent studies.[11,42] As mentioned above, a previous study reports that the main clinical reasons for hospitalization are cardiovascular disease and diabetes,[38] which are cited in the literature as conditions that result in physical frailty.[43,44]

No decline in IADL was associated to frailty, however the classic publication by Fried and collaborators discussed the functional decline in frail individuals over time.[11] A study involving community-dwelling Mexican older adults found that frailty was associated with functional dependence in a 10-year period.[45] A Canadian study involving 1643 older adults found similar results to those of the present investigation, reporting that the frailty criteria (with the exception of unintentional weight loss) were individually associated with the inability to manage one's own finances and medications in the model adjusted for sociodemographic characteristics, but when other criteria were incorporated into the model, these associations lost their significance.[46] Managing

finances and medications requires preserved cognition, which may demonstrate a possible overlapping of cognitive impairment and frailty. Functional loss in frail older adults is clear, but further studies are needed to gain a better understanding of the relation between physical status and specific activities of daily living.

Falls was not linked with frailty in this study, in the other hand the literature is clear regarding the prediction of frailty on this outcome. In cross-sectional analyses of the English Longitudinal Study of Ageing (ELSA) involving 4301 participants, frailty was significantly associated with falls in both women and men, but the effect was maintained only for women in the adjusted analysis.[47] The authors attribute this relation to the possible mediation of deficits in balance and muscle function.[48] Accordingly, the measurement of frailty in the present study included the investigation of walking speed and muscle strength however could not be enough to predict falls.

Separately, frailty and cognitive impairment were associated with hospitalizations and functional decline in using telephone and shopping. . Considering hospitalizations, studies report associations with frailty[49] and cognitive impairment[50] but found inconsistent statistics when the predictor was the concomitant cognitive impairment and frailty.. One study found that the combination of the Montreal Cognitive Assessment test and the Clinical Frailty Scale predicted hospitalizations in patients with liver problems.[51]

Considering the studies found in the literature, the discussion of functional decline regarding specific activities is limited. The smaller number of participants in comparison to large population-based studies, the way in which the older adults were selected and the restriction regarding the diagnosis of dementias are limitations that should be considered when interpreting the present results. The follow-up rate was relatively small, this happens because most of the participants changes address and do not update contact information with the health services, which difficult the following assessments. However, considering potential bias, the characteristic of the lost in follow-up participants were the same those were contacted again in 2018. Nonetheless, this is a pioneering study in Brazil aimed at understanding the effects of frailty and cognitive impairment on community-dwelling residents in a longitudinal follow-up investigation.

Conclusion

Frailty and cognitive impairment were associated with hospitalizations, functional decline but not falls among older adults. Both conditions exerted cumulative effects on the occurrence of hospitalizations and functional decline specific to the activity of managing medications. Moreover, the combination of the MMSE and CHS frailty criteria was capable of measuring cumulative effects. The physiological mechanisms behind the two conditions may clarify the effects found. However, further clinical investigations with specific samples and population-based surveys in Brazil and other developing countries are needed. This study has particular relevance, as it provides information that can assist in the establishment of prevention measures for adverse health outcomes, which currently account for considerable expenditures in the healthcare system and exert a negative impact on the wellbeing and quality of life of older adults.

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