ORIGINAL ARTICLE

PREVALENCE AND TRANSITION TO FRAILTY IN OLDER ADULTS WITH COGNITIVE IMPAIRMENT: A 1-YEAR COHORT STUDY

Prevalência e transição para a fragilidade em idosos com alteração cognitiva em uma coorte de um ano

Mariana Asmar Alencar[a], Aldalan Cunha de Oliveira[b], Luisa Costa Figueiredo[c], João Marcos Domingues Dias[a], Rosângela Corrêa Dias[a]

ABSTRACT

Cognitive impairment and frailty are often found in older people, and they appear to be related to each other. However, little is known about the prevalence and transition to frailty in older adults with cognitive impairment, especially in the Brazilian population. The present study aimed to determine the prevalence and transitions between frailty states in a cohort of older adults with cognitive impairment followed prospectively for 1 year. A cohort of 59 community-dwelling older adults (aged ≥ 65 years) with cognitive impairment was evaluated. Individuals were classified as frail by the presence of 3 or more of the following criteria: unintentional weight loss; reduced grip strength; exhaustion; slowness; and low physical activity level. Individuals meeting 1 or 2 criteria were classified as prefrail, and those meeting 0 criteria as nonfrail. Cognitive function was assessed by the Mini-Mental State Examination, and severity, by the Clinical Dementia Rating scale. Of 59 older adults evaluated at baseline, 28 (47.5%) were classified as frail, 28 (47.5%) as prefrail, and only 3 (5%) as nonfrail. Over 12 months, 33.3% of participants transitioned from prefrail to frail. The present study showed a high prevalence of frailty in older adults with cognitive impairment and, within 12 months, new cases of frailty were identified in this population. Therefore, more research is needed to further investigate the relationship between cognitive decline and frailty.

KEYWORDS: aged; frailty; cognitive dysfunction; mortality.

RESUMO

Alteração cognitiva e fragilidade são frequentemente encontradas em idosos e parece haver uma relação entre elas. Entretanto, pouco se sabe sobre a prevalência e a transição para a fragilidade nos idosos com alteração cognitiva, principalmente para a população brasileira. O objetivo do estudo foi avaliar a prevalência e a transição entre os estados de fragilidade em um grupo de idosos com alteração cognitiva em uma coorte prospectiva de um ano. Neste estudo de coorte foram avaliados 59 idosos comunitários com alteração cognitiva (≥ 65 anos). O indivíduo frágil foi identificado por apresentar pelo menos três dos seguintes critérios: perda de peso não intencional, fraqueza da força de preensão palmar, exaustão, lentidão na marcha e baixo nível de atividade física. Quando o indivíduo apresentou um ou dois critérios, foi considerado pré-frágil; quando não apresentou nenhum critério, foi considerado não frágil. A função cognitiva foi avaliada pelo Mini Exame do Estado Mental e a gravidade, pela *Clinical Dementia Rating Scale*. Do total de 59 idosos avaliados na linha de base, 28 (47,5%) eram frágeis, a mesma quantidade era de pré-frágeis e apenas 3 idosos eram não frágeis. Em 12 meses, verificou-se uma transição para fragilidade de 33,3%. Este estudo mostrou que a prevalência de fragilidade é alta entre os idosos com alteração cognitiva e, em um período de 12 meses, novos casos de fragilidade ocorreram entre os idosos com alteração cognitiva. Entretanto, mais estudos são necessários para investigar com melhor precisão uma relação existente entre o declínio cognitivo e a fragilidade.

PALAVRAS-CHAVE: idoso; fragilidade; disfunção cognitiva; mortalidade.

[a]Department of Physical Therapy, Universidade Federal de Minas Gerais – Belo Horizonte (MG), Brazil.
[b]Specialist in Geriatric Physical Therapy, Faculdade de Ciências Médicas de Minas Gerais – Belo Horizonte (MG), Brazil.
[c]Universidade de Brasília – Brasília (DF), Brazil.

Correspondence data
Mariana Asmar Alencar – Departamento de Fisioterapia, Escola de Educação Física, Fisioterapia e Terapia Ocupacional, Universidade Federal de Minas Gerais – Avenida Antônio Carlos, 6.627 – Pampulha – CEP: 31270-901 – Belo Horizonte (MG), Brasil – E-mail: masmaralencar@yahoo.com.br
Received on: 06/28/2018. Accepted on: 07/04/2018.
DOI: 10.5327/Z2447-211520181800037

INTRODUCTION

An important characteristic of the aging process is the heterogeneity in morphological, functional, psychological, and social aspects. Thus, a specific older population may consist of different individuals, from frail and vulnerable to strong and independent older adults.[1,2]

Given the increasing number of frail older people worldwide, there has been a growing interest and need to investigate frailty in this population.[2-4] Currently, frailty is considered a multifactorial clinical syndrome characterized by a state of physiological vulnerability, resulting from decreased energy reserves, and by reduced resistance to stressors, with a consequent decline in physiological systems.[3,5]

To identify frailty, Fried et al.[6] proposed a phenotype consisting of the following 5 components:

1. unintentional weight loss;
2. self-reported exhaustion;
3. reduced grip strength;
4. low physical activity level;
5. slowness.

Older adults with 3 or more of these components are classified as frail, those with 1 or 2 components as prefrail, and those with 0 components as nonfrail.[6] However, these criteria are limited to physical and functional aspects, disregarding cognitive and psychological aspects.[3,4,7]

Frail older adults are at high risk of falls, functional decline, hospitalization, and death, as their physiological reserves are insufficient to withstand stressors.[8,9] In the prefrail state, which is clinically silent, the organism still has physiological reserves to respond to external stressors, with a chance of complete recovery.[3,10]

However, an important aspect that has received little attention in prior studies of frailty is cognitive impairment, although some studies have shown a possible association between them.[7,11-15] Some researchers have identified poor cognition as a risk factor for frailty. Ottenbacher et al.[14] and Raji et al.[16] found an association between cognitive decline and increased risk of frailty over a 10-year period. In addition, Samper-Ternent et al.[17] found that the risk of frail older adults becoming cognitively impaired, over a 10-year period, was 1.3 times higher than that of nonfrail older adults.

Little is known about the transitions between frailty states in older adults with cognitive impairment. The present study aimed to determine the prevalence and transitions between frailty states in a cohort of older adults with cognitive impairment followed prospectively for 1 year. This knowledge of frailty in the Brazilian population and its relationship with cognitive impairment may pave the way for new advances in prevention and health promotion for older adults.

METHODS

Sample

This prospective cohort study was conducted from 2011 to 2012 (12 months) at Jenny de Andrade Faria Institute for Women's Health and Geriatric Care, located at Hospital das Clínicas of Universidade Federal de Minas Gerais (UFMG), in Belo Horizonte, Brazil. Public specialized geriatric care is provided through the Brazilian Unified Health System at the outpatient clinic of the institute.

To obtain a representative sample, the sample size calculation was based on the number of older adults receiving care at the institute and on studies of frailty. Considering a power of 80% and a significance level of 5%, simple random probability sampling was used to include the study participants.

Therefore, the sample consisted of 59 community-dwelling older adults aged ≥ 65 years with cognitive impairment. Bedridden older adults, wheelchair users, terminally ill patients, patients with auditory or visual impairment to perform the tests, with serious sequelae of stroke, or with severe Parkinson's disease that impaired their ability to perform the tests were excluded. Older adults with severe dementia, defined as Clinical Dementia Rating (CDR) 3,[18] were also excluded from the sample due to the low reliability of the grip strength test for assessing frailty in these patients.[19]

The study was approved by UFMG Research Ethics Committee (approval number ETIC 220/09). Written informed consent was obtained from all individual participants or their legally authorized representatives prior to inclusion in the study.

Frailty assessment

Frailty was assessed using the criteria developed by Fried et al.[6] The characteristics of frailty are as follows:

- unintentional weight loss of ≥ 4.5 kg or ≥ 5% of body weight in prior year;
- weakness, measured by grip strength adjusted for sex and body mass index (BMI);
- self-reported exhaustion, identified by two questions from the Center for Epidemiological Studies Depression (CES-D) scale;
- slowness, based on time (in seconds) to walk 4.6 meters adjusted for sex and standing height;

- low physical activity level, measured by energy expenditure per week, as assessed by the short version of the Minnesota Leisure Time Physical Activity Questionnaire.

As previously proposed, individuals with 3 or more of these characteristics were classified as frail, those with 1 or 2 characteristics as prefrail, and those with 0 characteristics as nonfrail.[6]

Cognitive function assessment

Cognitive function was assessed using a two-stage screening strategy (sequential testing) in order to increase the accuracy of the assessment, favoring the specificity of the measure.[20] First, the Mini-Mental State Examination (MMSE) was applied to all participants.[21] Those who screened positive for cognitive impairment were subsequently administered a drawing test (Brief Cognitive Screening Battery — BCSB).[20] Participants were considered to be cognitively impaired only if they screened positive for cognitive impairment in both tests.[20] The following cut-off scores were used for the MMSE: 17/18 for illiterate older adults; 20/21 for those with 1 to 4 years of schooling; 23/24 for those with 5 to 8 years of schooling; and 25/26 for those with 9 or more years of schooling. In the BCSB, participants who scored 7 or less were considered to have screened positive for cognitive impairment.

The CDR was used to assess the severity of dementia.[18] This instrument is divided into 6 cognitive-behavioral domains: memory; orientation; judgment and problem-solving; community affairs; home and hobbies; and personal care. Each of the 6 domains was rated as follows:

- 0 (none);
- 0.5 (questionable);
- 1 (mild dementia);
- 2 (moderate dementia);
- 3 (severe dementia), except for the personal care domain, which does not have the 0.5 level.

The global CDR score was derived from individual ratings in each domain, following a set of rules developed and validated by Morris et al.[18] Therefore, based on the final CDR score, older adults with cognitive impairment were categorized into 1 of 4 groups:

- questionable (CDR = 0.5);
- mild (CDR = 1);
- moderate (CDR = 2);
- severe (CDR = 3).[18]

Older adults were classified according to the stages of dementia severity by consensus between two researchers who had received previous training in the application of the CDR and were certified by the Alzheimer's Disease Research Center, Washington University, St. Louis.

Evaluation of sociodemographic and clinical characteristics

The sociodemographic characteristics included age, sex, education (years of schooling), marital status (married, single, separated/divorced, or widow/widower), and monthly income.

Nutritional status was measured and classified based on the BMI, according to the cut-off points recommended for older adults: those with BMI < 22 kg/m^2 were categorized as underweight; 22 kg/m^2 ≤ BMI ≥ 27 kg/m^2 as normal weight; and BMI > 27 kg/m^2 as overweight.

Medical conditions in the past 12 months were investigated and recorded. We investigated the occurrence of hospitalization, falls, the number of regularly used medications, the number of medical appointments, difficulty swallowing, and choking when eating or drinking.

To identify the presence of comorbidities and diseases, participants were asked whether they had a medical diagnosis of heart disease, hypertension, stroke, diabetes, cancer, rheumatic disease, pulmonary disease, osteoporosis, neurological disease, urinary incontinence, or fecal incontinence. The Cornell Scale for Depression in Dementia (CSDD) was used to assess depressive symptoms.

Procedures

In this cohort study, two assessments were performed: at baseline and at 12-month follow-up. For the assessment of older adults with cognitive impairment, the data were obtained from the participant's primary caregiver.

Older adults with cognitive impairment were considered to be transitioning to frailty if they were not frail (prefrail and nonfrail states) at baseline but were classified as frail after 12 months.

Statistical analysis

Descriptive statistics were used to characterize the sample and compare the groups. Nonfrail, prefrail and frail older adults were compared for sociodemographic characteristics and health status using Pearson's χ^2 test or Fisher's exact test for continuous variables and the F-test (ANOVA) or Kruskal-Wallis test for continuous variables. The Shapiro-Wilk test was used to determine the normality of data distribution. The R software, version 2.7.1 (R Foundation for Statistical Computing, New Zealand), and Epi Info, version

6.04 (Centers for Disease Control and Prevention, Atlanta, USA), were used to perform the analyses. The level of significance was set at 0.05.

RESULTS

Of 59 older adults who screened positive for cognitive impairment at baseline, 47.5% were classified as frail (n = 28), 47.5% as prefrail (n = 28), and only 5% as nonfrail (n = 3) (Table 1). The groups did not differ in age, sex, education, marital status, monthly income, MMSE score, nutritional status, number of comorbidities, loss of appetite, difficulty swallowing, choking, falls, depression screening, number of medications, hospitalization in the past year, or number of medical appointments ($p > 0.05$). The participants' sociodemographic characteristics and health status are shown in Table 1.

During 12 months of follow-up, 8 participants died. Of these, 6 were classified as frail and 2 as prefrail at baseline. Four participants were lost to follow-up, because

Table 1 Sociodemographic characteristics and health status of older adults with cognitive impairment.

Variable	Nonfrail	Prefrail	Frail	p-value
	n (%) or mean ± SD	n (%) or mean ± SD	n (%) or mean ± SD	
Total	n = 3 (5.0)	n = 28 (47.5)	n = 28 (47.5)	
Age (years)	82.67 ± 3.51	80.57 ± 9.25	82.79 ± 6.4	0.887
Women	3 (100)	23 (82.1)	20 (71.4)	0.401
Education (years)	1.33 ± 2.3	2.54 ± 2.65	1.78 ± 1.95	0.399
Marital status — widow(er)	3 (100)	10 (57.1)	15 (53.6)	0.795
Monthly income	290 ± 31.23	300.0 ± 169.90	324.95 ± 157.37	0.224
MMSE	13.0 ± 13.60	13.57 ± 3.99	13.68 ± 4.15	0.962
BMI				
Normal weight (22–27 kg/m^2)	3 (100)	9 (32.1)	11 (39.3)	0.252
Underweight (< 22 kg/m^2)	–	10 (35.7)	8 (28.6)	
Overweight (> 27 kg/m^2)	–	9 (32.1)	9 (32.1)	
Number of comorbidities	3.0 ± 1.0	2.96 ± 1.58	3.07 ± 1.63	0.968
Loss of appetite	3 (100)	15 (53.6)	16 (57.1)	0.302
Difficulty swallowing	7 (25)	4 (14.3)	–	0.410
Choking	11 (39.3)	10 (35.7)	1 (33.3)	0.952
Falls	1 (33.3)	12 (42.9)	17 (60.7)	0.337
CSDD	6.33 ± 4.9	7.04 ± 6.4	10.04 ± 7.67	0.249
Number of medications (min–max)	5.67 ± 1.53 (4–7)	4.04 ± 2.24 (1–8)	4.86 ± 1.51 (2–7)	0.158
Hospitalization	1 (33.3)	5 (17.9)	7 (25.0)	0.722
Number of medical appointments (min–max)	7.0 ± 0.0 (7–7)	7.93 ± 6.45 (1–30)	8.82 ± 6.27 (0–30)	0.810
Dementia rating				
Questionable	1 (33.3)	11 (39.3)	7 (25.0)	0.556
Mild	2 (66.7)	9 (32.1)	11 (39.3)	
Moderate	–	8 (28.6)	10 (35.7)	

n: number; %: percentage; SD: standard deviation; MMSE: Mini-Mental State Examination; BMI: body mass index; CSDD: Cornell Scale for Depression in Dementia; min: minimum; max: maximum.

we were unable to locate them. Of these, 1 was classified as nonfrail, 1 as prefrail, and 2 as frail at baseline. Therefore, 47 older adults with cognitive impairment completed the 12-month follow-up and were reassessed. Regarding transitions between frailty states, 9 participants (33.3%) transitioned from prefrail to frail after 12 months. No transition from nonfrail to frail was observed during the follow-up period.

DISCUSSION

This cohort study evaluated community-dwelling older adults and found a high prevalence of frailty and prefrailty among older adults with cognitive impairment, as well as a transition to frailty in 33.3% of the sample within 12 months of follow-up. The prevalence of both frailty and prefrailty was 47.5%; therefore, only a small proportion of older adults with cognitive impairment was classified as nonfrail (5%).

In population-based surveys, the estimated prevalence of frailty ranges from 5.8 to 27.3%.[22] Therefore, our data indicate that the prevalence of frailty in a population of cognitively impaired older adults is considerably higher than that in older adults without cognitive impairment. The present findings are supported by previous studies that have also identified a higher proportion of frail and prefrail older adults among individuals with cognitive impairment.[11,12]

Some studies suggest the existence of a biological association between frailty and cognitive impairment.[7,12,13,23] Thus, frailty and cognitive impairment appear to share common pathophysiological mechanisms that, in many cases, allow them to coexist.[7,12,13,23] The hypotheses of shared pathophysiological mechanisms are based on the fact that both frailty and cognitive impairment involve mechanisms of inflammatory activation and neuroendocrine dysregulation.[7,12,13,23] However, frailty and cognitive impairment are complex conditions in which other factors may be involved in their onset and course.

Approximately one-third of the older adults who were classified as not frail at baseline became frail after 12 months of follow-up, while all older adults who transitioned to frailty had been classified as prefrail at baseline. None of the nonfrail older adults became frail after 12 months, and none of the frail participants transitioned from a state of greater to lesser frailty.

However, population-based studies evaluating transitions between frailty states over time have found that transitions occur in both directions, worsening and improvement.[1,14,24-27] Also, frailty is a dynamic process with transitions in both directions even within a short period of time, such as 12 months.[1] These studies have shown that a higher proportion of patients transition to states of greater frailty than to states of lesser frailty.[1,14,24-27] Alencar et al.,[1] in a 12-month cohort study of older adults, found that 24.2% of participants transitioned to states of greater frailty, while 12.6% transitioned to states of lesser frailty. Li et al.,[24] over a 3-year follow-up period, reported that 34% of participants progressed to a more-frail status, while 20% showed improved transitions. Studies have reported that cognitively impaired older adults transition more often to the frail state than those without cognitive impairment.[14,16,28] In addition, frailty and cognitive impairment are associated with an increased risk of adverse health outcomes, especially when they coexist.[13] The combination of frailty and cognitive impairment appears to exacerbate the vulnerability of the individual, playing a role in the subsequent transition to a state of greater frailty.[13,23] Li et al.[24] found that transitions to a worsened state of frailty within a short period of time are associated with an increased risk of mortality over the following years. Therefore, further studies are needed to investigate the relationship between cognitive impairment and frailty as well as possible factors associated with such declines.

Over a 12-month follow-up period, mortality was higher for frail older adults with cognitive impairment (n = 6; 21.4%) than for prefrail (n = 2; 7.2%) and nonfrail (n = 0; 0%) participants. Previous studies have also found higher mortality in frail older adults with cognitive impairment.[11,12,29] Jacobs et al.[12] found that 5-year mortality was higher for community-dwelling frail older adults with cognitive impairment, while Aprahamian et al.[11] found that the presence of cognitive impairment increased the risk of death within 1 year for frail older adults admitted to a geriatric day-hospital. St John et al.,[29] evaluating a cohort of community-dwelling older adults, found that the hazard ratio for 5-year mortality was 2.28 (95% confidence interval [95%CI] 1.17–3.09) for those who were frail and cognitively impaired and 1.81 (95%CI 1.35–2.41) for those who were frail but cognitively intact.

Increased mortality rates have been reported for older adults with cognitive impairment, especially for those with more severe dementia, regardless of physical frailty.[30] Older adults with moderate to severe cognitive impairment are more likely to have multiple comorbidities, functional limitations, poorer nutritional status, and increased risk of complications, such as falls and clinical deterioration.[30] However, in the present study, although the sample consisted only of older adults with questionable (CDR = 0.5) to moderate (CDR = 2) cognitive

impairment, mortality was higher in the frail group than in the nonfrail and prefrail groups. These findings highlight the importance of screening and identifying frailty in individuals with cognitive impairment.

The present study demonstrated that transitions to a worsened state of frailty and mortality can occur even within a short period of time, such as 12 months. That is, cognitively impaired older adults can become more vulnerable and less resistant to stressors within 1 year.

A possible limitation of this study is that we did not investigate the underlying diseases or conditions associated with cognitive impairment in our cohort, since different conditions may result in heterogeneous rates of progression to cognitive impairment and, consequently, to frailty. Another possible limitation is that our study population was recruited from a center that provides specialized geriatric care. Therefore, older patients cared for in the center have been previously identified as requiring specialized treatment with a multidisciplinary team.

Increased frailty and mortality among cognitively impaired older adults within a short period of time is of considerable clinical and public health importance, since these findings indicate a need for prevention and health promotion strategies for older adults with cognitive impairment.

CONCLUSION

The present study showed a high prevalence of frailty in older adults with cognitive impairment and, within 12 months, new cases of frailty were identified in this population. Therefore, more research is needed to further investigate the relationship between cognitive decline and frailty.

CONFLICT OF INTERESTS

The authors declare no conflict of interests.

REFERENCES

1 Alencar MA, Dias JMD, Figueiredo LC, Dias RC. Transitions in frailty status in community-dwelling older adults. Top Geriatr Rehabil. 2015;31(2):105-12. https://doi.org/10.1097/TGR.0000000000000055

2. Crews DE, Zavotka S. Aging, disability and frailty: implications for universal design. J Physiol Anthropol. 2006;25(1):113-8.

3. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. Lancet. 2013;381(9868):752-62. https://doi.org/10.1016/S0140-6736(12)62167-9

4. Collard RM, Boter H, Schoevers RA, Oude Voshaar RC. Prevalence of frailty in community-dwelling older persons: a systematic review. J Am Geriatr Soc. 2012;60(8):1487-92. https://doi.org/10.1111/j.1532-5415.2012.04054.x

5. Morley JE, Vellas B, van Kan GA, Anker SD, Bauer JM, Bernabei R, et al. Frailty consensus: a call to action. J Am Med Dir Assoc. 2013;14(6):392-7. https://dx.doi.org/10.1016%2Fj.jamda.2013.03.022

6. Fried LP, Tangen C, Walston J, Newman A, Hirsch C, Gottdiener J, et al. Frailty in older adults: Evidence for a phenotype. J Gerontol. 2001;56A(3):M146-56.

7. Aubertin-Leheudre M, Woods AJ, Anton S, Cohen R, Pahor M. Frailty Clinical Phenotype: A Physical and Cognitive Point of View. Nestle Nutr Inst Workshop Ser. 2015;83:55-63. https://doi.org/10.1159/000382061

8. Harmand M, Meilon C, Bergua V, Tabue Teguo M, Dartigues JF, Avila-Funes JA, et al. Comparing the predictive value of three definitions of frailty: Results from the Three-City study. Arch Gerontol Geriatr. 2017;72:153-63. https://doi.org/10.1016/j.archger.2017.06.005

9. Lahousse L, Maes B, Ziere G, Loth DW, Verlinden VJA, Zillikens MC, et al. Adverse outcomes of frailty in the elderly: the Rotterdam Study. Eur J Epidemiol. 2014;29:419-27. https://doi.org/10.1007/s10654-014-9924-1

10. Lang PO, Michel JP, Zekry D. Frailty syndrome: a transitional state in a dynamic process. Gerontology. 2009;55(5):539-49. https://doi.org/10.1159/000211949

11. Aprahamian I, Suemoto CK, Aliberti MJR, Queiroz Fontes Filho S, Araújo Melo J, Lin SM, et al. Frailty and cognitive status evaluation can better predict mortality in older adults? Arch Gerontol Geriatr. 2018;77:51-6. https://doi.org/10.1016/j.archger.2018.04.005

12. Jacobs JM, Cohen A, Ein-Mor E, Maaravi Y, Stessman J. Frailty, cognitive impairment and mortality among the oldest old. J Nutr Health Aging. 2011;15(8):678-82.

13. Avila-Funes JA, Amieva H, Barberger-Gateau P, Le Goff M, Raoux N, Ritchie K, et al. Cognitive impairment improves the predictive validity of the phenotype of frailty for adverse health outcomes: the three-city study. J Am Geriatr Soc. 2009;57(3):453-61. https://doi.org/10.1111/j.1532-5415.2008.02136.x

14. Ottenbacher KJ, Graham JE, Al Snih S, Raji M, Samper-Ternent R, Ostir GV, et al. Mexican Americans and frailty: findings from the Hispanic established populations epidemiologic studies of the elderly. Am J Public Health. 2009;99(4):673-9. https://doi.org/10.2105/AJPH.2008.143958

15. Woods AJ, Cohen RA, Pahor M. Cognitive frailty: frontiers and challenges. J Nutr Health Aging. 2013;17(9):741-3. https://dx.doi.org/10.1007%2Fs12603-013-0398-8

16. Raji MA, Al Snih S, Ostir GV, Markides KS, Ottenbacher KJ. Cognitive status and future risk of frailty in older Mexican Americans. J Gerontol A Biol Sci Med Sci. 2010;65(11):1228-34. https://doi.org/10.1093/gerona/glq121

17. Samper-Ternent R, Al Snih S, Raji MA, Markides KS, Ottenbacher KJ. Relationship between frailty and cognitive decline in older Mexican Americans. J Am Geriatr Soc. 2008;56(10):1845-52. https://dx.doi.org/10.1111%2Fj.1532-5415.2008.01947.x

18. Morris JC, Storandt M, Miller JP, McKell DW, Price JL, Rubin EH, et al. Mild cognitive impairment represents early-stage Alzheimer disease. Arch Neurol. 2001;58(3):397-405.

19. Alencar MA, Dias JMD, Figueiredo LC, Dias RC. Handgrip strength in elderly with dementia: study of reliability. Rev Bras Fisioter. 2012;16(6):510-4.

20. Nitrini R, Caramelli P, Herrera Júnior E, Porto CS, Charchat-Fichman H, Carthery MT, et al. Performance of illiterate and literate nondemented elderly subjects in two tests of long-term memory. J Int Neuropsychol Soc. 2004;10:634-8. https://doi.org/10.1017/S1355617704104062

21. Folstein MF, Folstein SE, McHugh PR. Mini-mental state. A practical method for grading the cognitive state of patients for clinician. J Psychiatric Research. 1975;12(3):189-98.
22. Santos-Eggimann B, Cuénoud P, Spagnoli J, Junod J. Prevalence of Frailty in Middle-Aged and Older Community-Dwelling Europeans Living in 10 Countries. J Gerontol A Biol Sci Med Sci. 2009;64(6):675-81. https://doi.org/10.1093/gerona/glp012
23. Boyle PA, Buchman AS, Wilson RS, Leurgans SE, Bennett DA. Physical frailty is associated with incident mild cognitive impairment in community-based older persons. J Am Geriatr Soc. 2010;58(2):248-55. https://doi.org/10.1111/j.1532-5415.2009.02671.x
24. Li CY, Al Snih S, Karmarkar A, Markides KS, Ottenbacher KJ. Early frailty transition predicts 15-year mortality among nondisabled older Mexican Americans. Epidemiol. 2018;28(6):362-7. https://doi.org/10.1016/j.annepidem.2018.03.021
25. Gill TM, Gahbauer EA, Allore HG, Han L. Transitions between frailty states among community-living older persons. Arch Intern Med. 2006;166(4):418-23. https://doi.org/10.1001/archinte.166.4.418
26. Fallah N, Mitnitski A, Searle SD, Gahbauer EA, Gill TM, Rockwood K. Transitions in frailty status in older adults in relation to mobility: a multistate modeling approach employing a deficit count. J Am Geriatr Soc. 2011;59(3):524-9. https://doi.org/10.1111/j.1532-5415.2011.03300.x
27. Xue QL. The frailty syndrome: definition and natural history. Clin Geriatr Med. 2011;27(1):1-15. https://doi.org/10.1016/j.cger.2010.08.009
28. Lee JS, Auyeung TW, Leung J, Kwok T, Woo J. Transitions in frailty states among community-living older adults and their associated factors. J Am Med Dir Assoc. 2014;15:281-6. https://doi.org/10.1016/j.jamda.2013.12.002
29. St John PD, Tyas SL, Griffith LE, Menec V. The cumulative effect of frailty and cognition on mortality – results of a prospective cohort study. Int Psychogeriatr. 2017;29(4):535-43. https://doi.org/10.1017/S1041610216002088
30. Fogg C, Meredith P, Bridges J, Gould GP, Griffiths P. The relationship between cognitive impairment, mortality and discharge characteristics in a large cohort of older adults with unscheduled admissions to an acute hospital: A retrospective observational study. Age Ageing. 2017;46(5):794-801. https://doi.org/10.1093/ageing/afx022