THE JOURNAL OF LATIN AMERICAN GERIATRIC MEDICINE ORIGINAL ARTICLE

Risk factors for frailty syndrome in the Costa Rican population

José E. Picado-Ovares[1,2]*, Isabel C. Barrientos-Calvo[1,2], Fernando Morales-Martínez[1,2] and Alejandro Sandí-Jirón

[1]Hospital Nacional de Geriatría y Gerontología; [2]Universidad de Costa Rica, San Pedro. San José, Costa Rica.

Abstract

Objective: *The objective of this study was to identify the health risk factors related with the onset of frailty in the Costa Rican population.* **Methods:** *A subgroup of 3000 people from the CRELES study was analyzed. A frailty phenotype was constructed based on the variables of the phenotypic model: weight loss, exhaustion, weakness, slowness, and low level of physical activity. Patients were classified into frail, pre-frail, and robust. A multinomial logistic model was used, which included data from the 3 years of study (2205, 2007, and 2009). An exploratory analysis was made, using sociodemographic and health variables. Taking as reference the robust category, the odds ratio was obtained for the frail and pre-frail categories, with 95% confidence.* **Results:** *Of the analyzed variables, age, osteoarthritis, and living alone proved to be risk factors with statistical significance.* **Conclusions:** *In the Costa Rican population, age, osteoarthritis, and living alone represent risk factors for suffering frailty in the future.*

Key words: *Frailty. Risk factors. Elderly. Incidence.*

Corresponding author: *José Ernesto Picado-Ovares, jepicado@ccss.sa.cr*

INTRODUCTION

Between 2000 and 2050, the number of inhabitants on earth aged 60 years or older will double. A considerable number of them will have an elevated risk of becoming frail[1]. Frailty is considered a clinical state in which there is an increase in an individual's vulnerability for developing increased dependency and/or mortality when exposed to a stressor[2,3].

Although the operational definition of frailty is controversial, two approaches to defining frailty are widely accepted[3]. The deficit model, which consists of adding an individual's number of impairments and conditions to create a frailty index, and the second model, the phenotype model, which describes frailty as a clinical syndrome resulting from a combination of variables, such as weight loss, fatigue, weakness, diminished gait speed, and poor physical activity that reflects an underlying physiologic state of multisystem dysregulation[2,4].

Multiple population studies have shown the relationship between frailty and diverse conditions[5-7], and a few trials have been performed with Latin American populations and Central American populations[5].

The main goal of this study is to analyze the correlation of multiple health and sociodemographic variables and the risk of suffering from frailty in the future within the Costa Rican population.

MATERIALS AND METHODS

CRELES study

A longitudinal study design was established using The Costa Rican Longevity and Healthy Aging Study

Correspondence to:
*José Ernesto Picado-Ovares
Department of Geriatric Medicine
Hospital Nacional de Geriatría y Gerontología
San José, Costa Rica
E-mail: jepicado@ccss.sa.cr

(CRELES), which is a dataset of Costa Rican older adults born in or before 1946; it included a representative sample of ≥ 60-year-old adults from Costa Rica. A full description of sampling methods may be found elsewhere[8]. This study has three waves in which face-to-face interviews were conducted by trained and standardized staff at the homes of older adults including in-depth data collection on demographics, current activities, health-related issues, social support, health-care use, financial status, functionality, cognitive status, anthropometry, and blood sampling. The analysis of the present study was performed using a cohort of 2827 elderly people, 60 years and older, beginning in 2005, with follow-ups in 2007 and 2009.

Construction of the frailty variable

A frailty indicator was constructed based on the five variables from Fried's phenotype model[4], with certain modifications. The variables were built as follows:

- Weakness: To measure this variable, a grip strength test performed with a dynamometer in the CRELES study was used. The elderly individual was asked to extend his or her dominant arm to full length alongside his or her body, and when instructed by the interviewer, the person was to grip the handle with all their strength and immediately loosen the grip. Then, he or she would rest for 3 min, repeating the test for the second time. The result of the second grip strength test was used for this study. This variable was registered in the anthropometric questionnaire.

A regression model was calculated in which hand strength was the dependent variable and the independent variables were sex and body mass index. Then, the residual values were added to the adjusted average value to create a standardized grip strength variable. The 20th percentile was calculated, resulting in a cutoff value. The patient was considered to have an altered grip strength test if his or her result was below the 20th percentile or could not perform the test at all.

- Slowness: To determine this variable, information obtained from questions in the CRELES anthropometric chapter was considered. Gait speed measured the capacity and time necessary to perform the stand-up and walk test. This test consisted of asking the person to stand-up from a chair and walk at his or her usual rhythm for a distance of 3 m. This distance is divided by the elapsed time, resulting in the speed of the elderly individual. Afterward, the regression model was adjusted, where the dependent variable was the calculated speed and the independent variables were height and sex, obtained from the CRELES database. The predicted values were calculated, and an average value was obtained. The residual values were added to this average value, which results in a new speed variable from which the 20th percentile was calculated.

A decreased gait speed was considered if one of the following conditions was present: the patient had a gait speed lower than the 20th percentile value, or the person could not do the test at all, or if the person answered affirmatively to the question: "Do you have a problem that prevents you from doing any mobility or flexibility test?"

- Low level of physical activity: For this variable, the answer for the question "In the past 12 months, have you had regular exercise or rigorous physical activity such as sports, trotting, dancing, or heavy workloads 3 times a week?" Was used. The variable was taken as is from the CRELES study, and it was considered altered if there was no physical activity.
- Exhaustion or poor endurance: The answer to the question "Were you full of energy?" From the CRELES study was used for this variable. The variable was considered altered if the elderly responded that they felt they had no energy whatsoever.
- Weight loss: For this variable, the answer to the question, "In the past 6 months, have you lost > 5 kg of weight without planning it?" Was used. If the patient answered affirmatively, the variable was considered altered and was incorporated the frailty syndrome.

Once the five variables were defined, they were codified as 1 if they met the frailty criteria on a particular variable, and 0 if the criteria were not met. A classification of robust was given to those who did not present altered variables on any of the five variables analyzed (which translates to a total sum of 0 for all variables), a classification of pre-frail for those who presented one or two altered variables, and a classification of frail to those who presented three to five altered variables. It is worth mentioning that if any values were missing, the individual was not included, as there was a strict method to prevent biases for this categorization. This methodology was also used for the cohort follow-up years of 2005, 2007, and 2009.

With the goal of investigating possible risk factors for the frailty condition, an incidence analysis was

Table 1. Costa Rica: Results of the prevalence and incidence model for frailty according to sociodemographic indicators

Health and sociodemographic characteristics	Prevalence‡				Incidence§			
	Pre-frail		Frail		Pre-frail		Frail	
	OR	CI	OR	CI	OR	CI	OR	CI
Age								
80+	4.86	2.07; 9.06*	20.77	10.23; 42.15*	4.12	1.07;15.86*	18.69	1.89; 184.72*
70-79	1.69	1.31; 2.18*	2.25	1.51; 3.35*	1.46	0.89; 2.39	2.33	0.59; 9.22
Education level								
≤ 6th grade	2.09	1.53; 2.84*	1.77	1.00; 3.16	-	-	-	-
7-9th grade	1.83	1.19; 2.80*	1.64	0.74; 3.62	-	-	-	-
≥ 10th grade†	-	-	-	-	-	-	-	-
Sex								
Woman	1.15	0.88; 1.51	0.70	0.46; 1.08	1.34	0.78; 2.31	4.06	0.78; 21.17
Live alone								
Yes	1.17	0.78; 1.75	1.59	0.90; 2.79	1.43	0.55; 3.75	6.91	1.36; 35.20*
Health self-perception No healthy	2.34	1.82; 3.01*	5.60	3.78; 8.30*	2.00	1.11; 3.60	0.21	0.03; 1.37
Income								
≤ 100 US dollars	0.98	0.71; 1.34	1.23	0.75; 2.03	0.59	0.31; 1.12	1.62	0.31; 8.40
100-250 US dollars	1.01	0.75; 1.37	0.78	0.47; 1.28	1.01	0.55; 1.87	3.72	0.73; 18.87
≥ 250 US dollars†	-	-	-	-	-	-	-	-

*p < 0.05.
†category of reference.
‡model taking into account data of the year 2005.
§data of 2005, 2007, and 2009 are included.
CI: confidence interval at 95%; OR: odds ratio.

performed. For that analysis, data from the three follow-up years of the elderly cohort (2005, 2007, and 2009) were used. For this analysis, a multinomial logistic model was used, including data for those 3 years, as well as the elderly identifier. The frailty indicator for the study years was used as the dependent variable, divided into frail, pre-frail, and robust. As inclusion criteria for independent variables, the study focused on an exploratory analysis in which a widespread quantity of variables in the health and sociodemographic fields was considered based on expert judgment. Specifically, the included variables were obtained from the elderly questionnaire, Section C (health status) from CRELES, related to detected health conditions by the physician. Other socioeconomic factors were obtained from the same questionnaire from the section regarding personal identification data, as well as the employment and income sections. Variables that presented difficulties for model convergence were not included, nor were variables with missing information within their categories.

As a result, odds ratio for the frail and pre-frail categories was obtained, and the robust category was taken as reference, as it was considered the healthiest among the three categories. To compare relevance and possible error in the OR estimation with 95% confidence, intervals were created for each variable of interest.

RESULTS

For the year 2005 (base year for the study), after application of the inclusion criteria mentioned above, an initial base sample consisting of 2827 patients was used. Afterward, this sample was reduced for the years 2007 (n = 2364) and 2009 (n = 1863). During this period, a total of 964 cases were lost; a total of 525 due to death and 439 because it was impossible to contact the individual for follow-ups.

For the base year 2005, the final analysis shows a prevalence of frailty in the elderly population of 11%. The general characteristics of the frail patient in Costa Rica were analyzed in a previous publication[7].

Of the variables analyzed, only three proved to be statistically significant risk factors. These variables were age (OR 18.6, CI 1.89; 184.73), presence

Table 2. Costa Rica: Results of the prevalence and incidence model for frailty according to health and comorbidities indicators

Variable	Prevalence†				Incidence‡			
	Pre-frail		Frail		Pre-frail		Frail	
	OR	CI	OR	CI	OR	CI	OR	CI
Hypertension								
Yes	1.01	0.80; 1.27	1.52	1.04; 2.20*	1.31	0.85; 2.12	1.09	0.30 3.98
Cholesterol								
Yes	0.94	0.75; 1.20	0.64	0.44; 0.93*	0.78	0.48; 1.27	1.38	0.38; 5.06
Diabetes								
Yes	1.50	1.10; 2.03*	2.47	1.61; 3.79*	1.04	0.56; 1.94	3.74	0.63; 22.1
Cancer								
Yes	1.99	1.06; 3.76*	2.12	0.92; 4.88	-	-	-	-
Pulmonary disease								
Yes	1.62	1.16; 2.26*	1.82	1.14; 2.92*	0.49	0.21; 1.80	2.46	0.34; 17.9
Heart attack								
Yes	0.78	0.45; 1.37	0.55	0.24; 1.28	-	-	-	-
Cerebrovascular event						-		
Yes	2.87	0.77; 10.71	20.90	5.31; 82.33*	-		-	-
Arthritis								
Yes	1.48	1.01; 2.17*	3.19	1.95; 5.22*	0.77	0.29; 2.04	5.46	1.08; 27.7*
Osteoporosis								
Yes	1.43	0.91 ; 2.25	1.88	1.02; 3.46*	-	-	-	-
Smoking								
Yes	0.90	0.70; 1.16	0.83	0.55; 1.24	0.91	0.54; 1.53	1.88	0.39; 9.09
Falls								
Yes	0.86	0.69; 1.08	1.03	0.72; 1.47	0.87	0.511; 1.48	0.73	0.18; 3.03

*p < 0.05.
†model taking into account data of the year 2005.
‡data of 2005, 2007, and 2009 are included.
CI: confidence interval at 95%; OR: odds ratio

of osteoarthritis (OR 5.46 CI 1.076; 27.65), and living alone (OR 6.9 CI 1.36; 35.2).

Other variables, such as hypertension, diabetes mellitus, dyslipidemia, cancer, lung disease, osteoporosis, heart failure, strokes, smoking, falls, educational level, income, and health self-perception, did not show any significant association in this model (Tables 1 and 2).

DISCUSSION

In this study, age was shown to be a risk factor for the presence of frailty. Patients 80 years of age or older presented an increased risk for becoming frail. Furthermore, age 80 and above proved to be a risk factor for presenting a pre-frail condition when compared to the robust patients (OR 4.12 CI 1.07; 15.9).

This result was similar to multiple publications that have documented that age, per se, is a risk factor for the frail condition[7,9-11]. Various mechanisms can be mention as contributors, mainly the oxidative stress associated with aging and secondary cellular damage that triggers multiorgan and system failure, possibly resulting in vulnerability and decreased physiological reserves[12,13].

Although age as a risk factor for frailty is not a new concept in other parts of the world, this is the first study performed in a Central American location showing this correlation and is one of the few longitudinal studies in Latin America[5,14,15].

This study was also able to determine that osteoarthritis is a risk factor for the presence of frailty in the Costa Rican population. After adjusting for this variable, an increased risk for suffering frailty was documented. The risk was greater than what has been presented in other similar studies[14].

The association between frailty and arthritis has been documented in other cohorts and longitudinal studies previously performed[7,16]. Fried's study has already documented a link between self-reported

arthritis and frailty[4]. This finding has been reproduced in similar studies[17], including in a Latin American population cohort[7,18], as well as in longitudinal studies[9].

The association between osteoarthritis and frailty is due to the limitation in physical activity secondary to pain. There have been reports of an increase in the incidence of frailty syndrome and the presence of secondary pain resulting from diseases such as osteoarthritis[19,20]. Pain may lead to a decrease in physical activity, immobility, fatigue, and sarcopenia.

The "living alone" variable in this study was a risk factor for the onset of frailty syndrome. Fried suggested a frailty model that includes a "vicious cycle" that comprises frailty, chronic malnutrition, sarcopenia, poor chronic disease control, symptoms of depression, and sedentarism[4], all of which are more prevalent in the elderly who live alone.

To the author's knowledge, this is the first longitudinal study that demonstrated this correlation. Other cohort studies showed the relationship between living alone and frailty[4,17,21], including one trial that presented this condition as a protective factor[10]. This result warrants future investigations that include this variable as a risk factor for the presence of frailty syndrome and identifying mechanisms to protect the elderly from the consequences involved.

Given the longitudinal nature of the CRELES study, the analysis performed in the three study years involved many cases (n = 964) that were lost due to death and other unknown causes. This mainly affected the last year of the cohort. Loss of data significantly affected the construction of the frailty variable in the years under study, as five variables were used during the time span, of which some presented problems regarding missing information, therefore, affecting the final elaboration of the frailty variable.

In addition, the variables of interest with regard to the frailty syndrome present certain problems during the 3 years of the study, resulting in problems in the construction of the incidence model, as cases must be matched across all years to allow its estimation.

The main consequence in this study can be observed in the uncertainty reflected in the wide confidence intervals for the variables analyzed. This was caused by some large odds ratio and errors in estimation, which were also wide, resulting from a significant reduction of the sample size for some variables, along with their great variability. Therefore, when interpreting the final sample with less available cases, caution should be exercised regarding the results obtained.

Another limitation present in the study was the fact that many of the variables being analyzed were based on self-report of comorbidities. Many of the questions were written in non-technical language, so interviewees could understand what they were asked.

Despite the study limitations, the results generated do represent the Costa Rican population. Furthermore, the criteria used for this study were more similar to Fried's original criteria when compared to previous studies at a national and international level, which provided more robust results than in other similar studies.

The weight that certain comorbidities have in the onset of the frailty syndrome in the Costa Rican elderly population was demonstrated, being to the author's knowledge, one of the few Latin American studies and the only one in Central America that truly analyses these factors, allowing visualization of this important condition in this area of the American continent. This allows us to assess the needs for future investigations in this area and to take preventive actions involving specific elderly groups to avoid frailty syndrome and its consequences.

CONCLUSIONS

At present, there is little information regarding the risk factors that lead to the onset of the frailty syndrome in the Latin American population and, specifically, in the Central American population. In the Costa Rican population, age, the presence of osteoarthritis, and living alone are risk factors for suffering this syndrome in the future. Other variables did not show this association.

REFERENCES

1. World Health Organization. World Report on Ageing and Health. Available from: http://www.apps.who.int/iris/bitstream/10665/186471/1/WHO_FWC_ALC_15.01_spa.pdf?ua=1. [Last accessed on 2017 Dec 10].
2. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K Frailty in elderly people. *Lancet. 2013;381:*752-62.
3. Morley JE, Vellas B, van Kan GA, et al. Frailty consensus: a call to action. J Am Med Dir Assoc. 2013;14:392-7.
4. 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:M146-56.
5. Pérez-Zepeda MU Cesari M García-Peña C. Predictive value of frailty indices for adverse outcomes in older adults. Rev Invest Clin. 2016; 68:92-8.
6. Romero RL, Abizanda SP. Frailty as a predictor of adverse episodes in epidemiologic studies: a systematic review. Span J Geriatr Gerontol Rev Esp Geriatr Gerontol. 2013;48:285.
7. Picado-Ovares J, Barrientos-Calvo I, Morales-Martinez F, et al. Frailty in the elderly population of Costa Rica. Jpn J Med. 2018;1:5.
8. Rosero-Bixby L, Xinia F, William HD. CRELES: costa Rican Longevity and Healthy Aging Study. Costa Rica, Ann Arbor, MI: Inter-University Consortium for Political and Social Research; 2005.

9. Ottenbacher KJ, Graham JE, Al Snih S, et al. Mexican Americans and frailty: findings from the Hispanic established populations epidemiologic studies of the elderly. Am J Public Health. 2009;99:673-9.
10. Woods NF, LaCroix AZ, Gray SL, et al. Frailty: emergence and consequences in women aged 65 and older in the women's health initiative observational study. J Am Geriatr Soc. 2005;53:1321-30.
11. Semba RD, Bartali B, Zhou J, et al. Low serum micronutrient concentrations predict frailty among older women living in the community. J Gerontol A Biol Sci Med Sci. 2006;61:594-9.
12. Mulero J, Zafrilla P, Martinez-Cacha A. Oxidative stress, frailty and cognitive decline. J Nutr Health Aging. 2011;15:756-60.
13. Cutler RG. Human longevity and aging: possible role of reactive oxygen species. Ann N Y Acad Sci 1991;621:1-28.
14. Serra-Prat M, Papiol M, Vico J, et al. Incidence and risk factors for frailty in the community-dwelling elderly population. A two-year follow-up cohort study. J Gerontol Geriatr Res 2017;6:452.
15. Da Mata FA, Pereira PP, Andrade KR, et al. Prevalence of frailty in Latin America and the Caribbean: a systematic review and meta-analysis. PLoS One. 2016;11:e0160019.
16. León-Muñoz LM, Guallar-Castillón P, López-García E, Rodríguez-Artalejo F. Mediterranean diet and risk of frailty in community-dwelling older adults. J Am Med Dir Assoc. 2014;15:899-903.
17. Chang YW, Chen WL, Lin FG, et al. Frailty and its impact on health-related quality of life: a cross-sectional study on elder community-dwelling preventive health service users. PLoS One. 2012;7:e38079.
18. Masel MC, Graham JE, Reistetter TA, Markides KS, Ottenbacher KJ. Frailty and health related quality of life in older Mexican Americans. Health Qual Life Outcomes. 2009;7:70.
19. Danon-Hersch N, Rodondi N, Spagnoli J, Santos-Eggimann B. Prefrailty and chronic morbidity in the youngest old: an insight from the Lausanne cohort lc65+. J Am Geriatr Soc. 2012;60:1687-94.
20. Serra-Prat M, Sist X, Saiz A, et al. Clinical and functional characterization of pre-frailty among elderly patients consulting in primary care centers. J Nutr Health Age. 2016;20:653-8.
21. Yamanashi H, Shimizu Y, Nelson M, et al. The association between living alone and frailty in a rural Japanese population: the Nagasaki Islands study. J Prim Health Care. 2015;7:269-73.