

Frailty: What phenotype criteria have the most influence on the occurrence of this syndrome in older people?

Fragilidade: Quais critérios do fenótipo mais influenciam na ocorrência dessa síndrome em pessoas idosas?

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ABSTRACT

Objective: determine the extent to which each criterion of the frailty phenotype (either alone or grouped) contributes to the emergence of the syndrome in older people. **Methods:** observational and analytical study was conducted with 219 male and female older people in outpatient care. The evaluation of frailty syndrome was based on the phenotype proposed by Fried *et al.*, the criteria of which are unintentional weight loss, self-reported fatigue, low grip strength, insufficient physical activity and slow gait. Multinomial logistic regression analysis was employed to evaluate the influence of each criterion of the phenotype alone or grouped. **Results:** a total of 219 individuals participated in the study. The most common frailty criterion was slowness in both frail and pre-frail individuals. Pre-frail individuals with slow gait were 9.42-fold more likely to become frail (OR = 9.42, 95%CI: 7.27-13.40, p = 0.001). The model with all five criteria explained 99.5% of frailty in the sample. **Conclusion:** slow gait was the most frequent frailty criterion in frail and pre-frail individuals. Therefore, this criterion seems to be the best predictor of frailty in older people and warrants close observation on the part of healthcare providers.

Keywords: aging; frail elderly; frailty; gait; phenotype; odds ratio.

RESUMO

Objetivo: determinar o quanto cada critério do fenótipo de fragilidade (isolado ou agrupado) contribui para o surgimento da síndrome em pessoas idosas. **Métodos:** estudo observacional e analítico realizado com 219 idosos, de ambos os sexos, em atendimento ambulatorial. A avaliação da síndrome da fragilidade foi baseada no fenótipo proposto por Fried *et al.*, cujos critérios são perda de peso não intencional, fadiga autorreferida, baixa força de preensão palmar, atividade física insuficiente e lentidão de marcha. A análise da regressão logística multinomial foi empregada para avaliar a influência de cada critério do fenótipo isolado ou agrupado. **Resultados:** um total de 219 indivíduos participaram do estudo. O critério mais comum foi a lentidão de marcha tanto em frágeis quanto em pré-frágeis. Indivíduos pré-frágeis com lentidão de marcha tiveram 9,42 vezes mais chances de se tornarem frágeis (OR = 9,42, IC95%: 7,27-13,40, p = 0,001). O modelo com todos os cinco critérios explicou 99,5% da fragilidade da amostra. **Conclusão:** a lentidão de marcha foi o critério mais frequente entre os indivíduos frágeis e pré-frágeis. Sendo assim, esse critério parece predizer melhor a fragilidade em pessoas idosas, merecendo uma observação minuciosa por parte dos profissionais da saúde.

Palavras-chave: envelhecimento; idoso fragilizado; fragilidade; marcha; fenótipo; razão de chances.

INTRODUCTION

Aging is associated with numerous challenges and comorbidities and frailty is considered one of the main syndromes that affect older people.¹ Frailty syndrome increases the likelihood of falls, fractures, dependence, hospitalization and premature death.^{2,3}

This syndrome is characterized by slow gait, involuntary weight loss, fatigue, low grip strength and low physical activity level⁴ as well as reductions in energy reserves, physical and adaptive abilities and cognition, leaving individuals vulnerable

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Recebido em 09/05/2023 - Aceito para publicação em 15/06/2023.



to adverse health outcomes, with a negative impact on quality of life as well as a significant increase in healthcare costs.⁵

Several methods are used for the evaluation of frailty. The phenotype proposed by Fried *et al.*⁶ is one of the most widely employed in scientific research throughout the world. This is a non-invasive, low-cost method capable of revealing manifestations of the cycle of frailty based on the evaluation of five criteria (unintentional weight loss, fatigue, low grip strength, slow gait and low physical activity level). Although not considered the “gold standard”, this phenotype has satisfactory validity demonstrated by associations with chronic comorbidities, advanced age, cognitive function and depressive symptoms and is a predictor of adverse health outcomes.⁷

Scientific studies suggest that early identification and treatment can reverse frailty.^{8,9} In the clinical practice of healthcare providers who work with older people, the evaluation of the criteria of the phenotype and the determination of which criteria require greater attention for a timely intervention could contribute to the prevention of the progression of this syndrome and its consequences.

The aim of the present study was to evaluate the contribution of each criterion separately and grouped to the occurrence of frailty syndrome.

MATERIALS AND METHODS

Study design and participants

Observational and analytical study was conducted with male and female older people (≥ 60 years of age based on the classification determined for developing countries) recruited from outpatient clinics at a university hospital in northeast Brazil. The sample was selected based on spontaneous demand and defined statistically by the comparison of proportions.

The inclusion criteria were age 60 or older, either sex, in outpatient care, the absence of cognitive impairment (score ≥ 17 point on the Mini Mental State Examination)¹⁰ and meeting the criteria for frailty or pre-frailty proposed by Fried *et al.*⁶ The exclusion criteria were locomotion difficulty, restriction to a wheelchair or amputation of upper or lower limbs due to the impossibility of performing the gait speed and grip strength tests.

Variables

A questionnaire was administered addressing the following sociodemographic characteristics: sex (male or female), age (in complete years), marital status (single, married, divorced or widowed), schooling (years of formal study), income (retirement pension, other sources of income) and self-reported comorbidities.

Assessment of frailty

Individuals with at least three of the five criteria proposed by Fried *et al.*⁶ described below were considered frail and those with one or two criteria were considered pre-frail.

Unintentional weight loss

This criterion was based on the participants answer to the following question: “Have you lost ≥ 4.5 kg or $\geq 5\%$ of your body weight unintentionally (without diet or exercise) in the past year?” Individuals who answered affirmatively were considered to have met this criterion.

Self-reported fatigue

This criterion was investigated by scores of three or four points on at least one of following two items from the depression scale of the Center for Epidemiological Studies (CES-D): “I felt that I had to make an effort to do habitual tasks” and “I could not get ‘going’ (14). The response options are scored on a Likert scale considering the previous week as reference (never or rarely = 1, some of the time = 2, most of the time = 3, always = 4).^{6,11}

Low grip strength

This criterion was measured using a handgrip dynamometer (Saehan, model SH5001) and recorded in kilogram-force (kgf) using the dominant hand with the forearm forming a 90° angle with the upper arm. Three trials were performed with a one-minute rest interval between trials and the average was calculated. Individuals with mean values below the 20th percentile of the distribution adjusted for sex and body mass index were considered to have met this criterion.

Insufficient physical activity

This criterion was investigated using the questionnaire for physical activity in older people validated by Rauchbach and Wendling,¹² which has 20 items divided among three domains: housekeeping activities (seven items), physical activities (seven items) and subsistence/social/leisure activities (six items). The score was converted for the following classification: inactive (0-32 points), infrequently active (33-82 points), moderately active (83-108 points), active (109-133 points) and very active (≥ 134 points). Individuals classified as inactive or infrequently active were considered to have met this criterion.

Slow gait

Gait speed was measured using a stopwatch to determine the time in seconds required to walk 4.6 meters. The cutoff points for the sample were determined by the 80th percentile of time adjusted for sex and height (in meters). Thus, individuals with whose times were among 20% longest in the distribution were considered to have met this criterion. Reference values: women with height ≤ 1.53 m – time up to 5.72 seconds; women with height > 1.53 m – time up to 5.63 seconds; men with height ≤ 1.70 m – time up to 5.31 seconds; men with height > 1.70 m – time up to 5.2 seconds.

Statistical methods

The data were analyzed with the aid of the Statistical Package for Social Sciences (SPSS version 25.0, SPSS Inc., Chicago, IL, USA) and entered twice by different researchers to avoid possible errors. The Kolmogorov-Smirnov test revealed that all continuous variables had normal distribution. Pearson’s chi-squared test was used to evaluate associations



between qualitative variables. The frequency of each frailty criterion in the sample was calculated.

Multinomial logistic regression analysis was used to investigate the influence of each criterion of the frailty phenotype. Three multinomial logistic regressions were run for combinations of criteria. The first grouped unintentional weight loss and fatigue. The second grouped low physical activity level, low grip strength and slowness. The third grouped all five criteria. The strength of the associations between variables was expressed as odds ratios (OR) and respective 95% confidence intervals (CI). The level of significance for the rejection of the null hypotheses was set at 5% ($p < 0.05$) for all statistical tests.

Ethical aspects

This study received approval from the human research ethics committee (CAAE: 50159615.7.0000.5207, 2015).

RESULTS

The sample was composed of 219 participants, with a predominance of women (61.2%), the 60-to-69-year-old age group (45.7%), married individuals (43.4%), four to seven years of schooling (45.7%), an income per capita of two times the monthly minimum wage (48%) and less than three morbidities (62.1%). The prevalence of frailty was 44.8%. Significant differences between frail and pre-frail individuals were found for age group, schooling and number of comorbidities (Table 1). Among the frailty criteria, slowness was the most frequent in the overall sample (67.5%) as well as in the prefrail (44.6%) and frail (95.9%) groups (Table 2).

Table 1. Sociodemographic characteristics of frail and pre-frail older people in outpatient care at a university hospital in northeast Brazil.

Sociodemographic characteristics	Frailty status		Total sample n (%)	p*
	Frail n (%) ^Δ	Pre-frail n (%) ^Δ		
Sex				
Female	61 (27.9%)	73 (33.3%)	134 (61.2%)	0.881
Male	37 (16.9%)	48 (21.9%)	85 (38.8%)	
Age group				
60 to 69 years	37 (16.9%)	63 (28.8%)	100 (45.7%)	0.017**
70 to 79 years	40 (18.3%)	47 (21.4%)	87 (39.7%)	
80 years or older	21 (9.6%)	11 (5.0%)	32 (14.6%)	
Marital status				
Single	14 (6.4%)	16 (7.3%)	30 (13.7%)	0.272
Married	38 (17.4%)	57 (26.0%)	95 (43.4%)	
Separated	3 (1.4%)	16 (7.3%)	19 (8.7%)	
Widowed	43 (19.6%)	32 (14.6%)	75 (34.2%)	
Schooling				
0 to 3 years of study	50 (22.8%)	39 (17.8%)	89 (40.6%)	0.008**
4 to 7 years of study	40 (18.3%)	60 (27.4%)	100 (45.7%)	
≥ 7 years of study	8 (3.7%)	22 (10%)	30 (13.7%)	
Income <i>per capita</i>				
Up to monthly minimum wage	41 (18.7%)	40 (18.3%)	81 (37%)	0.073**
2 x monthly minimum wage	48 (22%)	57 (26%)	105 (48%)	
≥ 3 x monthly minimum wage	9 (4.1%)	24 (10.9%)	33 (15%)	
Morbidities				
0 to 3	47 (21.5%)	89 (40.6%)	136 (62.1%)	0.000
> 3	51 (23.3%)	32 (14.6%)	83 (37.9%)	

* chi-squared test ** linear trend chi-squared test

^Δ Percentages of all variables in “frailty status” column calculated in relation to value of overall sample (n = 219).



Table 2. Frequency of frailty phenotype criteria in frail and pre-frail older people in outpatient care at a university hospital in northeast Brazil.

Frailty phenotype criteria	Frail (n = 98)	Pre-frail (n = 121)
	n (%)	n (%)
↓ Gait speed	94 (95.9)	54 (44.6)
Fatigue	75 (76.5)	51 (42.1)
↓ Physical activity level	72 (73.5)	32 (26.4)
Unintentional weight loss	66 (67.3)	31 (25.6)
↓ Grip strength	56 (57.1)	23(19.0)

Slowness ($R^2 = 0.41$), fatigue ($R^2 = 0.36$) and low physical activity level ($R^2 = 0.31$) were the criteria that separately had the highest explanatory power for frailty in the individual model.

Pre-frail individuals with slow gait were 9.42-fold more likely to become frail (OR = 9.42, 95%CI: 7.27-13.40, $p = 0.001$) (Table 3).

Table 3. Influence of each frailty criterion on the development of the syndrome in frail and pre-frail older people in outpatient care at a university hospital in northeast Brazil.

Frailty criteria	R^2	OR	95%CI	p^*
↓ Gait speed	0.41	9.42	7.27-13.40	0.001
Fatigue	0.36	1.81	1.11-3.43	0.001
↓ Physical activity level	0.31	1.53	1.09-3.74	0.001
Unintentional weight loss	0.22	2.43	2.27-3.94	0.001
↓ Grip strength	0.21	1.34	1.17-3.77	0.001

The criteria were grouped differently depending on frailty status, as pre-frail individuals met only one or two criteria. Alternative models were run with the criteria with the highest and lowest individual odds ratios. The model with slow gait, low physical activity level and low grip strength

explained 78.9% of the frailty in the sample and slowness was the criterion that determined the greatest likelihood of a pre-frail individual becoming frail (OR = 17.55, 95%CI: 12.25-28.05, $p < 0.001$) (Table 4).

Table 4. Models with grouped criteria for evaluation of frailty in frail and pre-frail older people in outpatient care at a university hospital in northeast Brazil.

Frailty criteria	R ²	OR	95%CI	p*
All criteria	0.995			
↓ Gait speed		327.14	165.08-644.41	0.000
Fatigue		207.21	98.73-333.12	0.000
↓ Physical activity level		197.44	87.45-301.47	0.000
Unintentional weight loss		131.63	84.52-272.54	0.000
↓ Grip strength		94.31	77.65-222.67	0.000
3 criteria	0.789			
↓ Gait speed		17.55	12.25-28.05	0.000
↓ Physical activity level		13.23	9.34-15.68	0.000
Grip strength		14.71	9.53-16.92	0.000
2 criteria	0.584			
Fatigue		6.81	3.27-9.12	0.000
Unintentional weight loss		4.76	2.67-10.01	0.000

*Multinomial logistic regression analysis. Dependent variable reference category: frail.

The grouping of fatigue and unintentional weight loss explained 58.4% of the frailty in pre-frail individuals. In this model, fatigue was the criterion that determined the greatest likelihood of the progression to frailty, as pre-frail individuals with fatigue were 6.81-fold more likely to become frail (OR = 6.81, 95%CI: 3.27-9.12, $p < 0.001$) (Table 4).

In the model with all criteria together, the explanatory power for frailty was 99.5%. These criteria occurring concomitantly had a high odds ratio for the development of frailty. The slowness (OR = 327.14, 95%CI: 165.08-644.41, $p < 0.000$) and fatigue (OR = 207.21, 95%CI: 98.73-333.12, $p < 0.000$) criteria had the highest ORs (Table 4).

DISCUSSION

The frequency of frailty criteria varies considerably among studies depending on the characteristics of the population studied, methods employed and cutoff points adopted.¹³⁻¹⁶

The most frequent criteria in the present study were slowness and fatigue. The same criteria were the most frequent in a Brazilian study on cutoff points for frailty status.¹³ A study conducted in China also found that slowness was the most frequent frailty criterion.¹⁶ However, the study conducted by Fried and collaborators⁶ found a greater frequency for low physical activity level, followed by slowness, which is in agreement with data described in a study developed in Taiwan.¹⁴ Despite variations in the literature, the results point to issues related to physical aspects, underscoring the need for greater attention to be given to physical activity and body composition in older people.

In the present investigation, slow gait, fatigue and low physical activity level had the greatest explanatory power for frailty in the individual model. Pre-frail individuals with slow gait were 9.42-fold more likely to become frail.

Gait speed is a well-established consistent predictor of disability, cognitive impairment, institutionalization, falls and mortality and is a useful, sensitive criterion for identifying the progression of frailty; it can even be used as a single-item assessment tool in clinical practice, considered to be a fast, safe, inexpensive, highly reliable instrument.^{16,17}

Fatigue was the second most frequent criterion in this study. Pre-frail individuals with fatigue were 1.81-fold more likely to become frail. This finding may be due to the fact that the pre-frail individuals were mainly single, widowed and separated. According to the literature, living alone is associated with frailty. However, divergent results are found among studies with regards to this criterion.^{15,16} Such divergences may be due to the subjectivity of the criterion, which is one of its major limitations, as there is no exact measure for quantifying fatigue. Nonetheless, there is strong evidence of its association with depressive symptoms, which, in turn, are associated with frailty.¹⁸ On the other hand, this criterion is considered a frequent symptom related to aging and has been associated with several factors, such as social position, muscle weakness and comorbidities, and is the main clinical manifestation of different chronic diseases.¹⁹

The third most frequent criterion in the present sample was low physical activity level. Pre-frail individuals were 1.53-fold more likely to become frail. Previous studies with community-dwelling older people found this criterion to be one of the most frequent and with a greater power of prediction for frailty syndrome.^{15,16,20} In our study, we opted to use a questionnaire validated in Brazil for the measurement of physical activity level,¹² as this instrument addresses activities that are more common in Brazilian culture and therefore better reflects the situation of Brazilian older people.



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It is well established in the literature that a sedentary lifestyle exerts an influence on the reduction in the quantity and quality of muscle mass and, consequently, contributes to dysfunctionality in the older population, resulting in the emergence of frailty syndrome. Thus, the practice of regular physical activity is a therapeutic and prevention strategy to improve body composition and lower the risk of the occurrence of frailty in older people.^{21, 22}

Involuntary weight loss was the fourth most frequent criterion in the present study and one of the criteria with the lowest explanatory power for the development of frailty. This finding is in agreement with data reported by previous studies, in which weight loss had a more indirect association with frailty syndrome and was less capable of determining this condition in pre-frail older people when considered alone.^{15,23} Unintentional weight loss in older people is an independent risk factor for an increase in morbidity and mortality and is correlated with a high risk of specific nutritional deficiencies, disability, higher hospitalization rates and longer hospital stay.²⁴ Unintentional weight loss can suggest the occurrence of organic diseases, but may also be the result of other factors, such as the use of medications that affect the digestion and absorption of nutrients, level of appetite and satiety and general metabolism.²⁵ In the present sample, as most participants were single, divorced or widowed, this aspect may have exerted an influence on the determination of this criterion. Moreover, the presence of comorbidities can also affect diet quality and acceptance, exerting an influence on nutritional status.

The least frequent criterion in the present study was low grip strength, which had the lowest capacity for predicting frailty. In contrast, previous studies have found this criterion to be one of the most frequent in this clinical condition.^{15,16} Most of the present sample was in the youngest age group, which may have influenced this result. With the advance in age, individuals become more susceptible to musculoskeletal disorders, resulting in changes in body composition and a reduction in muscle mass, which exerts an impact on the reduction in muscle strength and physical performance, favoring the emergence of frailty syndrome.²⁶

In the combined models, the model with slowness, low physical activity level and low grip strength was capable of explaining 78% of the development of frailty in pre-frail individuals. Silva et al.¹⁵ reported a similar finding. The assessment tool for frailty syndrome with three criteria is capable of predicting mortality in the short term.²⁷ The combination of fatigue and unintentional weight loss had a lower explanatory power in the development of frailty, which suggests that these criteria need to be grouped with others in the determination of the syndrome.

The model with the five criteria combined was able to explain 99.5% of frailty. This result suggests that the criteria should perhaps not be isolated for the identification of frailty, as together they explain the development of the syndrome better. The frailty phenotype is an instrument influenced by several factors, which is justified, as it identifies a syndrome with a multifactorial cause.

Gobbens *et al.*²⁸ state that the criteria of the phenotype should always be present in any evaluation of frailty, as they represent the most widely cited and discussed concept in scientific research.²⁹

Although the present findings are relevant to the follow-up of older people, the cross-sectional design of the study does not enable the evaluation of causality. Nonetheless, these results contribute to explaining the influence of each criterion of the frailty phenotype in the determination of the syndrome, which can assist in the determination of appropriate interventions considering the specific capacity that each criterion has in predicting frailty.

CONCLUSION

The results of the present study underscore the importance of considering all criteria of frailty syndrome. However, slow gait was the more frequent criterion among both pre-frail and frail older people, suggesting that this criterion seems to be the best predictor of frailty and may enable the early identification of the syndrome. Thus, slowness warrants a detailed examination on the part of healthcare providers. Special attention should also be given to older people with fatigue and a low physical activity level, as such individuals are at greater risk of becoming frail and have greater susceptibility to negative outcomes associated with frailty.

DECLARATION OF COMPETING INTERESTS

The authors declare having no conflicts of interest.

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Como citar este artigo:

Araújo ACP, Cabral PC, Silva ABS, Santos ACO. Frailty: What phenotype criteria have the most influence on the occurrence of this syndrome in older people? *Rev Fac Ciênc Méd Sorocaba*. 2021;23(3/4):83-89. doi: 10.23925/1984-4840.2021v23i3/4a4



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