Clinical predictors of frailty in users of Secondary Care in Geriatrics and Gerontology

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Abstract

Objective: To analyze the health predictors associated with frailty in the older population treated at a Secondary Care Service in Geriatrics and Gerontology, Belo Horizonte, Minas Gerais state, Brazil. *Methods*: A cross-sectional observational study involving a sample of 4,323 individuals aged 60 years or older that underwent a clinical-functional evaluation was conducted. Sociodemographic and clinical-functional variables were analyzed and compared against the dependent variable of the study: clinical-functional stratum, as measured by the Visual Frailty Scale, dichotomized into frail and non-frail. Univariate logistic regressions were performed and the variables with p-value <0.2 were submitted to multivariate regression by stepwise and forward methods of selecting variables in the equation. *Results*: The potential explanatory value of the model was 70.4%. Seven variables were associated with frailty: age (OR 1.016; 95%CI: 1.001–1.028; p<0.001), dementia (OR 5.179; 95%CI: 3.839–5.961; p<0.001), depressive symptoms (OR 1.268; 95%CI: 1.090–1.475; p=0.002), urinary incontinence (OR 1.330; 95%CI: 1.153–1.535; p<0.001), changes in gait speed (OR 1.483; 95%CI: 1.287–1.709; p<0.001), calf circumference (OR 0.956; 95%CI: 0.932–0.982; p=0.001), and BMI (OR 1.026; 95%CI: 1.008–1.044; p=0.005). *Conclusion*: Advanced age, dementia, depressive symptoms, and continence and gait changes were associated with frailty. The study results reveal an association of reduced calf circumference and increased BMI values with frailty in older adults and that dementia diagnosis had the strongest association with the frailty syndrome.

Keywords: Health of Older adults. Frailty. Precipitating Factors. Secondary Care. Cross-Sectional Studies.

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INTRODUCTION

Population aging is a global phenomenon and a process that occurs heterogeneously, being influenced by physiological, functional and socioenvironmental factors[1]. The stratification of clinical-functional profile of older adults according to level of frailty can help inform public health actions targeting the needs of this population[2].

Frailty is a complex dynamic clinical syndrome characterized by a decline in functional reserves, such as cognition, functioning and mobility, which culminates in physical, psychological and social deficits[2]. The condition is associated with reduced resistance to external stressor events. Frailty is influenced by age, genetic and environmental factors, life habits and the presence of chronic diseases. The syndrome is associated with increased functional dependence, falls, hospitalizations and mortality[4-6].

Different conceptual models have been proposed to diagnose frailty in older individuals: phenotype, cumulative and multidimensional. Fried et al. defined frailty based on "frailty phenotype", characterized by the presence of 3 or more of the following criteria: unintentional weight loss, exhaustion, slowed gait, physical inactivity and reduced muscle strength[4]. In 2005, Rockwood et al. proposed the Frailty Index (FI), a cumulative model based on the accumulation of deficits/limitations related to aging and its unfavorable outcomes[7]. The FI is a broad measure, encompassing domains such as mobility, functioning, cognition, psychological aspects and presence of comorbidities[5]. Under the multidimensional model approach, frailty is regarded as multifactorial. Thus, physiological and psychological, cognitive, socioeconomic and environmental resources have similar importance in the subject´s ability to react to external adverse events[8].

The Brazilian Consensus on Frailty in Older Adults identified challenges for assessing frailty syndrome in Brazil, such as the need for simpler methods of evaluating frailty, establishing normative cut-off values for the scales employed for use in the Brazilian population, and strategies for population-wide screening for frailty[9]. A recent study on frailty in Latin America, India and China highlighted a number of other challenges, such as significant variation in prevalence and factors associated with the syndrome[10].

In view of the gap in knowledge on the underlying factors for identifying the Frailty Syndrome, the objective of the present study was to analyze the health predictors associated with frailty in older adults treated at a public referral Secondary Care service in Geriatrics and Gerontological medicine in Belo Horizonte, Minas Gerais state, Brazil.

METHOD

A cross-sectional observational study assessing Older Adult Care Plans (PCIs), devised based on a treatment protocol of a public secondary care Geriatrics service for patients seen between November 2016 and March 2020 was conducted[11,12]. The study participants, referred by Health Centers in Belo Horizonte were treated at the Centro Mais Vida (More Life Center) of the Hospital das Clínicas of the Federal University of Minas Gerais. The PCIs, based on the Broad Geriatric Assessment (AGA) and from multi-professional care, are employed for rereferrals to the Primary Care Units (UBS) of Belo Horizonte City Hall, Minas Gerais state. Older adults classified as frail and pre-frail are referred for follow-up at the secondary care services in geriatrics and gerontology of the city of Belo Horizonte[11,12].

The data from PCIs were collected between November 2020 and August 2021. PICs of patients aged ≥60 years containing results of instruments screening for frailty: the CFVI-20 (Clinical-Functional Vulnerability Index-20), and for level of vitality/frailty: the Visual Scale of Frailty (VSF)[3,10,12] were included. Sample selection was performed consecutively. All PCIs that met the inclusion criteria were included. Subsequently, PCIs not containing information on one or more of the independent variables outlined below were excluded. The data were keyed into the REDcap platform using double-entry.

The VSF constitutes a practical simple alternative tool, accessible to the levels of health care of older people, for assessing frailty syndrome. It is based on an assessment of performance (dependence or independent) for carrying out instrumental and basic

activities of daily living (ADLs) and in the presence of chronic diseases, cognitive impairment, sarcopenia and multiple comorbidities. A score of 6-10 points identifies the individual as frail and 1-5 points as non-frail[3].

The CFVI-20 is a multidimensional frailty screening instrument which measures cognition, mood, mobility, urinary/fecal continence, communication, age, self-rated health, polypharmacy, polypathology and recent hospitalization. [8] In the present study, the domains (including scales assessing these domains) of multi-dimensional frailty from the CFVI-20 instrument were employed as independent variables.

The following independent variables were selected to assess possible determinants of health: age (full years), sex (male and female), self-rated health (dichotomized into excellent, very good and good versus fair and poor), cognition (normal cognition, mild cognitive impairment, *delirium*, dementia, depressive symptoms, and mental disorder), presence or otherwise of depressive symptoms, urinary continence, slowed gait and polypharmacy (use of ≥5 medications). Anthropometric parameters measured were calf circumference (CC) with cut-off <31cm for sarcopenia, and body mass index (BMI) categorized as underweight (< 22kg/m^2), normal weight (22-27 kg/m^2) and excess weight (>27 kg/m^2)[12]. Only the variables available in the PCIs with missing data <10% were selected for the present study.

Cognitive status was determined using the records held in the PCIs and from analysis of results on the following cognitive screening tests: Mini-Mental State Exam (MMSE), 10-drawing recognition test, 10-word list from CERAD battery, semantic verbal fluency test (animals and fruit categories (cut-off = 9 for low educational level and 13 for high educational level) and Clock Drawing Test (cut-off = 3 points) scored according to Shulman. A cut-off of 18 points was defined for low educational level and 26 points for high educational level on the MMSE, and of 4 words and 5 drawings on the 10-word list recall from the CERAD and on the 10-drawing recognition test, respectively. The cut-off points were established based on validity studies of the scales for Brazilian Portuguese.[12]

Depressive symptoms were assessed based on record of mood changes on the PCI according to results on the 15 and 5-item Geriatric Depression Scales (GDS-15 and GDS-5), whose cut-offs were defined as ≥6 and ≥2 points, respectively, to indicate presence of depression, and also on records of the 5 criteria of major depression (with compulsory presence of at least one major criteria), according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)12. The cases of cognitive decline caused by mood disorders were subdivided into depressive symptoms and mental illness, with the latter reserved for mental disorders causing cognitive decline not associated with depression.

Mobility was assessed based on the results of the following tests: Timed Up and Go Test (cut-off ≥ 20 seconds), Get up and Go Test (TUGT), Nudge test, Romberg´s Test and 4m Gait speed test (cut-off < 0.8m/s)[12]. The presence of incontinence (urinary and/or fecal), self-rated health and use of medications were determined by self-report or using information from the caregiver.

The variables age and gender were expressed as median and quartiles, whereas qualitative variables were expressed as frequency. The Shapiro-Wilk test was employed to determine normality of the distribution. The Variance Inflation Factor (VIF) was applied to analyze the possibility of multicollinearity among variables prior to regression analysis. Univariate logistic regressions were performed. Variables with a p-value <0.2 on univariate analysis were input to the multivariable model using the stepwise forward method, confirmed by the backward method, for a significance level of 0.05.

The research project was approved by the Research Ethics Committee of the Federal University of Minas Gerais under permit no. 4198546.

RESULTS

After applying the inclusion criteria, the initial sample involved 18,009 PCIs. Of this total, 4,323 were selected for analysis. Sociodemographic and clinical-functional data for the study population are presented in Table 1. The sample population had a median age of 76 years (Q1=70; Q3=82), 74.1% were

female and 54.8% rated their health as fair or poor. Regarding cognition, 47.3% had normal cognitive status and 22.6% dementia. For mobility, 46.2% of the sample exhibited slowed gait. Overall, 36.3% of the sample met criteria for frailty as measured by the VFS.

The results of univariate logistic regression are presented in Table 2. Only the sex variable failed to obtain a p-value $p<0.2$. All other variables were retained for inclusion in the multivariate model.

The results of multivariate logistic regression are presented in Table 3. Seven variables were associated with frailty: age, cognition, depressive symptoms, urinary incontinence, slowed gait, CC and BMI. The strongest association detected was with the dementia variable (OR 5.179; CI 95% 3.839 – 5.961; p<0.001). Notably, higher CC values proved protective for frailty syndrome (OR 0,956), whereas high BMI favored greater likelihood of frailty (OR 1.026; 95% CI: 1.008 – 1.044; p=0.005).

The model found was able to correctly predict 70.4% of frailty present in the study. The Variance Inflation Factor (VIF) was 1, confirming no multicollinearity among the study variables.

Table 1. Descriptive qualitative and quantitative data for study population (N= 4,323), Belo Horizonte, Minas Gerais state, 2022.

Variable	Results
Sex (%)	
Male	1,123 (25.9)
Female	3,200 (74.1)
Self-rated health (%)	
Excellent, very good, good	1,958 (45.2)
Fair, poor	2,365 (54.8)
Hospitalization (%)	
No	2,980 (68.9)
Yes	1,343 (31.1)
Cognitive status (%)	
Normal cognition	2,049 (47.4)
Mild cognitive impairment	964 (22.3)
Delirium	5 (0.1)
Dementia	977 (22.6)
Depressive Symptoms	228 (5.3)
Mental Disorder	100 (2.3)
Depressive Symptoms (%)	
No	3,125 (72.2)
Yes	1,198 (27.8)
Slowed Gait (%)	
No	2,326 (53.8)
Yes	1,997 (46.2)

to be continued

Continuation of Table 1

Variable	Results
Urinary Incontinence (%)	
No	2,871 (66.4)
Yes	1,452 (33.6)
Visual Deficits (%)	
No	2,927 (67.7)
Yes	1,396 (32.3)
Auditory Deficits (%)	
No	3,489 (80.7)
Yes	834 (19.3)
Swallowing difficulties – dysphagia (%)	
No	4,094 (94.7)
Yes	229 (5.3)
Oral health problems (%)	
No	3,230 (74.7)
Yes	1.093 (25,3)
Sleep disturbances (%)	
No	3.299 (76.3)
Yes	1.024 (23.7)
Poor Family Support (%)	
No	3,736 (86.4)
Yes	587 (13.6)
Institutionalized (%)	
No	4,263 (98.6)
Yes	60 (1.4)
Clinical-Functional Stratum (%)	
Non-frail	2,754 (63.7)
Frail	1,569 (36.3)
Age (Q1-Q3)	76 (70-82)
Body Mass Index (Q1-Q3)	27 (23.3-30.5)
Calf Circumference (Q1-Q3)	35 (32-37)

n: Number of participants expressed as absolute value: Q1: First quartile, Q3: Third quartile.

Table 2. Univariate Logistic Regressions of study population (N=4,323). Belo Horizonte, Minas Gerais state, 2022.

Variable	OR	CI (95%)	*p*-value
Age	1.046	(1.039 – 1.053)	<0.001
Sex - Male (reference)			
Female	1.020	(0.895 – 1.162)	0.768
Self-rated health			
Fair/Poor (reference)			
Excellent/very good/good	0.772	(0.682 – 0.874)	<0.001
Cognition – Normal (reference)			
Mild Cognitive Impairment	1.384	(1.181 – 1.621)	<0.001
Delirium	4.002	(0.893 –17.936)	<0.001
Dementia	5.720	(4.919 – 6.651)	<0.001
Depressive Symptoms	1.554	(1.180 – 2.048)	<0.001
Mental Disorder	3.528	(2.448 – 5.086)	<0.001
Depressive Symptoms – No (reference)	1.169	(1.029 – 1.327)	0.016
Yes			
Urinary incontinence – No (reference)	1.759	(1.562 – 1.980)	<0.001
Yes			
Slowed Gait – No (reference)			
Yes	2.368	(2.108 – 2.660)	<0.001
Calf Circumference	0.928	(0.914 – 0.942)	<0.001
Body Mass Index	0.979	(0.968 – 0.989)	<0.001

OR: Odds Ratio; 95% Confidence Interval, level of significance <0.05.

Table 3. Multivariate Logistic Regressions of study population (n= 4,323). Belo Horizonte, Minas Gerais state, 2022.

Variables	OR	CI (95%)	*p*-value
Age	1.016	(1.001 –1.028)	<0.001
Cognition – Normal (reference)			
Mild Cognitive Impairment	1.231	(1.034 – 1.466)	0.020
Dementia	5.179	(3.839 – 5.961)	<0.001
Delirium	4.578	(0.848 – 31.631)	0.075
Depression	1.329	(0.982 – 1.798)	0.066
Mental Disorder	3.372	(2.222 – 5.117)	<0.001
Depressive Symptoms			
No (reference)			
Yes	1.268	(1.090 – 1.475)	0.002
Urinary incontinence – No (reference)			
Yes	1.330	(1.153 – 1.535)	<0.001
Slowed Gait – No (reference)			
Yes	1.483	(1.287 – 1.709)	<0.001
Calf Circumference	0.956	(0.932 – 0.982)	0.001
Body Mass Index	1.026	(1.008 –1.044)	0.005

OR: Odds Ratio; reference p: <0.05; Hosmer and Lemeshow Test: p=0.783.

DISCUSSION

Results showed that age, cognitive impairment, depressive symptoms, urinary incontinence, slowed gait, lower calf circumference and higher BMI scores were independently associated with frailty of the older population assessed, corroborating the multidimensional nature of the frailty syndrome.

In fact, age is one of factors exhibiting greatest evidence of correlation with frailty syndrome[13]. A higher prevalence of frailty was observed at more advanced ages, promoted by oxidative stress of endogenous and exogenous agents. The production of cellular oxygen increases and damage to DNA changes cells with deregulation of the inflammatory process. The final consequence of this process is functional loss and frailty syndrome[14,15]

Of the different cognitive variables examined, dementia was found to have the strongest association with frailty (OR 5.179- 95%CI: 3.839–5.961; p<0.001). There is evidence in the literature of a strong association between physical frailty and cognitive decline. Petermann-Rochat et al. found a 2.08 times increase (2.20 times after adjusting for life-style factors) in the probability of dementia in frail individuals[16]. A systematic review published in 2021 by Waite et al.[17] showed that frailty may be a predictor of dementia syndromes, given that frailty can occur even before individuals present the first symptoms of dementia. The frailty syndrome may correlate with dementia conditions as measured by pro-inflammatory, muscle stressor and neurodegeneration markers. Therefore, it is possible that more frail individuals, besides presenting physical decline, may have a higher risk of functional decline due to greater proneness to dementia. Nevertheless, these associations have not been fully elucidated in the literature[17-19].

The association between frailty and depressive symptoms has been reported in other studies at referral centers, such as the study by Silva et al.[20], which found similar results (OR=1.94; 95%CI: 1.41-2.66) in a population from the north of Minas Gerais state. Aprahamian et al. observed higher self-rated frailty in older adults with depression from an outpatient clinic in São Paulo state (OR 2,75; 95%CI= 1.84–4.11)[21]. In a cohort involving 6 Latin-American countries, depression increased the risk of developing frailty by 59%[22]. An integrative review published in 2021 suggested the possibility of depression and frailty being predictors of one another, given that frailty can be a predisposing factor for depression and behavioral problems, while reduced social interaction caused by depression can lead to physical frailty[23]. The role of chronic inflammation is highlighted, since high levels of interleukin 6 (IL-6), C-Reactive Protein and tumor necrosis factor-α are associated with frailty syndrome and depressive disorders in older adults[14,24,25].

The results of the present study suggest an association between urinary incontinence and frailty (OR 1.330; CI 95%: 1.153–1.535; p<0.001), consistent with the meta-analysis of Veronese et al. showing that incontinent older adults had a 2-fold higher frailty rate than their continent counterparts (OR 2.1; 95%CI: 1.20–3.60)[26]. Frail individuals tend to present slowed gait speed and exhaustion, contributing to poorer control of pelvic floor muscles, increasing the propensity for urinary incontinence[26,27]. These individuals often experience homeostatic dysregulation, culminating in declines in functioning, mobility, balance and cognition which lead to a greater prevalence of incontinence. However, the negative effects of urinary incontinence can lead to sufficient deficit accumulation to predispose to frailty[26].

The results of the present study corroborate previous investigations exploring the association between reduced mobility and frailty. The results revealed that 46.2% of frail individuals had mobility difficulties and that these are predictors of frailty (OR=1.483; 95%CI 1.287-1.709, p<0.001). A systematic review published in 2018 showed a clear association between gait speed in older people and frailty, underscoring the importance of assessing gait which yields objective sensitive parameters for evaluating functional decline during the aging process[28]. Gait is correlated with markers of functioning and body composition which contribute to balance and independence of older people for performing activities. Slow gait is associated with poor quality of life, increased risk of comorbidities, hospitalizations, falls and death[28-31].

A recent studying comparing frail and pre-frail institutionalized older residents showed that the frail group had slower gait speed, worse performance on the TUGT and lower knee extensor strength[29]. Consequences of frailty include risk of fractures, with an estimated 70% increase found in a 2016 meta-analysis[30]. Interestingly, a cohort of individuals aged >50 years reported that high levels of physical activity over the long-term can reduce predisposition to frailty. Therefore, on a public health level, stimulating physical activity in the older population constitutes a potential intervention for reducing the likelihood of developing frailty syndrome[31].

Lower CC values were associated with frailty, congruent with results reported by Xu et al. who found a protective effect of greater CC against frailty syndrome (OR 0.159; CI 0.064–0.396, P<0.001) in Chinese older inpatients[32]. Conversely, Wei et al., showed a 2.42 times increase in risk of death in individuals with low CC[33]. There is evidence that inflammation and changes in body composition and musculoskeletal and nervous systems act synergistically as risk factors for frailty[32].

The present study showed a positive association of elevated BMI and frailty, corroborating previous reports. Xu et al. reported that higher body fat mass, measured by analyzing body composition, increased the chances of frailty[32]. In a meta-analysis conducted by Amiri, Behnezhad & Hasani, a BMI≥25 was considered a risk factor for frailty (OR 1.43; 95%CI 1.13-1.81)[34]. It is also believed that increased inflammatory levels and peripheral insulin resistance predispose to decline in functional activities[32].

The present study has several strengths, such as the fact that the PCIs were applied by trained professionals from a cohesive multi-disciplinary team; the use of appropriate clinical protocols and tools recognized and validated for use in the older population, the large number of PCIs assessed; and the sample drawn from a single Referral Center which receives patients referred by Health Centers throughout the city of Belo Horizonte.

Study limitations include the cross-sectional design, precluding determination of cause-effect relationships for the results found. Additionally, the data were obtained from analyses of medical records (PCIs), introducing a possible bias regarding the quality of the documents accessed. Given that functioning is employed in the VSF, it was necessary to exclude basic and instrumental ADLs from among the independent variables. The information collected was derived from the first visit of users in secondary care, where this may have led to a higher rate of frailty and associated factors compared with the general population and limited the generalization of the results found. Lastly, the data were collected prior to the adoption of health measures during the COVID-19 pandemic and therefore do not reflect the changes in the older population arising in this period.

CONCLUSION

The results of the present study showed the association of frailty with advanced age, depression syndromes, depressive symptoms, slowed gait and urinary incontinence, consistent with previous reports in the scientific literature. The findings also revealed an association of frailty with high BMI and lower CC, suggesting that sarcopenic obesity might be a factor associated with the frailty syndrome. However, further studies are needed to confirm this hypothesis. Also, dementia proved the variable with the strongest association with the frailty syndrome.

These results emphasize the multidimensional nature of frailty in terms of cognitive aspects and both functional and physical characteristics. The findings also highlight factors which require vigilance by society and public agents to prevent the development of frailty in older individuals and among future generations within the Brazilian milieu. Future longitudinal studies involving diverse populations are needed to provide more in-depth analyses of the multiple problems involved in health care of older people, particularly early diagnosis of frailty.

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