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Hypertension and frailty in older adults

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The association between hypertension and frailty syndrome in older adults remains unclear. There is scarce information about the prevalence of hypertension among frail elderly patients or on its relationship with frailty. Up to one quarter of frail elderly patients present without comorbidity or disability, yet frailty is a leading cause of death. The knowledge and better control of frailty risk factors could influence prognosis. The present study evaluated: (1) the prevalence of hypertension in robust, prefrail, and frail elderly; and (2) factors that might be associated with frailty including hypertension. A cross-sectional study was conducted in 619 older adults at a university-based outpatient center. Study protocol included sociodemographic data, measures of blood pressure and body mass index, frailty screening according to the internationally validated FRAIL (fatigue, resistance, ambulation, illnesses, and loss of weight) scale, number of comorbidities, drug use assessment, physical activity, cognitive status, and activities of daily living. Ordinal logistic regression was used to evaluate factors associated with frailty. Prevalence of hypertension and frailty was 67.3% and 14.8%, respectively, in the total sample. Hypertension was more prevalent in the prefrail (72.5%) and frail (83%) groups than among controls (51.7%). Hypertension, physical activity, number of prescribed drugs, and cognitive performance were significantly associated with frailty status. Hypertension presented an odds ratio of 1.77 towards frailty (95% confidence interval, 1.21–2.60; $P = .002$). Hypertension was more prevalent in frail elderly patients and was significantly associated with frailty. Intensive control of hypertension could influence the trajectory of frailty, and this hypothesis should be explored in future prospective clinical trials.

1 | INTRODUCTION

Arterial hypertension is highly prevalent among older adults, consisting of reversible cardiovascular risk factors associated with high comorbidity and mortality.[1] The National Health and Nutrition Examination Survey (NHANES) showed that 67% of adults older than 60 years have hypertension in the United States.[2] It is estimated that the percentage of patients with hypertension rises with aging, especially isolated systolic hypertension.[3] Hypertension is also frequently associated with diabetes mellitus, dyslipidemia, and obesity, increasing cardiovascular risk and negative outcomes such as stroke, myocardial infarction, and renal failure.[4] Treatment of hypertension reduces the risk of stroke, cardiovascular events, and total mortality even among the oldest old, according to the HYVET (Hypertension in the Very Elderly Trial).[5] Moreover, a target systolic blood pressure (BP) < 120 mm Hg resulted in lower rates of major cardiovascular events and death from any cause

in the SPRINT (Systolic Blood Pressure Intervention Trial).[6] However, NHANES data between 2005 and 2008 showed that only 50.1% of patients with hypertension had controlled BP.[7,8] Whether treatment is of potential benefit for vulnerable elderly patients, such as those with frailty syndrome, must be balanced against inherent risks of drug treatment, such as orthostatic hypotension, falls, and polypharmacy.

Frailty syndrome is another great health concern for older adults. It has been defined by an international panel as a multiple etiology syndrome characterized by diminished strength and endurance and reduced physiologic function, leading to increased vulnerability for functional loss.[9] Frailty syndrome was the independent leading cause of death in elderly persons in a 10-year prospective cohort study.[10] Similar to hypertension, outcomes associated with frailty include functional and cognitive impairment, hospitalization, and death.[11] The prevalence of frailty in the elderly ranges from 7% to 16%, appears to be greater in women, increases with age, and reaches 28% in the oldest old.[12]

Only a few studies have explored the potential association between frailty syndrome and hypertension, and only two directly addressed the issue.[13–17] It appears that frailty is associated with hypertension, but the evidence is still scarce and based on studies with different criteria for the definition of frailty.[13–17] Moreover, hypertension treatment seems to positively affect unfavorable outcomes among older adults with frailty syndrome.[14] Frailty syndrome is present with comorbidity in 46.2% of the population.[11] This preliminary evidence shows that the association between hypertension and frailty syndrome is open to debate and in need of replication in different samples and using other criteria for frailty syndrome. Therefore, the aims of the present study were to evaluate: (1) the prevalence of hypertension and antihypertensive drug use in robust, prefrail, and frail elderly; and (2) factors associated with frailty status (ie, from robust to prefrailty, prefrailty to frailty), including hypertension.

2 | METHODS

2.1 | Participants and Procedures

Data collection for the CONFIDENT-VD (Cognitive and Functional Identification of Mild Deficits Among High Vascular Risk Associated Diseases) study occurred between June 2014 and July 2016 at the university-based outpatient center at the Faculty of Medicine of Jundiaí. The city of Jundiaí is located in the southwestern region of the state of São Paulo, Brazil, with 397,965 inhabitants, and it is classified as the fourth city in human development and eighth in economy in the state. The main objective of the CONFIDENT-VD study was to identify mild cognitive and functional impairments in patients with systemic hypertension, diabetes mellitus, and atrial fibrillation, conditions that are associated with higher cardiovascular risk. A second aim was to evaluate components of frailty and sarcopenia in a subsample of the study (n = 619), especially those 60 years or older, classified as elderly in Brazil. A total of 881 adults older than 50 years agreed to participate in the study. Random selection of participants was accomplished based on their scheduled appointment at any of the 20 medical specialized clinics in the outpatient center. The inclusion criteria were: age 50 years or older, stable medical conditions over the past month, and regular clinical follow-up at the outpatient center. Patients were excluded if they had suspected or diagnosed dementia, any severe limb plegia or paresis, important tremor, important functional impairment in hands, severe visual or auditory impairment, and presence of any kind of substance abuse. The present analyses were based on a subsample of 619 older adults (age ≥60 years) that completed the frailty and sarcopenia evaluations.

All participants were thoroughly evaluated by medical residents and attending physicians. Trained staff blinded to patient clinical diagnoses applied the study protocol. After the administration of the protocol, the research staff checked the patient's medical records to verify all exclusion criteria and to confirm current prescription regimen. The protocol included sociodemographic data, measures of BP and body mass index, frailty screening, cognitive status, and activities of daily living. Polypharmacy was defined by the use of five or more prescribed drugs. Patients were considered physically active if they reported walking or performing physical activities for ≥150 minutes, divided into two or three periods (each one with at least 45 minutes) weekly. Smoking was considered present if referred by the participant in any amount. Past episodes of myocardial infarction or stroke were confirmed by medical records. Baseline BP was measured twice (2-minute interval) in the right arm (the mean of the two scores was used), with participants in a seated position after 5 minutes of rest and without exercise, smoking, or alcohol or coffee consumption in the past 30 minutes. Standard aneroid sphygmomanometers were used for BP measurement. Diagnosis of hypertension was established as follows: systolic BP ≥140 mm Hg, diastolic BP ≥90 mm Hg, or the diagnosis of hypertension confirmed in medical records or current prescription of antihypertensive medications. Body mass index was calculated by dividing the weight in kilograms by the square of the height in meters. Cognition was evaluated by the Brazilian Portuguese version of the Montreal Cognitive Assessment (MoCA).[18] The cutoff for cognitive impairment was set at < 25 points, and one point was given if the patient had < 11 years of education.[19] The evaluation of activities of daily living was performed with the Functional Activities Questionnaire (FAQ).[20] Frailty was evaluated using the FRAIL-BR scale.[21]

2.2 | The FRAIL scale

The FRAIL (fatigue, resistance, ambulation, illnesses, and loss of weight) scale presents five simple questions to evaluate the presence of frailty components.[22,23] The scale is based on self-report without any objective measurement. Each question requires a "yes" or "no" answer, with one point for an affirmative response. Scores ranged from zero to five points, classifying patients as robust (0 points), prefrail (1 or 2 points), or frail (≥3 points). The scale assesses the presence of fatigue, muscle resistance, aerobic capacity, disease burden, and weight loss. Fatigue was evaluated by asking participants whether they felt tired most of the time; muscle resistance by participants' report of his/her capacity to climb a flight of stairs; aerobic reserve by participants' report of his/her capacity to walk a block independently; disease

burden by the presence of five or more of a total of 11 listed diseases; and loss of weight by a decline of ≥5% within the past 6 months.

2.3 | Ethics

The study was in accordance with the ethical standards of the Committee on Human Experimentation of both institutions as well as with the Declaration of Helsinki, and follows the standards established by the National Council of Health (resolution 466/12) in Brazil. All patients agreed to participate by signing an informed consent protocol approved by the local and national ethics committees (local protocol 13 466; national protocol CAAE: 48273214.6.0000.0068).

2.4 | Statistical analysis

R software was used for statistical analysis. Frequency tables were computed for categorical variables, and mean and standard deviations were computed for continuous variables. Shapiro-Wilk tests were used to determine which continuous variables followed the normality assumption. Comparisons between continuous variables were performed using analysis of variance in case the normality assumption was met, and using Kruskal-Wallis otherwise. Categorical variables were analyzed via chi-square tests. Ordinal logistic regression was performed to evaluate the association between independent variables (age, sex, physical activity, drug use, MoCA score, FAQ score, and hypertension) and frailty status from robust to prefrailty and frailty as the dependent variable. Level of statistical significance was set at 0.05 in two-tailed tests.

3 | RESULTS

3.1 | Baseline characteristics of the study population

The clinical and sociodemographic characteristics of the sample are described in Table 1. Frail patients were older and predominantly women. There was a higher presence of black race among prefrail and frail compared with robust older adults. Prefrail and frail groups had fewer years of formal education and lower income. Frail elderly showed lower

TABLE 1 Clinical and sociodemographic characteristics of the sample according to frailty status (n = 619)

	Robust (n = 201)	Prefrail (n = 324)	Frail (n = 94)	*P* value
Age, y	69.1 ± 7.1	70.0 ± 6.8	71.6 ± 7.7	.022[a,c]
Women	93 (46.7)	158 (48.8)	63 (65.6)	.006[a,c]
Race				
White	153 (80.5)	242 (78.3)	67 (72.8)	.002[b,d]
Black	9 (4.7)	43 (13.9)	14 (15.2)	
Other	28 (14.7)	24 (7.8)	11 (12.0)	
Education, y				
0–5	111 (55.8)	204 (63.0)	74 (77.1)	.004[b,c]
6–11	63 (31.7)	95 (29.3)	19 (19.8)	
>11	25 (12.6)	25 (7.7)	3 (3.1)	
Income, wages				
1–5	176 (88.4)	304 (93.8)	92 (95.8)	.03[b,c]
>5	23 (11.6)	20 (6.2)	4 (4.2)	
Physical activity	91 (45.7)	94 (29.0)	16 (16.7)	<.001[b,e]
Smoking	22 (11.1)	26 (8.0)	10 (10.4)	.477[b]
BMI	25.9 ± 4.4	27.3 ± 4.8	28.8 ± 5.4	<.001[a,f]
Stroke	9 (5.3)	17 (6.0)	10 (11.0)	.173[b]
Myocardial infarction	12 (7.1)	41 (14.4)	12 (13.2)	.06[b]
Polypharmacy[g]	41 (15)	152 (39)	66 (57.9)	<.001[b,f]
Disability	7 (3.48)	30 (9.26)	20 (21.28)	<.001[b,f]
MoCA test	21.2 ± 4.7	19.7 ± 4.8	17.5 ± 5.9	<.001[a,f]

Values are expressed as mean ± standard deviation or number (percentage).
Abbreviations: BMI, body mass index; MoCA, Montreal Cognitive Assessment; polypharmacy, ≥5 drugs; wages, US$258.06 according to current exchange rate (R1.00 = U$0.29).
[a]Analysis of variance.
[b]Chi-square test. Pairwise differences (test using Bonferroni-corrections).
[c]Robust vs frail.
[d]Prefrail vs frail.
[e]All groups differ except frail vs prefrail.
[f]All groups differ.
[g]Functional Activities Questionnaire ≥5 points.

physical activity and presented with higher body mass indexes compared with prefrail and robust older adults. The prefrail and frail groups showed significant polypharmacy. Frail patients presented with more disability (ie, higher FAQ scores), and the most frequent impairments consisted of difficulties in managing finances and transportation. The mean MoCA score observed was different in the three groups, with lower scores among prefrail and frail seniors.

3.2 | Prevalence of hypertension and association with frailty status

Prevalence of hypertension was 67.3% in the total sample and was higher among the frail (n = 78) ($P < .001$; Table 2) and prefrail (n = 235) ($P < .001$) groups. All three groups had different prevalence rates of hypertension. Participants with hypertension showed a mean systolic arterial pressure of 132.88 ± 17.92 mm Hg and a diastolic arterial pressure of 84.17 ± 10.97 mm Hg. Patients without hypertension presented with a mean systolic pressure of 124.48 ± 13.49 mm Hg and a diastolic pressure of 79.48 ± 10.12 mm Hg. Participants with and without hypertension were similar in clinical and sociodemographic characteristics except for age (70.5 ± 7.0 vs 68.9 ± 6.9, respectively; $P = .004$), history of stroke (32 vs 4, respectively; $P = .007$), and previous myocardial infarction (54 vs 11, respectively; $P = .005$). A significant difference was observed among robust, prefrail, and frail elderly in the use of antihypertensive drugs, except for the use of angiotensin-converting enzyme inhibitors (ACEIs) and calcium channel blockers (CCBs) (Table 2). Frail older adults used more diuretics (n = 49) followed by β-blockers (n = 41). Robust, prefrail, and frail elderly patients had significantly different prevalence rates of β-blocker, angiotensin receptor blocker, and diuretic use (Table 2).

The ordinal logistic regression model identified that physical activity, drug use, MoCA score, and hypertension were associated with a higher-order frailty status (Table 3). Practice of physical activity, one additional drug prescribed to the patient, one point lower score on the MoCA (cognitive performance), and having hypertension favored the progression from robust or prefrailty to the next step toward frailty. The odds ratio (OR) of hypertension was 1.77 ($P = .002$). Because of a higher prevalence of myocardial infarction and stroke in the hypertensive group, the same ordinal logistic regression was run with these two independent variables. Hypertension continued to be associated

TABLE 2 Prevalence of hypertension and antihypertensive drug class type used according to frailty status (n = 619)

	Robust (n = 201)	Prefrail (n = 324)	Frail (n = 94)	*P* value[a]
Hypertension				
Yes	104 (51.7)	235 (72.5)	78 (83.0)	< .001[b]
No	97 (48.3)	89 (27.5)	16 (17.0)	
Antihypertensive treatment				
β-Blocker				
Yes	36 (17.9)	111 (34.3)	41 (43.6)	< .001[b]
No	165 (82.1)	213 (65.7)	53 (56.4)	
ARB				
Yes	51 (25.4)	80 (24.7)	38 (40.4)	< .001[b]
No	150 (74.6)	244 (75.3)	56 (59.6)	
ACEI				
Yes	65 (23.9)	93 (23.9)	21 (22.3)	.824
No	163 (76.1)	297 (76.1)	73 (77.7)	
CCB				
Yes	12 (6.0)	35 (10.8)	12 (12.8)	.11
No	189 (94.0)	289 (89.2)	82 (87.2)	
Diuretics				
Yes	38 (18.9)	124 (38.3)	49 (47.9)	< .001[b]
No	163 (81.1)	200 (61.7)	45 (52.1)	
Others				
Yes	7 (3.5)	29 (9.0)	5 (5.3)	.042[c]
No	194 (96.5)	295 (91.0)	89 (94.7)	

Values are expressed as number (percentage).
Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker.
[a]Chi-square test with Monte Carlo correction. Pairwise differences (test using Bonferroni corrections).
[b]Found between all groups except frail vs prefrail.
[c]Found only in robust vs prefrail.

with frailty status (OR, 1.88; 95% confidence interval, 1.26–2.79 [*P* = .002]), but not myocardial infarction (OR, 1.02; 95% confidence interval, 0.659–1.593 [*P* = .914]) and stroke (OR, 0.923, 95% confidence interval, 0.475–1.794 [*P* = .002]).

4 | DISCUSSION

This is the first cross-sectional study with a large aleatory outpatient population of older adults to evaluate the association between hypertension and frailty syndrome. Hypertension was shown to be a risk factor for frailty syndrome according to the ordinal regression model used in this study. We highlight that the prevalence of frailty was 14.8% in this sample, consistent with the geriatric literature.[10] Prevalence of hypertension was also consistent with the literature,[2] and most older adults with frailty presented with hypertension (n = 78, 83% of the frail group; Table 2). The use of antihypertensive drugs was different among robust, prefrail, and frail elderly patients, except for the use of ACEIs and CCBs. Also, being sedentary, taking more prescribed drugs, showing lower cognitive performance, and having hypertension were significantly associated with a higher frailty status (Table 3).

Five previous studies have investigated the association between hypertension and frailty in observational and cross-sectional designs involving mostly community-dwelling older adults.[13,15–17] Their objectives varied as follows: (1) to investigate whether frailty status interfered with hypertension antihypertensive treatment (one study from the HYVET trial databank and another Chinese study); and (2) to evaluate the relationship between frailty and hypertension, and between frailty and kidney function of community-dwelling older adults with diabetes mellitus or hypertension (two Japanese and one Mexican study). Prevalence of hypertension varied from approximately 37% to 62% in previous studies, and its prevalence among participants with frailty was not reported in any of the trials. These studies also varied widely in their aims, methods, and frailty diagnostic criteria. In one previous study, the risk for frailty was associated with the presence of hypertension.[17] In multiple regression analyses, hypertension was associated with a 1.59 risk for frailty, in agreement with the present findings. However, in our study, we used an easy and common way to identify frailty, which is recommended by international societies.[21–23] The FRAIL scale is more suitable for use in clinical practice, especially in nonspecialized settings.

Chuang and colleagues[15] published a letter reporting a study with a convenience sample of 124 geriatric outpatients with hypertension (BP ≥160/90 mm Hg). CCB use was negatively associated with frailty (OR, 0.30; 95% confidence interval, 0.10–0.83). Frail (50%) and prefrail (54.9%) participants were less likely to use CCBs than robust elderly patients (74.1%). The authors suggested that CCBs could have a protective effect on frailty. Prevalence of frailty in this study was similar to that presented here (14% vs 14.8%, respectively). In our sample with a larger number of prefrail and frail participants, we did not observe a significant difference in the use of CCBs between robust and frail older adults (Table 2).

In the present study, we did not find that ACEIs were more prevalent among prefrail or frail groups compared with the use of other antihypertensive drugs. Previously, ACEIs were evaluated in relation to sarcopenia parameters and physical activity.[24–27] ACEIs were associated with larger lower extremity muscle mass,[26] and longitudinally they appear to slow muscle strength decline in older women with hypertension.[27] In a double-blind randomized trial of 20 weeks, perindopril improved exercise capacity in functionally impaired older adults without heart failure in a 6-minute walking distance.[24] Also, authors of this study reported a trend toward a reduction in the number of falls with perindopril. However, cross-sectional analyses of a large sample from a cohort study did not show a positive relationship between ACEI use and lean muscle mass, strength, and arm muscle quality or function.[27] Although controversies remain on the positive potential influence of ACEIs in frailty pathways, possible mechanisms may rely on the improvement of left ventricular and vascular function, reduction in the loss of skeletal muscle cross bridges, and improvement of skeletal muscle contractility mediated by increased nitric oxide production.[28–30] These issues should be explored in future studies.

TABLE 3 Ordinal logistic regression analyses with frailty status as outcome variable and age, male sex, physical activity, medication, cognitive performance, functional status, and hypertension as independent variables

Independent variable	β (95% CI)	OR (95% CI)	*P* value
Intercept 1	−2.19 (−4.21 to −0.16)	0.11 (0.01–0.85)	.017
Intercept 2	0.71 (−1.3 to 2.73)	2.04 (0.27–15.32)	.245
Age	0.00 (−0.03 to 0.02)	1.00 (0.97–1.02)	.444
Male	−0.22 (−0.54 to 0.10)	0.80 (0.59–1.10)	.088
Physical activity	−0.66 (−1.0 to −0.31)	0.52 (0.37–0.73)	< .001
Drug use	0.19 (0.12–0.26)	1.21 (1.13–1.30)	< .001
MoCA score[a]	−0.08 (−0.11 to −0.05)	0.92 (0.89–0.96)	< .001
FAQ score[b]	−0.42 (−1.01 to 0.17)	0.66 (0.37–1.19)	.083
Hypertension	0.57 (0.19–0.95)	1.77 (1.21–2.60)	.002

Abbreviations: CI, confidence interval; FAQ, Functional Activities Questionnaire; MoCA, Montreal Cognitive Assessment; OR, odds ratio (>1 indicates higher risk of frailty).

[a]Higher the score = better cognitive performance.

[b]Higher the score = more disability.

4.1 | Study limitations

Our study presents some limitations. The sample consisted of elderly patients from an outpatient clinic in a single center. Thus, our findings should be carefully extrapolated to community-dwelling or institutionalized samples.[11] In-depth diagnosis of depression or dementia was not performed, and these diagnoses could be present in the sample and associated with both hypertension and frailty, possibly increasing the prevalence of the latter. Finally, our study was observational and cross-sectional, and thus not designed to establish a causality relationship between hypertension and frailty.

5 | CONCLUSIONS

Hypertension was an associated risk factor for frailty and was more prevalent among frail older adults. Future longitudinal studies should investigate possible causality associations and the negative outcomes of the concomitant presence of hypertension and frailty.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

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