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Frailty and depression in the hypertensive older patients; a cross-sectional study

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Abstract

Hypertension (HT) is one of the most common chronic diseases in the elderly in our country and worldwide. HT alone can trigger depression and fragility, and it is possible that these three clinical conditions affect each other negatively. However, there is no study in the literature that evaluated the relationship between these variables. In this study, it was aimed to investigate the frequency of frailty and depression in a group of geriatric HT patients, as well as the relationship between these three variables. A total of 276 (mean age:73.0±7.2) HT elderly patients, 126 (mean age:73.6±7.8) of whom were female, were included in the study. All participants were evaluated with the Katz Activities of Daily Living (ADL) index, the Lawton-Brody instrumental activities of daily living (IADL) index, The Geriatric Depression Scale (GDS-15) and the Freid Frailty Index (FFI). Analyzes were performed by dividing them into three groups according to their FFI scores. According to the FFI scores, 94 (34.1%) as pre-frail, 87 (31.5%) as frail and 95 (34.4%) as robust. FFI scores were positively correlated with age and GDS-15. However, FFI scores were negatively correlated with HGS, ADL and IADL. Age (p<0.001, OR= 1.98[1.04-1.16]), ADL (p<0.01, OR= 0.51[0.36-0.71]), IADL (p=0.044, OR= 0.78[0.62-0.99]) and GDS-15 score (p<0.001, OR= 1.24[1.10-1.40]) were found as independent variables for frailty. Our results provide evidence of a consistent bidirectional relationship between frailty and depression in geriatric patients with HT. Additionally, our data show that three out of four people with frailty have depression and one in two people with depression have frailty. Therefore, interventions should be developed to reduce one of the two syndromes in the elderly diagnosed with HT.

Keywords: Frailty, depression, hypertension, elderly

Introduction

Hypertension (HT) is one of the most common chronic diseases in the older adults in Türkiye and worldwide [1]. The frequency of HT increases with age. In a study conducted in our country, the prevalence is 69% between the ages of 60-69, and it increases to 79% at the age of <80 years [2]. HT is associated with increased mortality and morbidity in the older adults [3]. Although its causality has not been fully determined, HT may cause frailty by creating complications such as cerebrovascular disease (CVD) and coronary artery disease (CAD) and impairing physical and cognitive functions [4-6]. In a study conducted with non-frail patients, it was shown that frailty may develop in the following three years in the presence of additional comorbid disease (CAD, CVD, Diabetes Mellitus or HT) in the older adults [7].

Frailty is a multidimensional geriatric syndrome that causes both physical and cognitive impairment due to loss of functional reserve [8]. Despite social differences, its prevalence varies between 4.0-59.1%. Frailty is clinically associated with adverse outcomes such as falls, decreased mobility, increased dependence, frequent hospitalizations, and death [9]. Therefore, it is important to investigate the fragility and related factors accompanying HT, which is the most common chronic disease especially in the elderly, in terms of early intervention and developing effective measures.

Another common disease in hypertensive older patients is depression. Recent studies have reported that approximately 26.8% of these patients have depression [10]. This result may develop due to the adverse biological effects of the deterioration in the stress response in depression, as well as the side effects of the drugs used [11]. Depression is also considered an independent risk factor for the development of frailty. Depression is also considered a risk

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factor in the development of frailty. While the rate of depression in frail older patients are 38%, 40% of depressed older patients are considered frail [12]. In addition, the probability of developing depression in frail older patients were found to be four times higher [12]. It may be possible to explain this mutual interaction between both frailty and depression with common symptoms (weight loss, decrease in physical activity, decrease in walking speed) and common biological substrates (chronic inflammation and oxidative stress) [13]. The coexistence of depression and frailty exacerbates the poor prognosis.

The most common chronic disease among the elderly living in the community is HT. It is important to develop effective and early interventions to investigate HT and other related geriatric syndromes triggered by it, which affects a large population. From this point of view, HT alone can trigger depression and frailty, and it is possible that these three clinical conditions affect each other negatively. However, studies evaluating the relationship between these variables are rare in the literatüre [14]. The main purpose of the study was investigate the frequency of frailty and depression in a group of geriatric HT patients, as well as the relationship between these three variables.

Material and Methods

Participants

The study is a cross-sectional study. Patients aged 65 years and older, who applied to the Inönü University Faculty of Medicine, Geriatrics outpatient clinic between March and December 2021, received anti-hypertensive therapy with the diagnosis of HT or were newly diagnosed with HT were included in the study. HT was defined as systolic blood pressure (SBP) ≥140 mm Hg and/or diastolic blood pressure (DBP) ≥90 mm Hg or chronic use of antihypertensive medication [15]. Anthropometric measurements and laboratory values of the patients were obtained from patient files. Patients with a diagnosis of HT without evidence of secondary causes were included in this study. Patients who were unable to complete tests due to cerebrovascular events or cognitive impairment, those on a cancer chemotherapy program and treated for an inflammatory disease were also excluded.

This study was evaluated and approved by the Inonu University Non-Interventional Ethics Committee (2022/3268). All patients gave informed consent.

Assesment for physical functions

The functional status of the participants was evaluated with the Katz Activities of Daily Living (ADL) index and the Lawton-Brody instrumental activities of daily living (ADL) index [16,17]. Eating, toilet, bathroom, continence, transfer and dressing status of the participants were questioned in ADL. In the IADL index, cooking, traveling, using the phone, shopping, housework, self-medication, planning financial affairs and mobility were questioned. Each item was given a score of zero (not disabled) or one (yes, disabled). High scores on both scales were associated with independence.

Assessment for depressive symptoms

Depressive symptoms were evaluated with the Geriatric Depression Scale (GDS-15). It was developed by Yesavage et al. in 1983 to screen for depression in older patients [18]. GDS-15 is a fast and easily applicable screening test. It contains a total of fifteen questions and a score of 5 or more is consistent with the presence of depressive symptoms. The validity and reliability of the scale in Turkey were confirmed by Durmaz et al. in 2018 [19]. All participants in our study were also evaluated by a clinical psychiatrist after the GDS-15 test.

Assessment for Frailty Syndrome

Freid Frailty Index (FFI) was used frailty [20]. The patients were evaluated with five questions; weakness (grip strength), slowness (4.57 m walking time), self-reported fatigue, low physical activity level (measured by expanded kilocalorie-weighted points per week), and self-reported weight loss. According to the answers given to each question, it was scored as 0 points and 1 point. Based on this score, patients were classified as non-frail or robust (0 components), pre-frail (1 or 2 components), or frail (≥3 components).

Assessment for Handgrip Strength

Hand grip strength (HGS) measured with a dynamometric instrument (Camry electronic hand dynamometer) was used to evaluate muscle strength. Handgrip strength was measured by instructing all participants to stand upright with their arms at their sides and to squeeze the dynamometer in their dominant hand. The HGS score was calculated by taking the highest of the three trials [21].

Statistical Analysis

Statistical analyzes were performed using SPSS-26. The normality of the distribution was tested with the Shapiro–Wilk and Kolmogorov–Smirnov tests for the variables. G-POWER analysis was used to calculate sample size. Accordingly, assuming 80% power and 0.05 bilateral alpha levels, the minimum number of patients required for the study was calculated as 180 [14]. Descriptive statistical analyzes were performed for continuous variables. Continuous variables of the groups were evaluated using independent samples t-test and analysis of variance (ANOVA). Relationships between parameters were investigated by Pearson correlation analysis. Multinomial logistic regression was used to simulate a model to identify factors affecting the presence of frailty. Statistical significance level was determined as $p < 0.05$.

Results

A total of 276 (73.0±7.2) HT older patients, 126 (73.6±7.8) of whom were female, were included in the study. According to the FFI scores, 95 (34.4%) of the participants were grouped as robust, 94 (34.1%) as pre-frail, 87 (31.5%) as frail and 95 (34.4%) as robust. Sociodemographic characteristics and anthropometric measurements of the participants are given in Table 1. The participants classified as frail and pre-frail were older than the robust participants ($p<0.001$). The rate of living alone and the number of drugs used were significantly higher in the frail group compared to the other groups ($p<0.001$ and $p=0.034$; respectively).

When five points and more were evaluated as depression according to their GDS-15 scores, 141 (51.1%) patients, 75 (27.2%) of whom were women, were found to be depressed. While the depression

rate in the frail group was 88.5%, the depression rate in the fit group was 14.9% (p<0.001).

In the correlation analysis, FFI scores were positively correlated with age and GDS-15 ((p<0.001, p=0.007; respectively). However, FFI scores were negatively correlated with HGS (p<0.001), ADL (p<0.001), IADL(p<0.001), and body mass index (p=0.049). GDS-15 scores were positively correlated with age (p=0.014) and negatively correlated with HGS (p<0.0050), ADL (p<0.001), and IADL(p<0.001) (Table 2).

Table 1. Sociodemographic characteristics and comprehensive geriatric assessment results of the participants (n=276)

Variables	Robust (n=95)	Pre-Frail (n=94)	Frail (n=87)	p
Age§†	**68 (65-86)**	**71 (65-91)**	**73 (65-97)**	**<0.001***
Sex				
Male	54 (56.8%)	56 (59.6%)	40 (46.0%)	0.156
Female	41 (43.2%)	38 (40.4%)	47 (54.0%)	
Education level				
Uneducated	28 (29.8%)	24 (25.5%)	22 (25.3%)	0.658
Primary/middle school	36 (38.3%)	42 (44.2%)	36 (41.4%)	
High school/university	31 (31.8%)	28 (30.3%)	29 (33.7%)	
Marrital status				
Married	26 (60.5%)	48 (76.2%)	74 (69.8%)	0.124
Other	17 (39.5%)	15 (23.8%)	32 (30.2%)	
Living alone#	4 (4.2%)	8 (8.4%)	12 (13.8%)	<0.001*
Smoking	18 (18.9%)	10 (10,6%)	4 (4.6%)	0.056
Alcohol	17 (17.9%)	14 (14.9%)	9 (10.3%)	0.785
Number of medications	5.00 (3.00-10.00)	5.00 (3.00-7.00)	5,00 (2,00-7,00)	0.034*
HGS#	18.7 (17-48.2)	17.9 (14-34.9)	11.9 (12.6-37)	0.002*
SBP	135 (120-140)	125 (115-140)	125 (115-140)	0.259
DBP§	75 (70-85)	75 (70-85)	70 (70-80)	0.044*
Number of additional diseases	1 (0-5)	2 (0-5)	2 (0-5)	0.032*
Diabetes mellitus#	15 (34.9%)	27 (42.9%)	42 (39.6%)	0.006*
Coronary artery disease#	7 (16.3%)	16 (25.4%)	23 (21.7%)	0.011*
Hyperlipidemia#	4 (9.3%)	7 (11.1%)	11 (10.4%)	0.020*
Asthma/COPD#	2 (4.7%)	8 (12.7%)	10 (9.4%)	<0.001*
Calf circumference (cm)	30.50 (20-41)	29 (20-38)	27 (20-38)	0.158
BMI (kg/m^2)	25.5 (17.2-44.9)	25.0 (15.8-43.7)	24.9 (15.5-44.9)	0.065
Physical Functions				
ADL#	6 (4-8)	6 (2-6)	4 (1-6)	<0.001*
IADL#	8 (4-8)	5 (2-8)	5 (0-8)	<0.001*
GDS-15#	11 (0-15)	9 (0-15)	12 (0-15)	<0.001*
Depression	14 (9.9%)	50 (35.5%)	77 (54.6%)	<0.001
Laboratory Values				
Hb	11.60 (9.7-13.5)	11.00 (9.6-13.2)	11.20 (9.5-12.0)	0.483
Urine	24.50 (16-41)	24 (12-41)	24 (12-57)	0.650
Creatinin	0.7 (0.6-1.2)	0.7 (0.4-1.2)	0.8 (0.4-1.4)	0.128
Na	136 (132-139)	136 (130-144)	135 (128-144)	0.718
K	4.92 (3.79 -7.13)	5.06 (3.46-7.29)	5.14 (3.52-7.43)	0.910
Vitamin D	8.80 (3.0-45.1)	8.49 (3.6-23.7)	8.58 (3.0-38.2)	0.952

HGS; Handgrip Strength, SBP; Systolic Blood Pressure, DBP; Diastolic Blood Pressure, COPD; Chronic Obstructive Pulmoner Disease; ADL; Activities Of Daily Living, IADL; Instrumental Activities Of Daily Living, GDS-15; Geriatric Depression Scale, cm; centimeter, , kg/m^2; kilogram per square meter, Hb; hemoglobin, Na; sodium, K; Potassium

*p<0.05; * Mann-Whitney U test

Data are presented as median (min-max)

Statistically significant difference between Frail vs. Pre-frail; Frail vs. Normal;

§ Statistically significant difference between Frail vs. Normal

† Statistically significant difference between Pre-frail vs. Normal

Table 2. Correlation analysis results between the variables

		FFI score	Age	BMI	HGS	ADL	IADL	GDS-15
FFI score	r	1	0.445**	-0.645**	-0.467**	-0.711**	-0.635**	0.162**
	p		0.000	0.000	0.000	0.000	0.000	0.007
Age	r		1	-0.380**	-0.191**	-0.302**	-0.324**	0.445**
	P			0.000	0.001	0.000	0.000	0.000
BMI	r			1	0.393**	0.536**	-0.603**	-0.645**
	p				0.000	0.000	0.000	0.000
HGS	r				1	-0.379**	-0.365**	-0.467**
	p					0.000	0.000	0.000
ADL	r					1	0.528**	-0.711**
	p						0.000	0.000
IADL	r						1	-0.635**
	p							0.000
GDS-15	r							1
	p							

FFI; Fried Frailty Index, BMI; Body Mass Index, HGS; Hand Grip Strength, ADL; Activities Of Daily Living, IADL; Instrumental Activities Of Daily Living, GDS-15; Geriatric Depression Scale.
Spearman rank correlation coefficient; *. Correlation is significant at the 0.05 level, **. Correlation is significant at the 0.01 level

Logistic regression analysis was performed to determine the parameters affecting the risk of frailty development in the older patients followed up with the diagnosis of HT. Age (p<0.001, OR= 1.98[1.04-1.16]), ADL (p<0.01, OR=0.51[0.36-0.71]), IADL (p=0.044, OR=0.78[0.62-0.99]) and GDS-15 score (p<0.001, OR=1.24[1.10-1.40]) were found as independent related factors for frailty (Table 3).

Table 3. EEG characteristics of GEFS+

	Frailty	
Variable	OR [95% CI]	P value
Age	1.98[1.04-1.16]	0.001*
BMI	1.05[0.99-1.13]	0.113
ADL	0.51[0.36-0.71]	<0.001*
IADL	0.78[0.62-0.99]	0.044*
GDS-15 score	1.24[1.10-1.40]	<0.001*

*p < 0.05 according to multivariate binary logistic regression analysis.
CI, confidence interval; OR, odds ratio.

Discussion

This cross-sectional study is the first in our country to evaluate frailty and depression in the hypertensive older patients. The findings here may provide clues for the development of intervention strategies to prevent the development of both frailty and depression in older patients with HT. In our study, we found frail in three of every ten HT patients. In addition, the rate of depression in the frail group was approximately six times higher than in the healthy group. Age, ADL, IADL and GDS-15 scores were found to be independent related factors in the development of frailty in the older patients followed up with the diagnosis of HT.

Chronic diseases and frailty represent the clinical expression of the biological deteriorations that occur with aging. With the increasing older patients and the aging of individuals with cardiovascular disease, the theme of frailty is gaining more and more importance day by day. Frailty and chronic diseases are often considered separate clinical entities. However, these two concepts are intertwined and although there are different opinions, the general opinion is that the presence of chronic disease contributes to the onset of frailty [22]. In the systematic review of Vetrano et al., it was determined that seven out of ten older patients who were evaluated as frail had HT and one out of seven HT patients showed frailty [23]. Rockwood et al. showed a linear relationship between frailty and SBP [24]. Conversely, in the study of Anker et al., older frail and pre-frail individuals were reported to have lower SBP than healthy individuals [25]. In observational studies to identify frailty precursors in the older patients, however, no effect of hypertension on the onset of frailty was found [26, 27] However, it is also known that antihypertensive treatment-related adverse events are more common in frail patients [28]. In our study, there was no difference between the SBP values between the three groups, while the DBP values of the frail group were found to be lower. The reason for the inconsistency between the results of the studies is not clear. However, variables such as the presence of additional comorbid diseases, age, number of drugs, target organ damage, anti-hypertensive treatments and methods used in frailty assessment may be the reason for this difference. Or, dietary restrictions due to HT may have triggered the development of frailty.

There are multiple mechanisms that facilitate the development of HT in the older patients, such as mechanical and hemodynamic changes that occur with advancing age, arterial stiffness, neurohumoral and autonomic disorders [29]. According to data from the US National Health and Nutrition Examination survey, 70% of older adults have HT [30]. Song et al. also showed that 46.5% of patients over the age of 65 with a diagnosis of HT have frailty syndrome [31]. Frailty increases the risks of adverse health outcomes, including dependence, falls, the need for long-term care, and mortality [32]. Gobbens et al showed that frailty is associated with ADL and IADL [33]. In another study, frailty was associated with age, gender, number of chronic diseases, ADL and IADL

disability [34]. In this study, the ADL and IADL scores of the frail and pre-frail patients were found to be lower than the healthy patients, and their age was higher. In addition, frailty development was associated with age, ADL and IADL score.

The aging population brings with it social problems as well as medical problems. The addition of chronic diseases to psychosocial stressors such as cognitive decline, sleep disorders, social isolation, loss of spouse that occur with aging facilitates the development of depressive symptoms [35]. This association may also lead to a further decrease in the quality of life. In a study, it was shown that the rates of depression increase in the presence of hypertension [14]. In our study, we found that depressive symptoms developed in approximately one in two HT patients. Considering that the treatment of depression in the older patients with chronic diseases such as HT is difficult and is associated with a poor prognosis [36], this result was noteworthy in terms of showing that depression is common in the older patients with HT and its screening is important.

There is a bidirectional relationship between frailty and depressive symptoms in the older patients [37]. While limitations in physical functions and loss of independence increase the risk of developing depression in frail older patients, depressive symptoms may contribute to the development of frailty by negatively affecting physical functionality [38–40]. This association has been attributed to the common pathophysiological mechanisms of hormonal changes and local inflammation on the hypothalamic-pituitary-adrenal axis [38]. In addition, the increasing prevalence of comorbidity with age increases the risk of depression by causing both physical and psychological difficulties. Chiu et al. found that among the factors predicting frailty, depressive symptoms were the most important risk factor for both men and women [39]. Masoli et al. showed in their study that the severity of depressive symptoms in the older patients had the highest independent effect on frailty [40]. Kennedy et al. suggested that increasing disability in the older patients significantly increases the occurrence of depressive symptoms, but facilitating factors are needed for the development of depression and disability [41]. Similarly, in this study, the GDS-15 scores of the frail and pre-frail group were significantly higher than the healthy group, and two-thirds of these patients had depression. Again, comorbid disease rates of frail patients were higher than the healthy group.

Limitation

Our study has several limitations. First, we did not classify patients according to subtypes of depression (major, minor, bipolar disorder, dysthymic disorder, etc.) in our study. Second, due to the cross-sectional nature of our study, the participants could not be evaluated at regular intervals. For this reason, it could not be followed whether depressive symptoms developed in those with pre-frail/frail without depressive symptoms. On the other hand, the barriers to treatment compliance in patients diagnosed with depression could not be determined. Despite its limitations, our study is the first in our region to evaluate frailty and depressive symptoms in hypertensive older patients.

Conclusion

Finally, the presented study provides important evidence of a reciprocal interaction between frailty and depression in hypertensive older patients. However, the mechanisms that support these associations in the elderly with chronic disease deserve further investigation. This results show that three out of four people with frailty have depression, and one in two people with depression are vulnerable. Therefore, interventions should be developed to reduce one of the two syndromes in the older patients diagnosed with HT.

Conflict of interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that they have received no financial support for the study.

Ethical approval
This study was evaluated and approved by the Inonu University Non-Interventional Ethics Committee (2022/3268).

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