



What is the relationship between frailty and orthostatic hypotension in older adults?

Suleyman Emre Kocyigit¹, Pinar Soysal², Esra Ates Bulut¹, Ali Ekrem Aydin¹, Ozge Dokuzlar¹, Ahmet Turan Isik¹

¹Unit for Aging Brain and Dementia, Department of Geriatric Medicine, Faculty of Medicine, Dokuz Eylul University, Izmir, Turkey

²Department of Geriatric Medicine, Bezmialem Vakif University, Faculty of Medicine, Istanbul, Turkey

Abstract

Background Frailty and orthostatic hypotension (OH), which is common in older adults, is associated with morbidity and mortality. The relationship between them remains unclear. The aim of the study is to determine whether there is a relationship between frailty and OH. **Methods** A total of 496 patients who were admitted to the geriatric clinic and underwent comprehensive geriatric assessment were retrospectively reviewed. In a cross-sectional and observational study, OH was measured by the Head-up Tilt Table test at 1, 3, and 5 min (respectively, OH₁, OH₃, and OH₅) and the frailty was measured by the Fried's frailty scale. **Results** The mean age of all patients was 75.4 ± 7.38. The prevalence of females was 69.8%. When the frail people were compared with the pre-frail and the robust ones, the frailty was associated with OH₁. There was no relationship between the groups in terms of OH₁ when the pre-frail group was compared with the robust group. OH₃ were higher in the frail group than in the pre-frail group ($P < 0.05$) and the OH₅ were higher in the frail group than in the pre-frail and robust group ($P < 0.05$), but OH₃ and OH₅ were not associated with frailty status when they were adjusted for age ($P > 0.05$). Slowness and weakness were associated with OH₁ ($P < 0.05$), whereas the other components of the Fried's test were not. **Conclusions** Frailty may be a risk factor for OH₁. The 1st min measurements of OH should be routinely evaluated in frail older adults to prevent OH-related poor outcomes.

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1 Introduction

Frailty and orthostatic hypotension (OH), two geriatric syndromes are not only prevalent in older adults but also cause adverse health outcomes in this population. Frailty is characterised by a physiological reserve reduction and ability to resist physical or psychological stresses.^[1] Several important multi-system pathophysiological processes, including chronic inflammation and immune activation, and those found in the musculoskeletal and endocrine systems occur in the pathogenesis of frailty syndrome.^[2] Frailty is also associated with adverse effects such as falls, hospitalisation, disability, institutionalisation, and premature mortality.^[3] Fried's frailty scale is a well-known and frequently

used measurement for the evaluation of frailty in the literature.^[4]

The prevalence of OH in people over 65 years of age is about 30%,^[5] but its prevalence is different from various diseases such as type 2 diabetes mellitus, Parkinson's disease, multiple system atrophy, dementia with Lewy Bodies, and autonomic neuropathies in older adults.^[5] It has been shown that OH is associated with falls, cardiac events, heart failure, stroke, reduced quality of life due to orthostatic symptoms, and an increase in the risk of overall mortality in these patients.^[5–7] Homeostatic ability to maintain blood pressure while standing is based on adequate blood volume and the integrity of the nervous system, heart, blood vessels, and muscle pump.^[8] However, in older adults, some age-related factors can contribute to the development of OH. For example, decreased baroreflex sensitivity, α-1 adrenergic vasoconstrictor response to sympathetic stimuli, parasympathetic activity, renal salt and water conservation, increased vascular stiffness and decreased ventricular diastolic filling, prone to dehydration due to thirst response, normal function

Correspondence to: Pinar Soysal, MD, Bezmialem Vakif University, School of Medicine, Fatih, Turkey. E-mail: dr.pinarsoysal@hotmail.com

Telephone: +90-352-3368888 **Fax:** +90-352-336-8857

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of the Renin-Angiotensin Aldosterone System (RAAS), and concentrated capacities of the kidney which may be associated with changes in postural blood pressure.^[9,10] It is assumed that these factors may be more severely affected; therefore, the development of OH may be easier in frail older people.

The aim of this study was to determine the frequency of OH in frail and pre-frail patients and the relationship between frailty and orthostatic blood pressure changes in older adults.

2 Methods

2.1 Study design

This retrospective and cross-sectional observational study included 497 elderly adults who were admitted to the geriatrics clinic at Dokuz Eylul University Hospital between January 2016 and December 2017. After obtaining informed written consent from the geriatric patients, a Comprehensive Geriatric Assessment (CGA), including the Head-up Tilt Table test (HUT), was performed.

2.2 Inclusion criteria

Patients over 65 years of age who were admitted to our centre regardless of the reason, and had none of the exclusion criteria, were included in the study.

2.3 Exclusion criteria

Patients with severe anemia (hemoglobin < 10 g/dL), critical mitral and/or aortic valve stenosis, acute or chronic renal insufficiency, decompensated cardiac and/or hepatic insufficiency, severe carotid artery stenosis and/or coronary artery stenosis, a history of a cerebrovascular incident, myocardial infarction or lower extremity fracture in the past week, hypotensive shock, bradycardia or tachycardia during examination, dehydration, electrolyte imbalance, acute hemorrhage, severe metabolic acidosis, sepsis and similar severe comorbid conditions, immobility due to severe osteoarthritis or neuromuscular disease, and delirium, all of which are contraindications for the Head-up Tilt Table test (HUT) and the Freid's frailty scale, were excluded.^[4,11]

2.4 Patient characteristics^[12]

Demographic data (age, gender, education status, marriage status) from the patients, history of falls (according to information obtained from the patient or their relative, the presence of more than one fall not associated with seizures or acute stroke in the previous year), and the presence of postural symptoms such as dizziness, blackout, nausea,

sweating, and imbalance in the upright position were collected and recorded from all patients. A history of personal chronic disease (hypertension, diabetes mellitus, coronary artery disease, congestive heart failure, cerebrovascular disease, hyperlipidemia, peripheral vascular disease, depression, Parkinson's Disease, and dementia), the type and number of medications the patients took, and polypharmacy were questioned in detail. In addition, the comorbid conditions of the patients were evaluated using the Charlson Comorbidity Index (CCI). All patients underwent a CGA including a Mini Mental State Examination (MMSE), Yesavage's Geriatric Depression Scale (YGS),^[13] Tinetti Performance Oriented Mobility Assessment (POMA), Barthel Activities of Daily Living index (ADL), Lawton-Brody Instrumental Activities of Daily Living (IADL), and Mini Nutritional Assessment-Short Form (MNA-SF).

2.5 Laboratory findings

Specific laboratory tests were performed to evaluate the biochemical, metabolic, and nutritional status of the patients. Thus, a complete blood count, kidney and liver function, cholesterol levels, thyroid-stimulating hormone (TSH), HbA1c, vitamin D, vitamin B12, and folic acid levels were obtained for laboratory records. All these biochemical tests were performed on a Diagnostic Modular Systems autoanalyser (Roche E170 and P-800, Roche Diagnostics, Germany). Serum 25-Hydroxyvitamin D [25-OH vitamin D] was measured with radioimmunoassay.

2.6 Orthostatic hypotension

The Head-up Tilt Table test was performed for the diagnosis of OH. The test was performed in the morning after the patients received their daily medications. The patients were advised not to smoke, limit caffeine intake, and not to exercise 30 min prior to the test. The latter was carefully noted and recorded. HUT was performed by the Tilt Table (Gemesan1 Tilt Table G-71, Turkey). Monitoring over the course of HUT was performed by Biolight1 BIOM69 (Australia) with reusable adult arm cuffs. After allowing the patients to rest in a 20–24 °C silent room for at least 10 minutes in the supine position, the Tilt Table was rapidly and fluently raised to a 60–80° angle. The patient's blood pressure, mean arterial blood pressure, heart rate, electrocardiogram (ECG), and pulse oximeter were monitored over the course of the HUT.^[14] The data in the 1st, 3rd, and 5th min (OH₁, OH₃, and OH₅, respectively) were recorded, and the patients were questioned whether they had postural symptoms such as dizziness, blackout, and nausea. The diagnosis of OH was made in the event of a 20 mmHg and higher decrease in systolic pressure and/or a 10 mmHg and higher

decrease in diastolic pressure during the transition from supine position to at least 60° head-up position during HUT.^[14,15] According to this definition, orthostatic blood pressure changes in the 1st, 3rd, and 5th min were evaluated by taking the data from the supine position as the basis. Additionally, the consensus definition for OH was updated in 2011 with the addition of initial and delayed OH, which is described as a sustained reduction within the first 15 s of standing and after 3 min of standing.^[16]

2.7 Frailty phenotype

The frailty was measured by Fried's physical frailty scale.^[4] The components of frailty are weakness, slowness, low level of physical activity, exhaustion, and weight loss in accordance with Fried's criteria.^[4] Patients were divided into three groups according to their frailty scales: intact (0 points), pre-frail (1–2 points) or frail (3–5 points).

2.8 Statistical analysis

Continuous variables were presented as means ± SD and were evaluated by the Kolmogorov-Smirnov test for normal distribution. Because all of the continuous variables were of non-normal distribution, they were evaluated with the Mann-Whitney *U* test. Differences between categorical variables were evaluated by the Chi-square and Fisher's exact Chi-square tests. Binary logistic regression analysis was performed for the relationship between frailty and OH₁, OH₃, and OH₅ according to age, gender, dementia, falls, and other covariates. It was also performed for the relationship between the Fried's frailty components and OH₁, OH₃, and OH₅ according to age, a disorder of balance, the presence of dementia, gait-balance test scores, ADL indices, and MNA scores. A probability < 0.05 was considered significant. All statistical analyses were performed using the SPSS 22.0 (SPSS Inc.) package program. Sufficient sample size was calculated (245 patients in a 95% confidence interval)

2.9 Ethical issues

The study was carried out in accordance with the Declaration of Helsinki and was approved by the Ethics Committee at the School of Medicine, Dokuz Eylul University in Izmir, Turkey (2017/06/15).

3 Results

Of the 496 patients admitted to our geriatric clinic, 38.6%, 41.2%, and 20.1% were in the frail, pre-frail, and robust groups, respectively. The prevalence of OH₁, OH₃, and OH₅ were 22.8%, 21.8%, and 23.1%, respectively. The

mean ages were 78.16 ± 7.00, 74.77 ± 7.13, and 71.39 ± 6.46 years in the frail, pre-frail, and robust groups, respectively. The patients' characteristics, comorbidities, laboratory findings, CGA parameters were summarized in Table 1. The rates of falls, dementia and depression, CGA parameters including gait-balance assessment tests, and ADL indices were statistically significant in the frail group compared to the pre-frail and robust groups ($P < 0.05$). Polypharmacy was higher in the frail and pre-frail groups compared to the robust group ($P < 0.05$). Alpha-blockers, anti-depressants, calcium channel blockers, and diuretic drug use were found to be higher in the frail group compared to the robust group ($P < 0.05$).

The OH₁ ratios were statistically higher in the frail group in comparison to the pre-frail and robust groups ($P < 0.05$) and higher in the pre-frail group compared to that of the robust group ($P < 0.05$). The rates of OH₃ and OH₅ were higher in the frail group compared to the pre-frail group ($P < 0.05$) (Table 2).

The frequency of OH₁ was statistically significant in the frail group compared to the robust group when adjusted for age, sex, year of education, presence of dementia, hypertension, Parkinson's disease, depression and falls, use of calcium channel blocker, alpha-blocker, diuretic and antidepressant drugs, level of hemoglobin, albumin and estimated glomerular filtration rate (GFR), and basic and instrumental ADL indices (Odds Ratio: 3.39; 95% CI: 1.08–10.59; $P = 0.032$). It was statistically significant in the frail group compared to the pre-frail group even when adjusted to the same confounders (Odds Ratio: 2.02; 95% CI: 1.14–3.55; $P = 0.015$). There was no significant difference between the pre-frail and robust group in terms of OH₁ when adjusted for the same confounding factors ($P = 0.098$) (Table 3). However, the significant relationship between frailty status and OH₃ and OH₅ disappeared, after adjusting for all covariates. Within the OH₁ groups, frequencies of robust, pre-frail, and frail people were 8.8%, 38.9%, and 52.2%, respectively. Frailty status was associated with OH₁ after adjusting for age, dementia, hypertension, up and go test, POMA score, and ADL indices (Odd Ratio: 1.66; 95% CI: 1.14–2.41; $P = 0.007$)

When the relationship between frailty components (weakness, slowness, low level of physical activity, exhaustion, and weight loss) and OH was evaluated separately and following adjustment for age, the presence of dementia, POMA, ADL indices, and MNA scores, only slowness was associated with OH₁, OH₃, and OH₅ ($P < 0.05$). However, weakness was only associated with OH₁. Other components were not associated with OH ($P > 0.05$) (Table 4).

Table 1. Comparison of demographic characteristics, comorbidities, laboratory findings and comprehensive geriatric assessment parameters according to frailty status.

	Robust (n = 99)	Prefrail (n = 205)	Frail (n = 192)	¹P value	²P value	³P value
Age, yrs	71.41 ± 6.49	74.77 ± 7.13	78.16 ± 7.00	< 0.001	< 0.001	< 0.001
Female	52.5%	69.8%	81.3%	< 0.001	0.008	0.003
Education year	8.62 ± 4.60	6.90 ± 4.47	5.39 ± 4.30	< 0.001	0.001	0.001
BMI, kg/m ²	27.61 ± 4.54	28.46 ± 4.68	28.81 ± 5.75	0.083	0.616	0.127
Comorbidities (%)						
Falls	32.7	35.1	52.9	0.001	0.001	0.710
Dementia	13.1	19.9	31.2	0.001	0.011	0.148
Cerebrovascular disease	8.1	4.9	7.3	0.809	0.313	0.268
Peripheral vascular disease	7.1	9.3	6.3	0.788	0.263	0.521
Depression	36.4	41	57.8	0.001	0.001	0.441
Hypertension	54.5	66.3	70.3	0.008	0.396	0.046
Diabetes mellitus	23.2	29.3	31.8	0.128	0.588	0.268
Hyperlipidemia	15.2	22.9	15.1	0.991	0.048	0.115
Coronary artery disease	20.2	19.5	19.3	0.850	0.952	0.887
Congestive heart failure	2	4.4	10.4	0.01	0.021	0.300
COPD	12.1	7.8	13.5	0.733	0.063	0.223
Hypothyroidism	15.2	26.8	18.2	0.510	0.041	0.023
Polypharmacy	45.5	58	61.5	0.009	0.489	0.039
Parkinson's disease	5.8	5.4	8.2	0.378	0.254	0.861
Class of drugs (%)						
ARB	29.3	34.1	35.4	0.294	0.791	0.397
ACEI	15.2	13.7	11.5	0.370	0.509	0.726
Beta-blockers	32.3	30.7	30.7	0.781	1.000	0.779
Calcium channel blockers	16.2	25.9	32.3	0.003	0.158	0.059
Diuretics	27.3	35.6	42.2	0.013	0.179	0.147
Alfa-blockers	14.1	8.8	5.7	0.015	0.243	0.153
Insulin	2	7.8	7.8	0.046	0.998	0.045
Antidepressant	31.3	36.1	44.8	0.026	0.078	0.411
Antipsychotic	3	5.4	8.3	0.130	0.241	0.363
Anti-parkinson	6.1	5.9	9.9	0.269	0.134	0.943
Laboratory findings						
Hemoglobin, g/dL	13.44 ± 1.25	12.63 ± 1.34	12.35 ± 1.32	< 0.001	0.068	< 0.001
Glucose, mg/dL	106.84 ± 38.9	112.67 ± 54.14	117.16 ± 47.83	0.005	0.029	0.283
Albumin, g/L	4.12 ± 0.33	4.04 ± 0.32	3.92 ± 0.36	< 0.001	< 0.001	0.039
TSH, mg/dL	1.46 ± 0.90	1.67 ± 1.40	1.87 ± 3.26	0.894	0.596	0.592
Vitamin B12, pg/mL	422.71 ± 365.15	420.44 ± 320.70	438.97 ± 341.23	0.294	0.953	0.306
25(OH)D, ng/mL	25.81 ± 10.07	23.51 ± 10.56	24.95 ± 16.95	0.111	0.878	0.026
Geriatric assessment						
MMSE	25.89 ± 5.16	23.81 ± 6.33	20.35 ± 6.90	< 0.001	< 0.001	0.022
YGDS	1.90 ± 2.55	2.90 ± 2.98	5.62 ± 3.86	< 0.001	< 0.001	0.003
Basic ADLs	95.43 ± 5.67	90.53 ± 9.90	79.32 ± 15.62	< 0.001	< 0.001	< 0.001
Instrumental ADLs	20.37 ± 3.74	17.94 ± 5.70	12.79 ± 6.74	< 0.001	< 0.001	< 0.001
Tinetti-Gait	11.48 ± 1.16	10.98 ± 1.59	9.02 ± 2.63	< 0.001	< 0.001	0.001
Tinetti-Balance	15.29 ± 1.42	14.59 ± 1.89	11.54 ± 3.81	< 0.001	< 0.001	< 0.001
POMA	26.77 ± 2.34	25.57 ± 3.30	20.56 ± 6.08	< 0.001	< 0.001	< 0.001
Up&Go Test	10.57 ± 3.08	12.73 ± 5.45	22.36 ± 14.61	< 0.001	< 0.001	< 0.001
MNA score	13.01 ± 1.52	12.70 ± 1.69	11.43 ± 2.35	< 0.001	< 0.001	0.029

Data are presented as mean ± SD or %. 25(OH)D: 25-hydroxyvitamin D; ACEI: angiotensin-converting enzyme inhibitor; ADLs: activities of daily living; ARB: angiotensin receptor blockers; BMI: body mass index; COPD: chronic obstructive pulmonary disease; MMSE: mini-mental state examination; POMA: performance-oriented mobility assessment; TSH: thyroid-stimulating hormone; YGDS: Yesavage Geriatric Depression Scale. ¹P: comparisons for between frail and robust group; ²P: comparisons for between frail and pre-frail group; ³P: comparisons for between pre-frail and robust group.

Table 2. Comparisons for OH₁, OH₃ and OH₅ according to frailty status.

	Fried robust (n = 99)	Fried pre-frail (n = 205)	Fried frail (n = 192)	¹ P value	² P value	³ P value
Systolic OH ₁	7.1%	17.1%	25%	< 0.001	0.05	0.018
Diastolic OH ₁	5.1%	6.8%	14.1%	0.02	0.018	0.548
OH ₁	10.1%	21.5%	30.7%	< 0.001	0.035	0.015
Systolic OH ₃	13.1%	12.7%	25.1%	0.017	0.001	0.913
Diastolic OH ₃	10.1%	5.9%	11.5%	0.715	0.044	0.180
OH ₃	19.2%	16.1%	29.3%	0.062	0.002	0.502
Systolic OH ₅	12.1%	17.1%	22.5%	0.032	0.174	0.263
Diastolic OH ₅	8.1%	6.3%	17.3%	0.033	0.001	0.575
OH ₅	17.2%	19.5%	30.4%	0.015	0.012	0.624

OH₁: Orthostatic hypotension within 1st minutes measured by head-up Tilt Table Test; OH₃: orthostatic hypotension within 3rd minutes measured by head-up Tilt Table Test; OH₅: orthostatic hypotension within the 5th min measured by head-up tilt table test. ¹P: comparisons for between frail and robust group; ²P: comparisons for between frail and pre-frail group; ³P: comparisons for between pre-frail and robust group.

Table 3. The relation between OH and frailty status by Binary Logistic Regression Analysis.

Between robust and frail group*			
Odds ratio	95% CI		P
OH ₁	3.392	1.086–10.598	0.032
OH ₃	1.008	0.395–2.557	0.986
OH ₅	1.162	0.452–2.991	0.755
Between pre-frail and frail group*			
Odds ratio	95% CI		P
OH ₁	2.025	1.144–3.585	0.015
OH ₃	1.973	1.095–3.558	0.067
OH ₅	1.568	0.893–2.754	0.117
Between pre-frail and robust group*			
Odds ratio	95% CI		P
OH ₁	2.034	0.879–4.709	0.097
OH ₃	0.517	0.241–1.109	0.090
OH ₅	0.663	0.316–1.390	0.276

*Independently age, sex, year of education, presence of dementia, hypertension, Parkinson's disease, depression and falls, use of calcium channel blocker, alpha blocker, diuretic and antidepressant drugs, level of hemoglobin, albumin and eGFR, basic and instrumental ADLs. ADLs: Barthel Activities of Daily Living index. eGFR: estimated glomerular filtration rate; OH₁: orthostatic hypotension within 1st min measured by head-up Tilt Table Test; OH₃: orthostatic hypotension within 3rd min measured by head-up Tilt Table Test; OH₅: orthostatic hypotension within the 5th min measured by head-up tilt table test.

Table 4. The relationship between OH and fried frailty components.

	OH ₁ (%)	P value	OH ₃ (%)	P value	OH ₅ (%)	P value
Exhaustion	27.0	0.077	25.5	0.113	23.9	0.757
Weight loss	25.0	0.668	32.1	0.335*	30.4	0.177
Weakness	26.3	0.046*	23.9	0.063	25.3	0.072
Slowness	29.9	0.022*	28.0	0.031*	31.0	0.030*
Low level of physical activity	27.0	0.061	25.6	0.084	28.1	0.611*

*Chi-square test and binary logistic regression analysis adjusted as age, disorder of balance, the presence of dementia, gait-balance test scores, ADLs, MNA scores. ADLs: Basic and Instrumental Activities of Daily Living index; MNA: Mini Nutritional Assessment.

4 Discussion

In this study, it has been shown that OH measured in the

first minute may be related to frailty status. The robust and pre-frail groups were similar in relation to OH₁. OH₃ and OH₅ were not associated with frailty status.

In our study, the frequency of OH was 22.8%, 21.8%, and 23.1% at the 1st, 3rd, and 5th minute, when transitioning from supine to standing position, respectively. The prevalence of OH was 30.7% in the frail people and 17.7% in the non-frail individuals. In addition, as the severity of frailty increases in older adults, the frequency of OH is also increased.^[17] Therefore, it is not surprising that in our study, OH was more common in frail older patients. As known, OH increases with age with a reported rate of 5%–30% in older adults.^[18,19] The prevalence of frailty was 38.7%. In a systematic review, the prevalence of frailty in the population ranged from 4.0% to 59.1% and increased with age.^[20] Therefore, this study is parallel to the literature in terms of both the frequency of frailty and orthostatic hypotension.

OH and frailty may be seen together in many medical situations. For example, the frequency of heart failure, dementia with Lewy Bodies, Parkinson's Disease, and malnutrition is higher in both frailty and OH.^[21–24] OH may develop with the treatment of hypertension, heart failure, and coronary heart disease, cause disability, syncope, and traumatic injuries, and substantially reduce the quality of life. Despite asymptomatic or minimal symptoms, the presence of OH independently increases mortality and the incidence of myocardial infarction, stroke, heart failure, falls, and atrial fibrillation.^[18,25] It is known that frailty is more common in those with Parkinson's disease or Dementia with Lewy bodies.^[26,27] The frequency of OH is higher in these two diseases.^[5] It is also known that there is an excess of comorbidity as a component of Fried's Frailty Scale^[4] and some comorbidities may cause OH, which may explain the relationship between frailty and OH in terms of similarity. Nutritional status may be associated with frailty and weight loss is another component of Fried's Frailty Scale.^[4] In a recent study, it was highlighted that malnutrition and malnutrition-risk might be associated with OH.^[24] On the other hand, the present study also showed that frailty can associate with OH. As such, it is important for healthcare professionals to be aware that both conditions can be a risk factor for each other.

There are several possible mechanisms for the development of frailty and OH. First, frailty has been related to impaired autonomic cardiovascular control.^[28,29] Any damage of the autonomic nervous system, such as functional or lesional, chronic or transient, causes OH which is defined as neurogenic OH.^[8] Reduced baroreceptor sensitivity was proposed as a contributing factor to OH in older adults.^[30] Baroreceptor responsiveness might be deteriorated earlier in frail people. Since autonomic dysfunction may cause immobility^[25] and malnutrition due to impaired gastrointestinal motility,^[24] the development of frailty might be easier in

frail people compared to robust ones. Therefore, autonomic dysfunction might affect both frailty and OH. Second, OH has been associated with poor peripheral motor nerve function in older adults.^[31] Slower gait speed as a part of frailty may be linked to impaired orthostatic response in elderly people. Decreased calf blood flow may impair the upright ejective ability of the skeletal muscle to pump and further contributes to the overall reduced blood flow and orthostatic intolerance in these patients.^[32] Besides, a decrease in muscle mass resulting in frailty may lead to OH by increasing venous pooling. In our study, it was emphasised that slowness and weakness are two components of sarcopenia and frailty and may be related to OH. Third, the anti-muscarinic effect of atropinic drugs can cause significant OH.^[33,34] Consequently, the anti-muscarinic effect can be a shared mechanism for frailty and OH. Fourth, inflammation is a common mechanism in frailty. Frailty and pre-frailty are associated with higher inflammatory parameters.^[35] In the literature, OH may be independently associated with systemic inflammation in nondiabetic adults.^[36] As a result, the inflammation may be a shared mechanism for explaining the relationship between frailty and OH.

The OH measurement is usually done in the third minute with the Head-up Tilt test. However, orthostatic blood pressure changes determined in the first minute might be more important for geriatric practice in a study.^[37] In our study, it was observed that the relationship between the frail group and OH measured in the first minute compared to both pre-frail and robust group was stronger, and this relationship remained independent of age. In geriatric practice, orthostatic blood pressure measurements are sufficient within the first minute for the state of frailty, and hence time loss is prevented during the examination. In addition, pre-frail individuals are similar to robust individuals according to OH. The latter suggests that necessary measures should be taken to avoid the individuals identified in the pre-frail phase from reaching the frail status.

There are a number of strengths in this study. First, orthostatic blood pressure was measured as a gold standard test for OH by the Head-up Tilt Table test. Second, the frailty status was considered to be quite extensive. The analyses were performed by removing the effects of confounding factors such as age, drug use, dementia, comorbidities, and other factors. However, there were some limitations. First, this study is a cross-sectional and observational study. Second, patients were not evaluated in terms of heart rate variability and orthostatic symptoms.

In conclusion, OH is a very widespread condition in frail older adults, especially when measured in the first minute. Frailty status might be a risk factor for OH, and both OH

and frailty may interplay and affect each other. Since frailty can exacerbate age-related physiological changes and is usually associated with other comorbidities and drugs, OH may occur in the early period by disrupting the compensatory responses to orthostatic changes. Therefore, changes in orthostatic blood pressure in the first minute may have higher clinical significance for frail older adults.

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