



Overlap between Osteosarcopenia and Frailty and their Association with Poor Health Conditions: The Bushehr Elderly Health Program

Gita Shafiee¹, Ali Sam Aryan¹, Saba Maleki Birjandi¹, Narges Zargar Balajam¹, Farshad Sharifi², Afshin Ostovar³, Noushin Fahimfar³, Iraj Nabipour⁴, Bagher Larijani⁵, Ramin Heshmat¹

¹Chronic Diseases Research Center, Endocrinology and Metabolism Population Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran
²Elderly Health Research Center, Endocrinology and Metabolism Population Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran
³Osteoporosis Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran
⁴The Persian Gulf Tropical Medicine Research Center, Bushehr University of Medical Sciences, Bushehr, Iran

⁵Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

Corresponding Author: Gita Shafiee, MD, PhD Chronic Diseases Research Center, Epidemiology, Endocrinology and Metabolism Research Institute, No. 10, Jalale-Al-Ahmad Ave, Chamran Highway, Tehran, Iran E-mail: gshafiee.endocrine@gmail.com ORCID: https://orcid.org/0000-0003-3441-3578

Ramin Heshmat, MD, PhD Chronic Diseases Research Center, Epidemiology, Endocrinology and Metabolism Research Institute, No. 10, Jalale-Al-Ahmad Ave, Chamran Highway, Tehran, Iran E-mail: rheshmat@tums.ac.ir ORCID: https://orcid.org/0000-0002-9498-6397

Received: December 29, 2023 Revised: March 17, 2024 Accepted: March 29, 2024 Background: The aim of this study was to investigate the association of osteosarcopenia with frailty and poor health conditions among older Iranian adults. Methods: This cross-sectional study analyzed data from the Bushehr Elderly Health Program. Osteosarcopenia was defined as the presence of osteopenia/osteoporosis and sarcopenia, while the Fried criteria were used to assess frailty. We assessed the history of falls and health-related quality of life (HRQoL), including physical and mental component summaries (PCS and MCS, respectively), history of fractures, activities of daily living (ADL), and instrumental activities of daily living (IADL), as indicators of poor health conditions. Results: This study included a total of 2,371 older adults. The prevalence rates of osteosarcopenia-only, frailty-only, and osteosarcopenia with frailty were 17.4%, 3%, and 4.8%, respectively. The prevalence of a history of falls, poor ADL, and poor IADL was significantly higher in the frailty-only and osteosarcopenia with frailty groups. Osteosarcopenia with frailty was significantly associated with a history of falls (adjusted odds ratio [adjOR]=1.94; 95% confidence interval [CI], 1.20-3.15), poor ADL (adjOR=2.85; 95% CI, 1.81-4.50), and poor IADL (adjOR=5.09; 95% Cl, 2.85–9.11). However, the frailty-only group also showed an association with falls and poor ADL and IADL. Only osteosarcopenia was associated with an increased OR for fracture. Frailty had the greatest effect on the MCS and PCS scores, whereas osteosarcopenia with frailty had a moderate impact. Conclusion: Osteosarcopenia with frailty significantly increased the odds of falls, poor ADL, poor IADL, and lower HRQoL compared with the robust group. Combined osteosarcopenia and frailty were not associated with poor health. These findings indicate the importance of diagnosing osteosarcopenia and frailty as separate entities to provide appropriate interventions and treatment.

Key Words: Osteosarcopenia, Frailty, Quality of life, Accidental Falls, Fractures, Bone, Disability Evaluation

INTRODUCTION

Aging leads to changes in body mass composition and can increase the risk of chronic diseases such as osteoporosis and sarcopenia.¹⁾ These diseases share common mechanisms, risk factors, and adverse outcomes. The coexistence of both conditions, known as osteosarcopenia, can occur in many older adults. Moreover, the risks of falls, fractures, and mortality are higher than those associated with either disease alone. Therefore, the concomitant occurrence of sarcopenia and osteoporosis may have additive effects on ad-

^{© 2024} by The Korean Geriatrics Society

This is an open access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (https://creativecommons.org/licenses/by-nc/4.0/) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

verse outcomes.²⁾

Frailty is another increasingly prevalent aging syndrome characterized by the inability of body systems to maintain homeostasis³⁾ in response to stressors such as pain or psychologically stressful incidents.⁴⁾ Frailty often manifests as the deterioration of cognitive function, muscle, nervous system, and cardiopulmonary reserve.⁵⁾

These two geriatric syndromes, osteosarcopenia and frailty, are musculoskeletal conditions causing devastating morbidity and mortality in older adults.⁶⁾ The prevalence of osteosarcopenia varies from 11% to 30% among community-dwelling older adults.^{7,8)} In addition, the prevalence of frailty increases with age, independent of the tools used to assess this condition, ranging from 4% to 59% in older adults.⁹⁾ Moreover, both disorders are commonly associated with adverse outcomes.^{10,11)}

Factors such as inflammation, hormonal imbalance, and malnutrition lead to musculoskeletal aging and frailty syndrome.¹²⁾ Additionally, many older adults have coexistence of some geriatric syndromes. Identifying the link between osteosarcopenia and frailty may inform the implementation of effective interventions to prevent and control chronic diseases, improve quality of life, and reduce disability and death among older adults.

Therefore, the present study aimed to determine the overlap between osteosarcopenia and frailty and its association with poor health conditions in older adults.

MATERIALS AND METHODS

Study Population

This cross-sectional study included 2,426 older adults in the second stage of the Bushehr Elderly Health (BEH) Program, a population-based prospective cohort study. This program aims to assess the incidence of non-communicable diseases and their risk factors among men and women aged > 60 years. The participants were selected for phase one based on multi-stage randomized sampling in Bushehr, Iran.¹³⁾

The prevalence of cardiovascular risk factors was investigated in 3,000 older people in the first phase of the BEH Program. The second stage of the first phase of the study was conducted 2.5 years later on eligible people from the first stage, and examined cognitive and musculoskeletal disorders.¹⁴⁾ The study included older adults ≥ 60 years of age of both sexes with sufficient physical and mental ability to participate. The exclusion criterion was the absence of a residence in Bushehr.

The Research Ethics Committee of Bushehr University of Medical Sciences and the Endocrinology & Metabolic Metabolism Research Institute approved this study (IR.TUMS.EMRI.REC. I 394.0036). All participants provided written informed consent. Also, this study complied the ethical guidelines for authorship and publishing in the *Annals of Geriatric Medicine and Research*.¹⁵⁾

Measurements

Trained personnel interviewed the participants privately and faceto-face using valid questionnaires. Initially, information on sociodemographic characteristics, lifestyle factors, general health, medical history, mental and functional health, and medication use was collected.¹⁴⁾ Height and weight were measured with a fixed stadiometer and digital scale, respectively, with shoes removed and the participants wearing lightweight clothing. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2) . Waist circumference (WC) was recorded midway between the iliac crest and the lowest rib with the participants in a standing position. After 15 minutes in a sitting position, systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured on the right arm, with the average of the two measurements considered the participant's blood pressure. Daily dietary intake was assessed using a 24-hour dietary recall questionnaire. Physical activity levels were assessed using the Physical Activity questionnaire described by Aadahl and Jorgensen.¹⁶⁾

Body composition was measured using dual X-ray absorptiometry (DXA Discovery Wi; Hologic Inc., Waltham, MA, USA). The bone mineral density of the lumbar spine (L1–4) and total hip were measured in the correct position. The appendicular skeletal muscle mass (ASM) for each participant was derived as the sum of the upper and lower limb muscle masses, and the skeletal muscle mass index (SMI) was calculated as ASM/height² (kg/m²). Muscle strength was measured based on handgrip strength using a digital dynamometer. The measurement was performed three times for each hand, and the maximum grip strength was calculated by taking the average of the highest measurements from both hands. The usual walking speed (m/s) on a 4.57-m course was used as an objective measure of physical performance.

Blood samples were collected from each participant for biochemical analyses after overnight fasting. Details of the measurements of fasting plasma glucose (FPG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglyceride (TG) levels in this population have been reported elsewhere.¹⁴⁾

Definitions of Terms

The coexistence of osteopenia/osteoporosis and sarcopenia was defined as osteosarcopenia. Participants with a T-score > -2.5 standard deviation (SD) and < -1.0 SD of the average value of normal young adults in either the femoral neck, lumber spine or total hip densitometry were defined as having osteopenia while those with

a T-score \leq -2.5 SD were defined as having osteoporosis.¹⁷⁾ Sarcopenia was defined according to the European Working Group on Sarcopenia in Older People (EWGSOP-2) guidelines as follows: low handgrip strength, slow gait speed, and low SMI.¹⁸⁾ The muscle strength cutoff was < 26 kg for men and < 18 kg for women. Furthermore, the cutoff for low physical function was difficulty in normal walking at a speed of < 0.8 m/s for both sexes.¹⁹⁾ A low SMI was defined as < 7.0 kg/m² for men and 5.4 kg/m² for women based on Iranian cutoff values.²⁰⁾ Frailty was determined based on the criteria defined by Fried et al.,²¹⁾ with \geq 3 of the following components present: unintended weight loss, exhaustion, low muscle strength, slow gait speed, and low physical activity. In this study, we classified the participants into four groups: robust (without osteosarcopenia and frailty), osteosarcopenia-only, frailty-only, and osteosarcopenia with frailty.

We defined diabetes mellitus as current FPG $\geq 126 \text{ mg/dL}$, glycated hemoglobin (HbA1c) ≥ 6.5 , the participant's self-report of diabetes mellitus based on a doctor's diagnosis, or current use of anti-diabetic drugs.²²⁾ Hypertension was defined as current SBP $\geq 140 \text{ mmHg or DBP} \geq 90 \text{ mmHg}$, the participant's self-report of hypertension based on a doctor's diagnosis, or the current use of anti-hypertension drugs.²³⁾ Smoking refers to the current use of cigarettes or waterpipes. High WC was defined as a WC > 102 cm in men and > 88 cm in women. Low HDL-C was defined as HDL-C < 40 mg/dL in men and < 50 mg/dL in women. High LDL-C was defined as LDL-C $\geq 110 \text{ mg/dL}$ and high serum TG as serum TG $\geq 150 \text{ mg/dL}$.²⁴⁾

Outcomes

A history of falling was defined as a self-reported unintentional fall on the ground in the previous year.²⁵⁾ History of fracture was defined as a self-reported fracture after 45 years of age.²⁶⁾

Health-related quality of life (HRQoL) was assessed using a translated and validated Persian version of the 12-item Short-Form Health Survey (SF-12). The SF-12 is a self-reported generic HRQoL measure consisting of 12 questions that can be scored to provide a physical component summary (PCS) score and a mental component summary (MCS) score. The PCS subscale measures physical problems, pain, and self-rated health, while the MCS subscale measures daily functioning related to psychological issues and vitality. The subscale scores range from 0 to 100, with higher scores indicating a greater HRQoL.²⁷⁾

The degree of disability was measured using two questionnaires: activities of daily living (ADL) and instrumental activities of daily living (IADL), which have previously been validated and translated in Iran.²⁸⁾ Participants with total ADL scores < 95 were considered to have poor ADL, while those with total IADL scores ≤ 7

were considered to be dependent.^{29,30)}

Statistical Analysis

The data are presented as mean ± SD and as percentages for continuous and categorical variables, respectively. To compare the data between groups (robust, osteosarcopenia-only, frailty-only, and osteosarcopenia with frailty), we applied analysis of variance and Pearson chi-square test to continuous variables and categorical data, respectively. We used logistic regression analysis to assess the associations between poor health conditions (falls, history of fracture, poor ADL, and poor IADL) and osteosarcopenia-frailty groups. In addition, we used multivariate linear regression to test for osteosarcopenia and frailty status on the MCS and PCS of the HRQoL.

All multivariate analyses included variables with p < 0.2; the final significance level for multivariate analyses was p < 0.05. All tests were two-sided, we defined p < 0.05 as statistically significant. We performed the statistical analyses using Stata 16 software (StataCorp, College Station, TX, USA).

RESULTS

After excluding participants with missing values for osteosarcopenia or frailty (n = 55), the analysis included 2,371 older adults. The prevalence rates of osteosarcopenia-only, frailty-only, and osteosarcopenia with frailty were 17.4% (n = 413), 3% (n = 71), and 4.8% (n = 114), respectively. Table 1 illustrates the baseline characteristics of the participants according to their osteosarcopenia and frailty statuses. Participants with osteosarcopenia and frailty were older and had lower BMI and energy and protein intakes than those in the other groups (p < 0.001). Furthermore, this and the frailty-only group had lower levels of physical activity than the other groups. In addition, the frailty scores were significantly higher in both the frailty-only and osteosarcopenia with frailty groups than in the robust group (p < 0.001).

Fig. 1 shows the prevalence of poor health among the four groups according to the osteosarcopenia and frailty statuses. The prevalence of a history of falls, poor ADL, and poor IADL was significantly higher in both the frailty-only and osteosarcopenia with frailty groups than in the robust group (p < 0.001). However, the prevalence of fractures in each of the groups was the same and was higher than that in the robust group. In addition, the scores of the HRQoL components differed significantly between the groups. The MCS ($50.00 \pm 13.32 \text{ vs. } 59.30 \pm 9.16$; p < 0.001) and PCS ($39.19 \pm 8.80 \text{ vs. } 53.43 \pm 8.40$; p < 0.001) scores in the frailty-only group were lower compared with the robust group (data not shown).

The odds ratios for poor health conditions in the osteosarcope-

	Osteosarcopenia_frailty status				1
	Robust (n = 1,773)	Osteosarcopenia only $(n = 413)$	Frailty only $(n = 71)$	Osteosarcopenia with frailty $(n = 114)$	p-value
Sex, male	892 (50.3)	189 (45.8)	24 (33.8)	50 (43.9)	0.014
Age (y)	67.87 ± 5.15	72.14 ± 6.85	74.75 ± 8.76	77.16 ± 7.78	< 0.001
Education (y)	5.85 ± 5.11	3.73 ± 4.43	3.01 ± 4.44	2.86 ± 3.84	< 0.001
Current smoking (%)	357 (20.2)	103 (24.9)	16 (22.5)	21 (18.4)	0.159
Physical activity (%)	476 (26.8)	67 (16.2)	3 (4.2)	5 (4.4)	< 0.001
Protein intake (gr)	56.93 ± 23.94	51.81 ± 23.88	48.78 ± 20.39	45.68 ± 22.25	< 0.001
Energy intake (kcal)	1,637.14±581.82	$1,517.47 \pm 567.26$	$1,448.23 \pm 549.42$	1,337.77±553.93	< 0.001
$BMI(kg/m^2)$	28.53 ± 4.62	24.04 ± 3.10	27.58 ± 5.77	23.37 ± 3.46	< 0.001
High TG (%)	602 (34.0)	110 (26.6)	19 (26.8)	21 (18.6)	< 0.001
High LDL-C (%)	517 (29.2)	126 (30.5)	18 (25.4)	40 (35.4)	0.431
Low HDL-C (%)	867 (48.9)	185 (44.8)	36 (50.7)	59 (52.2)	0.371
High WC (%)	1,111 (62.7)	167 (40.4)	47 (66.2)	40 (35.1)	< 0.001
Hypertension (%)	1,306 (73.7)	282 (68.3)	55 (77.5)	85 (74.6)	0.114
Diabetes (%)	567 (32.0)	141 (34.1)	28 (39.4)	32 (28.3)	0.367
Frailty scores	0 (0–1)	1 (0–2)	3 (3–4)	3 (3–4)	< 0.001

Table 1. Demographic and clinical characteristics of the study participants

Values are presented as number (%) or mean±standard deviation or median (interquartile range).

BMI, body mass index; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; WC, waist circumference.





nia-only, frailty-only, and osteosarcopenia with frailty groups among older adults are shown in Table 2.

Osteosarcopenia with frailty was significantly associated with a history of falls (adjusted odds ratio [adjOR] = 1.94; 95% confidence interval [CI], 1.20–3.15), poor ADL (adjOR = 2.85; 95% CI, 1.81–4.50), and poor IADL (adjOR = 5.09; 95% CI, 2.85–9.11) in the crude and full models. However, frailty-only was associated with a history of falls and poor ADL and IADL in the crude and adjusted models. Regarding the association between a history of fracture and osteosarcopenia and frailty status, only the osteosarcopenia-only group showed an increased OR of fracture in the

crude and full models (adjOR = 1.48; 95% CI, 1.10–1.98).

Regarding the quality of life, frailty-only showed the greatest effect on MCS and PCS scores (β = -9.62 [95% CI, -12.19 to -7.05] and β = -10.68 [95% CI, -12.74 to -8.62], respectively), while osteosarcopenia with frailty had a moderate impact on MCS and PCS scores (β = - 5.25 [95% CI, -7.48 to - 3.02] and β = -7.99 [95% CI, -9.74 to -6.16], respectively).

DISCUSSION

The results of this study demonstrated the overlap of osteosarco-

		Crude model	Full model ^{a)}
History of falls	Robust	Ref.	Ref.
	Osteosarcopenia only	1.14 (0.87, 1.51)	1.18 (0.87, 1.60)
	Frailty only	1.88 (1.10, 3.23)	1.80 (1.03, 3.16)
	Osteosarcopenia with frailty	1.76 (1.13, 2.73)	1.94 (1.20, 3.15)
History of fracture	Robust	Ref.	Ref.
	Osteosarcopenia only	1.38 (1.08, 1.76)	1.48 (1.10, 1.98)
	Frailty only	1.44 (0.85, 2.45)	1.43 (0.80, 2.56)
	Osteosarcopenia with frailty	1.44 (0.94, 2.20)	1.38 (0.83, 2.31)
Poor ADL	Robust	Ref.	Ref.
	Osteosarcopenia only	1.03 (0.79, 1.35)	0.75 (0.55, 1.02)
	Frailty only	6.48 (3.95, 10.63)	3.78 (2.17, 6.58)
	Osteosarcopenia with frailty	4.69 (3.18, 6.93)	2.85 (1.81, 4.50)
Poor IADL	Robust	Ref.	Ref.
	Osteosarcopenia only	1.84 (1.46, 2.32)	1.16 (0.87-1.55)
	Frailty only	9.38 (5.36, 16.42)	4.84 (2.58, 9.10)
	Osteosarcopenia with frailty	11.56 (7.20, 18.56)	5.09 (2.85, 9.11)
MCS score of QoL	Robust	Ref.	Ref.
	Osteosarcopenia only	0.35 (-0.71, -1.40)	-0.54 (-1.80, -0.73)
	Frailty only	-9.03 (-11.37, -6.70)	-9.62 (-12.19, -7.05)
	Osteosarcopenia with frailty	-2.44 (-4.30, -0.59)	-5.25 (-7.48, -3.02)
PCS score of QoL	Robust	Ref.	Ref.
	Osteosarcopenia only	-0.99 (-1.90, -0.08)	0.57 (-0.44, -1.59)
	Frailty only	-14.25 (-16.26, -12.23)	-10.68 (-12.74, -8.62)
	Osteosarcopenia with frailty	-11.08 (-12.67, -9.48)	-7.99 (-9.74, -6.16)

 Table 2. Association osteosarcopenia
 frailty status with poor health conditions

Values are presented as adjusted odds ratio (95% confidence interval) in multivariate logistic regression or linear regression analyses. Bold font indicates statistical significance.

ADL, activity of daily living; IADL, instrumental activity of daily living; QoL, quality of life; MCS, mental component summary; PCS, physical component summary.

^{a)}In full model, the outcome variables of each health condition: history of falls (age, sex, smoking, education, high waist circumference, diabetes, physical activity), history of fracture (age, sex, education, high waist circumference, diabetes, protein intake, energy intake, Ca/VitD supplement), poor ADL (age, sex, smoking, education, high waist circumference, diabetes, physical activity, hypertension, protein intake, energy intake), poor IADL (age, sex, smoking, education, high waist circumference, diabetes, physical activity, hypertension, protein intake, energy intake, Ca/VitD supplement), MCS (age, sex, smoking, education, high waist circumference, diabetes, physical activity, protein intake, energy intake, Ca/VitD supplement), and PCS (age, sex, smoking, education, high waist circumference, diabetes, physical activity, protein intake, energy intake, Ca/VitD supplement), and PCS (age, sex, smoking, education, high waist circumference, diabetes, physical activity, protein intake, energy intake, Ca/VitD supplement).

penia with frailty and its association with poor health conditions in a population of community-dwelling older adults in Bushehr, Iran. Our findings revealed that the prevalence of coexisting osteosarcopenia with frailty was 4.8%, while the prevalence of frailty-only and osteosarcopenia was 3% and 17.4%, respectively.

Osteosarcopenia and frailty are closely associated with common factors such as lifestyle behaviors, nutritional status, genetic predisposition, hormones, and biological pathways.³¹⁾ The dysregulation of the growth hormone (GH)/insulin-like growth factor1 (IGF-1) pathway plays an essential role in the pathogeneses of osteoporosis, sarcopenia, and frailty.^{32,33)} In addition, our data showed poorer energy and protein intake among patients with osteosarcopenia and frailty compared with those with osteosarcopenia or frailty alone. These findings are consistent with those of previous studies that revealed that nutrition mediates the relationship between osteosar-

copenia and frailty.^{31,34)}

Little is known about the natural histories of frailty and osteosarcopenia. The overlap between frailty and sarcopenia was discussed in the EWGSOP consensus, which showed that most frail participants had sarcopenia as a parameter of osteosarcopenia and vice versa. Our findings revealed a low coexistence of osteosarcopenia and frailty compared to osteosarcopenia only (4.8% vs. 17.4%). The different definitions and methodologies of osteosarcopenia and frailty used across studies make it difficult to compare results. Muscle strength is included in the definitions of both disorders. However, the cutoff points of this parameter differ between osteosarcopenia and frailty definitions.^{35,36)} In addition to muscle function, other components of frailty are independent of the musculoskeletal system. In our study, this discrepancy can be explained by the fact that the mean age of our study population was 69.3 years and relatively few participants in this age range showed frailty; in contrast, musculoskeletal diseases were observed more frequently. Moreover, our population comprised community-dwelling older adults; thus, people in care settings who were more likely to have frailty were not included. In addition, while people with osteopenia were included in the definition of osteosarcopenia, those with prefrailty were not considered.

Frailty and osteosarcopenia are potential risk factors for poor health conditions, such as functional decline, disability, poor quality of life, and mortality.^{37,38)} In this study, we assessed the risk of adverse outcomes in patients with combined osteosarcopenia and frailty compared with those with osteosarcopenia alone, frailty alone, or neither. Unintentional falls are a major health problem in older people and impose high health-related costs and morbidity.³⁹⁾ Osteosarcopenia is strongly associated with falls and fractures.⁴⁰⁾ Osteoporosis and sarcopenia interact through biomarkers such as osteokines, myokines, and adipokines. However, frailty increases the risk of falls and fractures in older people.⁴¹⁾

Declines in gonadal hormone, vitamin D, GH, and IGF-1 levels and elevations in pro-inflammatory cytokine levels and malnutrition may be important markers for the association between frailty and adverse outcomes. Our data showed that frailty alone and osteosarcopenia with frailty were associated with falls, with ORs of 1.80 and 1.94, respectively, compared with the robust group. In addition, the OR of fracture increased in patients with osteosarcopenia alone compared with the other groups. Osteoporosis is a risk factor for fractures, while sarcopenia is a risk factor for falls.^{42,43)} However, as most people who experience a fracture do not have a body mineral density (BMD) reaching the threshold for osteoporosis,⁴⁴⁾ increased attention is needed in people with BMD less than -1 SD (osteopenia). Our reanalysis of the association between osteosarcopenia and health-related outcomes based on the definition of osteoporosis showed similar results using only osteoporosis to define osteosarcopenia, thus demonstrating that osteopenia/osteoporosis along with sarcopenia are risk factors for poor health conditions (Supplementary Table S1).

Therefore, muscle mass and function, which are used to define frailty, may be important predictors of falls. Other frailty parameters such as weight loss, exhaustion, and low activity are also important factors for falls. Therefore, in our study, frailty alone was more important than osteosarcopenia in terms of fall risk. In contrast, low bone mass (osteoporosis) plays a critical role in fractures, and frailty is not an essential risk factor compared with osteosarcopenia.

We evaluated functional disability using the Barthel and Lawton scales for ADL and IADL, respectively. The results of the crude and adjusted models suggested a significant association between frailty and ADL disability in this population. This association was stronger in the frail-only group than that in the osteosarcopenia with frailty group. In addition, osteosarcopenia with frailty and, to a lesser degree, frailty alone were powerful and independent predictors of developing dependence in IADL (osteosarcopenia with frailty, adjOR = 5.09; frailty-only, adjOR = 4.84). These results confirm that frailty is associated with a higher risk of disability than osteosarcopenia in our population. This is consistent with the results of previous studies showing that frailty is associated with functional disability.^{45,46)} However, while some studies have shown an association between osteosarcopenia and disability,^{47,48)} in our study, osteosarcopenia was only associated with IADL and not with ADL. Both osteosarcopenia and frailty are associated with disability; however, our results showed that the role of frailty was more prominent and significant when these two disorders were combined.

Our findings revealed significantly lower physical and mental HRQoL in the frail-only and osteosarcopenia with frailty groups than in the robust group. Previous studies have shown that low muscle strength and physical performance are related to reductions in both components of HRQoL.⁴⁹⁾ Both factors were lower in the osteosarcopenia and frailty groups in the present study. In addition, exhaustion, as a component of frailty, through psychological and immunological mechanisms such as increased cytokine production, contributes to low HRQoL.⁵⁰⁾ Thus, our results showed that frailty had a greater role in reducing HRQoL and that frailty should be diagnosed at an early stage in older people.

This population-based study with a large sample size revealed an overlap between osteosarcopenia and frailty in older adults. To our knowledge, this is the first study to demonstrate the effect of the coexistence of two important geriatric syndromes on poor health conditions in Iran. However, this study has some limitations. While our study results showed a cross-sectional association between osteosarcopenia and frailty in poor health conditions, we could not make causal inferences, and further longitudinal studies are needed. Additionally, disability was measured using two self-reported scales based on limitations in ADL and IADL. The main disadvantage of self-reported questionnaires is the possibility of invalid answers. In the BEH study, we attempted to ask sensitive and important questions to the participants' companions and minimize information bias. In addition, the fracture data were based on history and self-reports and not on radiographic views. These points should be considered when interpreting the results of this study.

In conclusion, the results of this study demonstrated that older adults with osteosarcopenia with frailty and frailty alone were associated with significantly increased falls, poor ADL, poor IADL, and lower physical and mental HRQoL compared with robust older adults. The limited overlap of osteosarcopenia and frailty in our population suggests that combined assessments have no additional odds of detecting poor health conditions. Osteosarcopenia affects only the musculoskeletal system, whereas frailty is a multifactorial and complex disorder. Thus, frailty has a higher incidence of functional disorders than osteosarcopenia, and the odds of skeletal disorders such as fractures are higher in individuals with osteosarcopenia alone. Our findings highlight the importance of early diagnosis and intervention strategies for osteosarcopenia and frailty as separate entities. Comprehensive clinical guidelines are recommended for use in primary healthcare or community-based health promotion settings to facilitate early identification and lifestyle interventions. Routine screening for osteosarcopenia and frailty is recommended in all people aged ≥ 60 years. In addition, raising awareness among health and social care professionals, healthcare policymakers, and older adults regarding geriatric disorders may help in diagnosing and treating individuals with osteosarcopenia or frailty and decrease the risk of their developing poor health conditions.

ACKNOWLEDGMENTS

We thank the personnel of the Persian Gulf Tropical Medicine Research Center and the study participants.

CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

FUNDING

None.

AUTHOR CONTRIBUTIONS

Conceptualization, GS, RH; Data curation, AO; Investigation, NF; Methodology, SMB, FS; Project administration, IN; Supervision, BL; Writing–original draft, ASA; Writing–review & editing, NZB. All authors read and approved the final manuscript.

SUPPLEMENTARY MATERIALS

Supplementary materials can be found via https://doi.org/ 10.4235/agmr.23.0220.

REFERENCES

- 1. Dawson A, Dennison E. Measuring the musculoskeletal aging phenotype. Maturitas 2016;93:13-7.
- 2. Drey M, Sieber CC, Bertsch T, Bauer JM; Schmidmaier R; FiAT

intervention group. Osteosarcopenia is more than sarcopenia and osteopenia alone. Aging Clin Exp Res 2016;28:895-9.

- **3.** Thompson C, Dodds RM. The ageing syndromes of sarcopenia and frailty. Medicine 2021;49:6-9.
- 4. Morley JE, Vellas B, van Kan GA, Anker SD, Bauer JM, Bernabei R, et al. Frailty consensus: a call to action. J Am Med Dir Assoc 2013;14:392-7.
- 5. Abellan van Kan G, Rolland YM, Morley JE, Vellas B. Frailty: toward a clinical definition. J Am Med Dir Assoc 2008;9:71-2.
- 6. Paintin J, Cooper C, Dennison E. Osteosarcopenia. Br J Hosp Med (Lond) 2018;79:253-8.
- 7. Fahimfar N, Zahedi Tajrishi F, Gharibzadeh S, Shafiee G, Tanha K, Heshmat R, et al. Prevalence of osteosarcopenia and its association with cardiovascular risk factors in Iranian older people: Bushehr Elderly Health (BEH) program. Calcif Tissue Int 2020;106:364-70.
- **8.** Inoue T, Maeda K, Satake S, Matsui Y, Arai H. Osteosarcopenia, the co-existence of osteoporosis and sarcopenia, is associated with social frailty in older adults. Aging Clin Exp Res 2022; 34:535-43.
- 9. Rohrmann S. Epidemiology of frailty in older people. Adv Exp Med Biol 2020;1216:21-7.
- 10. Salech F, Marquez C, Lera L, Angel B, Saguez R, Albala C. Osteosarcopenia predicts falls, fractures, and mortality in Chilean community-dwelling older adults. J Am Med Dir Assoc 2021; 22:853-8.
- Pohl JS, Cochrane BB, Schepp KG, Woods NF. Falls and social isolation of older adults in the national health and aging trends study. Res Gerontol Nurs 2018;11:61-70.
- Greco EA, Pietschmann P, Migliaccio S. Osteoporosis and sarcopenia increase frailty syndrome in the elderly. Front Endocrinol (Lausanne) 2019;10:255.
- 13. Ostovar A, Nabipour I, Larijani B, Heshmat R, Darabi H, Vahdat K, et al. Bushehr Elderly Health (BEH) programme, phase I (cardiovascular system). BMJ Open 2015;5:e009597.
- 14. Shafiee G, Ostovar A, Heshmat R, Darabi H, Sharifi F, Raeisi A, et al. Bushehr Elderly Health (BEH) programme: study protocol and design of musculoskeletal system and cognitive function (stage II). BMJ Open 2017;7:e013606.
- 15. Noh JH, Jung HW, Ga H, Lim JY. Ethical guidelines for publishing in the Annals of Geriatric Medicine and Research. Ann Geriatr Med Res 2022;26:1-3.
- 16. Aadahl M, Jorgensen T. Validation of a new self-report instrument for measuring physical activity. Med Sci Sports Exerc 2003;35:1196-202.
- 17. Akkawi I, Zmerly H. Osteoporosis: current concepts. Joints 2018;6:122-7.

- 18. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyere O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing 2019;48:601.
- Chen LK, Liu LK, Woo J, Assantachai P, Auyeung TW, Bahyah KS, et al. Sarcopenia in Asia: consensus report of the Asian Working Group for Sarcopenia. J Am Med Dir Assoc 2014; 15:95-101.
- 20. Shafiee G, Ostovar A, Heshmat R, Keshtkar AA, Sharifi F, Shadman Z, et al. Appendicular skeletal muscle mass reference values and the peak muscle mass to identify sarcopenia among Iranian healthy population. Int J Prev Med 2018;9:25.
- 21. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001;56:M146-56.
- 22. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2014;37 Suppl 1:S81-90.
- 23. Williams B, Mancia G, Spiering W, Rosei EA, Azizi M, Burnier M, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension. Kardiol Pol 2019;77:71-159.
- 24. Grundy SM, Brewer HB Jr, Cleeman JI, Smith SC Jr; Lenfant C; American Heart Association, et al. Definition of metabolic syndrome: report of the National Heart, Lung, and Blood Institute/ American Heart Association conference on scientific issues related to definition. Circulation 2004;109:433-8.
- 25. Pasquetti P, Apicella L, Mangone G. Pathogenesis and treatment of falls in elderly. Clin Cases Miner Bone Metab 2014;11:222-5.
- **26**. Gregson CL, Dennison EM, Compston JE, Adami S, Adachi JD, Anderson FA Jr, et al. Disease-specific perception of fracture risk and incident fracture rates: GLOW cohort study. Osteoporos Int 2014;25:85-95.
- 27. Montazeri A, Vahdaninia M, Mousavi SJ, Omidvari S. The Iranian version of 12-item Short Form Health Survey (SF-12): factor structure, internal consistency and construct validity. BMC Public Health 2009;9:341.
- 28. Hassani Mehraban A, Soltanmohamadi Y, Akbarfahimi M, Taghizadeh G. Validity and reliability of the Persian version of Lawton Instrumental Activities of Daily Living Scale in patients with dementia. Med J Islam Repub Iran 2014;28:25.
- **29.** Instrumental Activities of Daily Living (IADL) Scale. Self-rated version. Incorporated in the Philadelphia Geriatric Center. Multilevel Assessment Instrument (MAI). Psychopharmacol Bull 1988;24:789-91.
- **30.** Wade DT, Collin C. The Barthel ADL Index: a standard measure of physical disability? Int Disabil Stud 1988;10:64-7.
- **31.** Chew J, Yeo A, Yew S, Tan CN, Lim JP, Hafizah Ismail N, et al. Nutrition mediates the relationship between osteosarcopenia and frailty: a pathway analysis. Nutrients 2020;12:2957.

- 32. Perrini S, Laviola L, Carreira MC, Cignarelli A, Natalicchio A, Giorgino F. The GH/IGF1 axis and signaling pathways in the muscle and bone: mechanisms underlying age-related skeletal muscle wasting and osteoporosis. J Endocrinol 2010;205:201-10.
- 33. Chew J, Tay L, Lim JP, Leung BP, Yeo A, Yew S, et al. Serum myostatin and IGF-1 as gender-specific biomarkers of frailty and low muscle mass in community-dwelling older adults. J Nutr Health Aging 2019;23:979-86.
- **34.** O'Connell ML, Coppinger T, McCarthy AL. The role of nutrition and physical activity in frailty: a review. Clin Nutr ESPEN 2020;35:1-11.
- **35.** Mijnarends DM, Schols JM, Meijers JM, Tan FE, Verlaan S, Luiking YC, et al. Instruments to assess sarcopenia and physical frailty in older people living in a community (care) setting: similarities and discrepancies. J Am Med Dir Assoc 2015;16:301-8.
- **36**. Spira D, Buchmann N, Nikolov J, Demuth I, Steinhagen-Thiessen E, Eckardt R, et al. Association of low lean mass with frailty and physical performance: a comparison between two operational definitions of sarcopenia-data from the Berlin Aging Study II (BASE-II). J Gerontol A Biol Sci Med Sci 2015;70:779-84.
- **37.** Inoue T, Maeda K, Nagano A, Shimizu A, Ueshima J, Murotani K, et al. Related factors and clinical outcomes of osteosarcopenia: a narrative review. Nutrients 2021;13:291.
- 38. Cunha AIL, Veronese N, de Melo Borges S, Ricci NA. Frailty as a predictor of adverse outcomes in hospitalized older adults: a systematic review and meta-analysis. Ageing Res Rev 2019;56: 100960.
- **39.** Kwan MM, Close JC, Wong AK, Lord SR. Falls incidence, risk factors, and consequences in Chinese older people: a systematic review. J Am Geriatr Soc 2011;59:536-43.
- **40.** Teng Z, Zhu Y, Teng Y, Long Q, Hao Q, Yu X, et al. The analysis of osteosarcopenia as a risk factor for fractures, mortality, and falls. Osteoporos Int 2021;32:2173-83.
- 41. Tom SE, Adachi JD, Anderson FA Jr, Boonen S, Chapurlat RD, Compston JE, et al. Frailty and fracture, disability, and falls: a multiple country study from the global longitudinal study of osteoporosis in women. J Am Geriatr Soc 2013;61:327-34.
- 42. Hirschfeld HP, Kinsella R, Duque G. Osteosarcopenia: where bone, muscle, and fat collide. Osteoporos Int 2017;28:2781-90.
- **43.** Kirk B, Zanker J, Duque G. Osteosarcopenia: epidemiology, diagnosis, and treatment-facts and numbers. J Cachexia Sarcopenia Muscle 2020;11:609-18.
- 44. Tomasevic-Todorovic S, Vazic A, Issaka A, Hanna F. Comparative assessment of fracture risk among osteoporosis and osteopenia patients: a cross-sectional study. Open Access Rheumatol 2018;10:61-6.

- **45.** Sanchez-Garcia S, Garcia-Pena C, Salva A, Sanchez-Arenas R, Granados-Garcia V, Cuadros-Moreno J, et al. Frailty in community-dwelling older adults: association with adverse outcomes. Clin Interv Aging 2017;12:1003-11.
- **46.** Nguyen TT, Nguyen AT, Vu TT, Dau NT, Nguyen PQ, Nguyen TX, et al. Association of frailty status and functional disability among community-dwelling people aged 80 and older in Vietnam. Biomed Res Int 2021;2021:7109452.
- 47. Lopez-Teros MT, Rosas-Carrasco O, Sanchez-Garcia S, Castro-Porras L, Luna-Lopez A, Agudelo-Botero M. The association of osteosarcopenia with functional disability in communi-

ty-dwelling Mexican adults 50 and older. Front Med (Lausanne) 2021;8:674724.

- 48. Laskou F, Patel H, Cooper C, Dennison E. Functional capacity, sarcopenia, and bone health. Best Pract Res Clin Rheumatol 2022;36:101756.
- 49. Rizzoli R, Reginster JY, Arnal JF, Bautmans I, Beaudart C, Bischoff-Ferrari H, et al. Quality of life in sarcopenia and frailty. Calcif Tissue Int 2013;93:101-20.
- **50.** Fillit H, Butler RN. The frailty identity crisis. J Am Geriatr Soc 2009;57:348-52.