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Frailty syndrome in women with osteoporosis, should physicians consider screening? A cross-sectional study

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ABSTRACT

Despite its high prevalence and profound impact, frailty syndrome often goes undiagnosed. The study revealed a significant correlation between osteoporosis and frailty syndrome, with predictive accuracy exceeding 75 %. Given these findings and the existing recommendation for osteoporosis screening in older women, we underscore the importance of concurrently screening osteoporotic women for frailty.

Introduction: Frailty syndrome, a prevalent and significant geriatric condition, impacts healthcare costs and quality of life. Previous reviews have associated frailty syndrome with osteoporosis, but original research on this link is limited and has produced conflicting results. This study aims to investigate the relationship between frailty syndrome, osteoporosis, bone mineral densitometry T-score, and other influencing factors.

Methods: In this cross-sectional study, post-menopausal women underwent screening for osteoporosis and frailty syndrome using bone mineral densitometry and the Fried phenotype. Exclusion criteria included a history of diseases related to bone loss or medications affecting bone metabolism. Bivariate and multivariable tests were used to examine the correlation between frailty syndrome and various covariates, including the diagnosis of osteoporosis.

Results: A total of 272 women aged 60 to 89 years (mean age 68.57 $\pm$ 6.22) were evaluated. Osteoporosis was prevalent in 44.9 % of participants, and frailty syndrome was identified in 36.4 %. The regression model identified age, menopausal age, and the diagnosis of osteoporosis as variables significantly and independently associated with frailty syndrome. A T-score lower than -2.5 in the femur neck or lumbar spine exhibited a sensitivity of 86.6 % and specificity of 76.5 % in predicting frailty syndrome.

Conclusion: Older adults with osteoporosis face an increased risk of frailty syndrome. Therefore, we recommend that primary care providers screen osteoporotic women for frailty syndrome and, when appropriate, refer this group to geriatric specialists for further evaluation.

1. Introduction

Frailty is undoubtedly one of the most significant global public health concerns we have confronted in the 21st century (Dent et al., 2019a). Because of an increase in life expectancy, most people live in their sixties or beyond. This will lead people aged 60 years or older to increase from 1 billion in 2020 to 2.1 billion in 2050 (Organization, W.H, 2022). In addition, older adults are the principal consumers of medical and social care services (Organization, W.H, 2022; Bock et al., 2016); Hence, the planning and delivery of health and social care will be profoundly impacted by a failure to pay greater attention to the health concerns of older adults (Ensrud et al., 2018).

Frailty syndrome is a significant and prevalent geriatric disease. According to the diagnostic criteria and age, the prevalence of this

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syndrome, which is characterized as a clinically recognizable state in which the ability of older adults to adapt to acute stressors is diminished due to age-related declines in physiological reserve and function across multiple organs, ranges from 3.9 % in China to 51.1 % in Cuba (Fried et al., 2021; Siriwardhana et al., 2018). This widespread condition increases the chance of early death and a variety of adverse health outcomes, such as falls, fractures, disability, and dementia among frail individuals, all of which may cause lower quality of life and higher costs (Kojima et al., 2019). Moreover, frailty is associated with higher total healthcare expenses (Ensrud et al., 2018; Hajek et al., 2018).

Despite the considerable impact of frailty syndrome on the lives of individuals and the expenses borne by governments, there is still confusion regarding the identification, measurement, and management of frailty (Hanlon et al., 2020). Because of the complexity and multifaceted character of frailty, it is essential to comprehend the elements related to this condition to develop more effective methods for its prevention, screening, and treatment. Multiple factors, including age, female sex, living alone, low levels of exercise, smoking, malnutrition, and low levels of exercise, have been linked to frailty syndrome (Wang et al., 2022; Fried et al., 2001). Additionally, many review publications asserted that osteoporosis and frailty syndrome are associated (Greco et al., 2019; Li et al., 2017). However, this assertion is controversial among the few original studies evaluating this correlation. Furthermore, the World Health Organization fracture risk assessment tool (FRAX), which provides estimations of the likelihood of osteoporotic fracture during a 10-year period, was exhibited to have an association with frailty syndrome. This fact further underscores the significance of investigating osteoporosis and frailty syndrome correlation (Hillier et al., 2011; Tembo et al., 2020).

Therefore, we aim to investigate the relationship between frailty syndrome, osteoporosis, bone mineral densitometry T-score, and other factors influencing this syndrome, in a cross-sectional study. With a proven correlation between osteoporosis and frailty syndrome, physicians will focus on the diagnosis of frailty syndrome in osteoporotic patients, and further research on the effect of osteoporosis prevention and treatment on frailty syndrome will contribute to an improvement in the quality of life, life expectancy, and healthcare system costs of older adults.

2. Material and methods

2.1. Participants and study design

This cross-sectional study was conducted on menopausal women aged 60 years and above who presented in the geriatric outpatient clinic of Firoozabadi Hospital affiliated with the Iran University of Medical Sciences, Tehran, Iran, between January and September 2022. Convenience sampling is the method used for the sampling. The inclusion criteria were female gender, age $\geq$ 60 years, history of menopause, and referral to the mentioned geriatric outpatient clinic. The exclusion criteria were abnormal serum levels of calcium or phosphorus, a history of hospitalization in the past three months, acute disease, physical disabilities including loss of hearing or vision loss, a history of diseases related to bone loss or frailty (heart failure, Alzheimer's disease, rheumatological diseases, cancers, inflammatory bowel disease, chronic kidney or liver diseases, and thyroid and parathyroid diseases), self-report of osteoporotic fracture, usage of drugs which affects bone metabolism (corticosteroids, antiepileptics, antiandrogens, progestins, thiazolidinediones, anticoagulants, and immunosuppressants).

The investigation had the University ethics committee's agreement (Ethics code: IR.IUMS.FMD.REC.1401.275), and the researchers adhered to the Helsinki ethical principles. Written consent was obtained from all included participants.

2.2. Data collection

Participants' demographic and health information, including age, marital status, race, BMI, history of diseases, and drug history, was collected and recorded using a checklist and by a researcher.

A geriatrician examined all participants using Fried's frailty phenotype, which comprises five criteria, including (i) weakness, (ii) slowness, (iii) unintentional weight loss, (iv) exhaustion, and (v) low physical activity. Participants are considered frail if they meet at least three criteria, and not frail if they meet fewer than three (Fried et al., 2001).

(i) Weakness was measured using handgrip strength. The grip strength of the dominant hand was measured using digital dynamometers, with participants standing in an upright position with both arms at their sides. Weakness was considered grip strength in the lowest 20 % at baseline, adjusted for gender and body mass index (Fried et al., 2001).
(ii) Slowness was evaluated based on the required time to walk 15 ft, adjusting for gender and standing height (Fried et al., 2001).
(iii) Weight loss was defined as unintentional weight loss of over 5 % of the body weight or over ten pounds in the previous year (Fried et al., 2001).
(iv) Exhaustion was assessed using the CES–D Depression Scale, and the following two statements were asked. (a) I felt that everything I did was an effort; (b) I could not get going. Fried, CES–D Depression Scale (Fried et al., 2001; Lewinsohn et al., 1997).
(v) Low physical activity was assessed by the question, “How often do you practice any of the following activities (dancing, walking, farmer work, or gardening)?”. Participants who reported “never/almost never” or “up to three times a month” were considered not active (Alves et al., 2020).

Bone mineral densitometry test with the Dual-energy X-ray absorptiometry (DXA) method (BMD-DXA) was performed on the femoral neck and lumbar spine to detect osteoporosis in patients. A T-score of -2.5 or below in the femoral neck or lumbar spine was considered diagnostic for osteoporosis (Kanis et al., 2019). The information gathered was eventually entered for statistical analysis.

2.3. Statistical analysis

Quantitative data were described by the mean and standard deviations or median and interquartile range, whereas qualitative data were described by absolute frequencies and percentages. The normality of the data was determined by evaluating the graphical representation of the data distribution in a Q-Q plot and the Shapiro-Wilk test. The Mann-Whitney *U* test was utilized for non-normally distributed quantitative data, the independent *t*-test for normally distributed quantitative variables, and the chi-square test for qualitative variables to compare groups.

The relationship between frailty syndrome and covariates with significant chi-square or Mann-Whitney *p*-values was evaluated using univariate logistic regression. Then, binary logistic regression was performed to evaluate variables with a p-value of 0.1 or less in univariate logistic regression. The significance level was considered <0.05.

Finally, Receiver operator characteristic (ROC) curves were generated to estimate the accuracy of three variables (0-femurT-score, 0-lumbarT-score and 0-the lower T-score between femoral and lumbar T-scores) in predicting frailty syndrome. The area under each ROC curve (AUC) was calculated to identify an accurate predicting covariate.

3. Results

3.1. Demographic data

After excluding 79 individuals who satisfied the exclusion criteria,

272 patients remained for final evaluation. The average age of participants was 68.57 ± 6.22 years, ranging from 60 to 89 years. The average menopause age was 47.25 ± 3.88 years, with a minimum of 30 and a maximum of 57 years.

All included patients were Iranian; 67.2 % were married, and 32.8 % were unmarried, divorced, or widowed. Thirty percent of older women did not mention any comorbidities. High blood pressure and diabetes mellitus were reported in 66.1 % and 36 %, respectively. Thirty-two percent of participants mentioned PPI use. Patients' characteristic is depicted in Table 1.

3.2. Bone densitometry results

According to the bone mineral densitometry using the DEXA method, the average T-score of the study participants was −2.04 ± 0.97 in the femoral neck and -2.09 ± 0.98 in the lumbar spine. (Table 1.)

The minimum T-score was −5.3 in the femoral neck and − 5.2 in the lumbar spine, while the maximum value in each area was 0.5. The lower T-score was taken into consideration for each participant, and the results showed that 44.9 % of older adults had a T-score that was diagnostic of osteoporosis, and 45.2 % of older adults had a T-score that was diagnostic of osteopenia. Only 4.8 % of participants had a T-score that showed normal bone density.

3.3. The prevalence of frailty syndrome and Fried's criteria

The prevalence of frailty was 36.4 %. Weakness (decreased grip strength) was the most common criterion, accounting for 49.7 % of all cases, followed by slowness (45.2 %), exhaustion (46.4 %), and low physical activity (36.4 %). Weight loss had the lowest prevalence among older adults., equal to 18.2 %.

3.4. Correlation analysis between frailty syndrome and demographic and clinical characteristics of participants

The association between Frailty syndrome and clinical and demographic characteristics of participants is demonstrated in Table 1. Frailty syndrome was significantly increased with aging, a lower menopause age, and a lower body mass index (*p*-values: <0.001, 0.003, 0.029, respectively).

History of smoking and unmarried status were also significantly related to frailty, while there was no correlation between alcohol consumption and frailty (p-values: 0.04, <0.001, and 0.56, respectively).

The presence of chronic illnesses comprising hypertension and diabetes mellitus were significantly associated with frailty syndrome with *p*-values of 0.005 and 0.001 respectively. Moreover, proton pump inhibitors were significantly correlated with frailty with a p-value of <0.001.

3.5. Correlation analysis between the frailty syndrome and osteoporosis

Among 122 older adults with osteoporosis, 83 patients (68 %) were frail, and 39 (31 %) were not frail. In comparison, the prevalence of frailty syndrome in people without osteoporosis was 11.9 % (16 out of 134). According to the Chi-Square test, the prevalence of frailty syndrome in the osteoporotic group was significantly higher than in the non-osteoporotic group, with a p-value of <0.001 (Table 1). Each of the frailty phenotype's five criteria was separately related to osteoporosis. The intensity of this correlation was higher between the decrease in grip strength and osteoporosis (Phi-value: 0.514).

According to the Mann-Whitney *U* test, frailty syndrome was significantly associated with T-score in both the femoral neck and lumbar spine (*P*-values<0.001).

3.6. Regression analysis

Table 2 demonstrates the results of univariate and multivariable logistic regression. As indicated, all the variables in the table had a P-value < 0.1 in univariate analysis and were entered multivariable logistic regression. According to the model, age, menopausal age, and osteoporosis diagnosis according to the WHO criteria were the variables with a significant correlation with frailty syndrome. The final model had a sensitivity of 80 %, a specificity of 84.6 %, and an overall 83 % of cases were correctly classified.

Table 1
Participants characteristics by frailty status.

Variables	Frail participants (mean ± SD) / (number)	Non-frail participants (mean ± SD) / (number)	All participants (mean ± SD) / (number)	p-value
Age	66.11 ± 4.30	72.44 ± 6.81	68.57 ± 6.22	<0.001
Menopause age	47.28 ± 4.28	46.32 ± 2.72	47.25 ± 3.88	0.003
Body mass index	27.00 ± 3.86	25.65 ± 5.12	26.51 ± 4.39	0.029
Weight	65.82 ± 14.00	70.89 ± 11.08	69.04 ± 12.44	0.003
Lumbar T-score	−2.640 ± 0.958	−1.79 ± 0.85	−2.09 ± 0.98	<0.001
Femoral neck T-score	−2.646 ± 0.88	−1.74 ± 0.90	−2.04 ± 0.97	<0.001

Variables		Frail participants (Number)	Non-frail participants (Number)	All participants (Number)	*p*-value
Marital status	Married	43 (43.5 %)	140 (81 %)	183 (67.2 %)	<0.001
	Non-married	56 (56.5 %)	33 (19 %)	89 (32.7 %)	
Smoking	Negative	89 (89.9 %)	165 (95.9 %)	254 (93.7 %)	0.04
	Positive	10 (10.1 %)	7 (4.1 %)	17 (6.3 %)	
Alcohol consumption	Negative	97 (98 %)	171 (98.8 %)	268 (98.5 %)	0.56
	Positive	2 (2 %)	2 (1.2 %)	4 (1.5 %)	
History of fall >2 times	Negative	58 (58.6 %)	161 (93.1 %)	219 (80.5 %)	<0.001
	Positive	41 (41.4 %)	12 (6.9 %)	53 (19.5 %)	
Diabetes mellitus	Negative	53 (53.5 %)	127 (73.4 %)	180 (66.1 %)	0.005
	Positive	46 (46.5 %)	46 (26.7 %)	92 (33.9 %)	
Hypertension	Negative	25 (25.3 %)	73 (42.2 %)	98 (36 %)	0.001
	Positive	74 (74.7 %)	100 (57.8 %)	174 (64 %)	
Osteoporosis	Negative	16 (16.2 %)	134 (77.5 %)	150 (55.1 %)	<0.001
	Positive	83 (83.8 %)	39 (22.5 %)	122 (44.9 %)	
Proton pump inhibitors	Negative	53 (53.5 %)	130 (75.1 %)	183 (67.3 %)	<0.001
	Positive	46 (46.5 %)	43 (24.9 %)	89 (32.7 %)	

Table 2
The association between frailty and included variables, assessed by binary logistic regression analysis.

Variable	Univariate		Multivariable (Model 1)		Multivariable (Model 2)	
	EXP(B) (95%CI)	P-Value	EXP(B) (95%CI)	P-Value	EXP(B) (95%CI)	P-Value
Age	1.24 (1.15–1.32)	<0.001	1.24 (1.03–1.49)	0.018	1.32 (1.09–1.60)	0.003
menopause age	0.91 (0.82–0.99)	0.045	0.82 (0.69–0.98)	0.032	0.87 (0.73–1.03)	0.112
Body mass index	0.93 (0.87–098)	0.020	0.90 (0.73–1.12)	0.286	0.96 (0.77–1.20)	0.761
Married / not married	0.16 (0.08–0.34)	<0.001	0.42 (0.06–2.70)	0.367	0.51 (0.09–2.74)	0.436
History of falling>2 times	9.48 (4.66–19.28)	<0.001	1.99 (0.33–11.91)	0.448	5.43 (0.99–29.72)	0.051
Osteoporotic/Non-Osteoporotic	17.82 (9.36–33.90)	<0.001	15.56 (2.80–86.27)	0.002	–	–
Hypertension	2.16 (1.25–3.72)	0.006	0.79 (0.09–6.83)	0.836	0.65 (0.99–4.27)	0.654
Diabetes mellitus	2.44 (1.45–4.11)	<0.001	1.31 (0.30–5.72)	0.712	1.52 (0.37–6.16)	0.554
Proton pump inhibitors	2.62 (1.51–4.43)	<0.001	3.96 (0.75–20.85)	0.104	3.45 (0.75–15.81)	0.111
Smoking	2.64 (0.97–7.19)	0.056	0.49 (0.05–4.29)	0.523	0.38 (0.04–3.05)	0.368
Femoral T-score	0.37 (0.27–0.51)	<0.001	–	–	0.67 (0.21–2.06)	0.485
Lumbar T-score	0.36 (0.26–0.50)	<0.001	–	–	1.04 (0.34–3.17)	0.936

Univariate analysis: Included each variable separately. Model 1: The binary logistic regression analysis included osteoporosis diagnosis, age, menopause age, body mass index, marital status, falling history, history of proton pump inhibitors usage, smoking, diabetes mellitus, and hypertension Model 2: The binary logistic regression analysis included bone mineral densitometry T-score, age, menopause age, body mass index, marital status, falling history, and history of proton pump inhibitors usage, smoking, diabetes mellitus, and hypertension.

3.7. Receiver Operating Characteristic Curve (ROC)

For T-scores lower than zero, performing –(femoral T-score), -(lumbar T-score), and -(lower T-score), is shown in Fig. 1. -(lower T-score) indicated the lower T-score between lumbar and femoral T-scores for each participant. The area under the curve for –(femoral T-score) estimated as 0.761 ($P < 0.001$), for –(lumbar T-score) as 0.744 ($P < 0.001$), and for –(lower T-score) as 0.807 ($P < 0.001$). Respectively, the thresholds of 2.5, 2.0, and 2.5, were estimated as the best cut-off points. The sensitivity and specificity for these cut-off points are shown in Table 3.

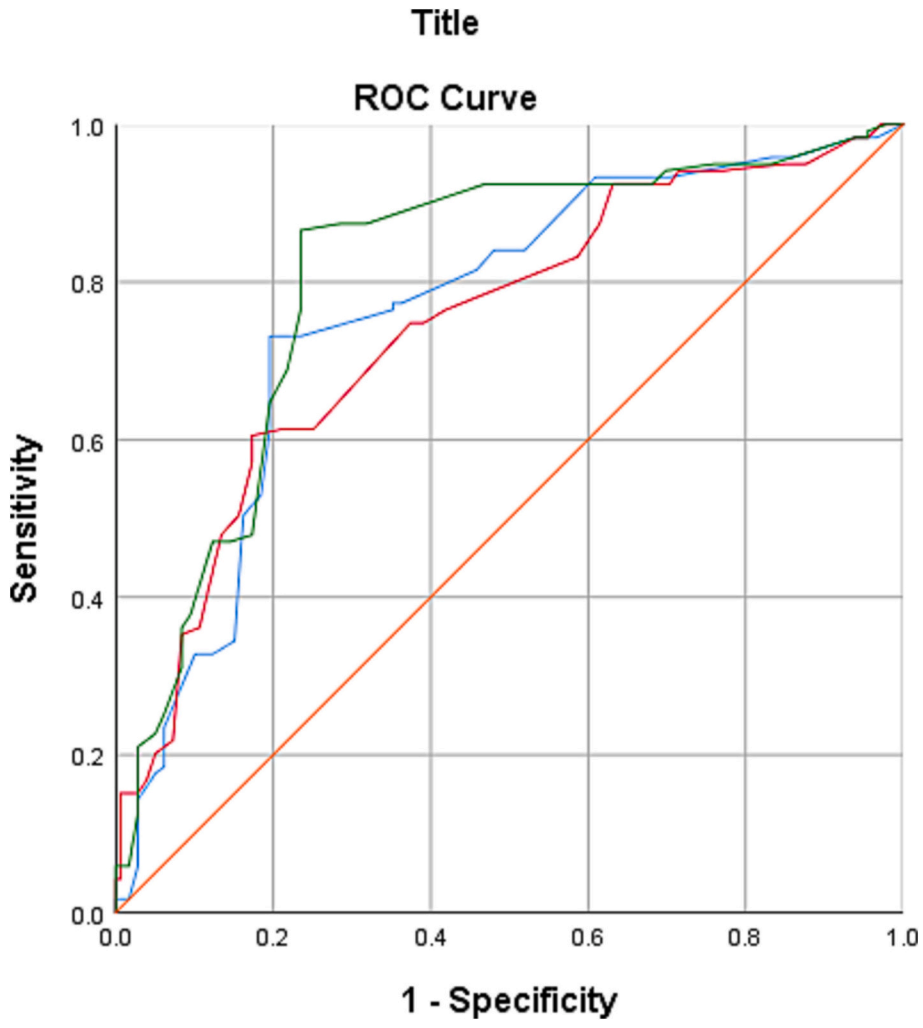

Fig. 1. ROC curve for blue:-(femoral T-score), red:-(lumbar T-score), green:-(lower T-score).

Table 3
ROC curve analysis for predictive variables.

Variable	Threshold	P-Value	AUC	Sensitivity	Specificity
-(femoral T-score)	2.5	<0.001	0.761 (0.705–0.817)	0.731	0.804
-(lumbar T-score)	2.0	<0.001	0.744 (0.686–0.802)	0.748	0.626
-(lower T-score)	2.5	<0.001	0.807 (0.754–0.859)	0.866	0.765

4. Discussion

This study was set out to determine the relationship between frailty syndrome, osteoporosis diagnosis, BMD T-score, along with other factors influencing this syndrome. We discovered that frailty syndrome is significantly and independently related to osteoporosis, age, and menopause age. Frailty syndrome is a prevalent and prominent disease of older adults, associated with osteoporosis in many review articles. However, the few original studies on the correlation between frailty and the diagnosis of osteoporosis documented controversial results. We investigated the aforementioned relationship in a single-gender population. Furthermore, we propose a T-score cutoff point for frailty syndrome prediction. These findings warrant further discussion.

The prevalence of frailty syndrome in this study's population was 36.4 %. There is inadequate available data about the prevalence of frailty syndrome based on Fried's phenotype among older women in Iran. A community-based cross-sectional study estimated a 14.3 % prevalence of frailty syndrome among adults aged 60 years and older in five cities in Iran's southwest. However, it cannot be compared to our study due to its inclusion of both men and women and its use of the frailty index of cumulative deficit to diagnose frailty syndrome. (Delbari et al., 2021).

Meanwhile, a review study and meta-analysis reported the prevalence of this disease different from 3.9 % to 51.4 % worldwide, with an average of 17 % based on Fried's phenotype (Siriwardhana et al., 2018). As a result, frailty syndrome in our sample had a significant prevalence. The fact that all older adults in this study were women can be the reason, considering various studies reported a higher prevalence of frailty syndrome in women compared to men (Wang et al., 2022). The poor income and education levels in the study's sampling area could be another factor contributing to the high prevalence found (Fried et al., 2001).

4.1. Frailty syndrome and osteoporosis

The osteoporosis prevalence in this study's population was 44.9 %. Previously, a meta-analysis estimated the prevalence of osteoporosis at 34.4 % in Iranian women aged 60 years or older (Nourmohammadi et al., 2022). The higher prevalence of osteoporosis in our study could be related to the low socioeconomic status in the sampling area, as it was shown that socioeconomic status pertained to osteoporosis in Iranian women (Asadi-Lari et al., 2018). In this study, frailty syndrome was significantly associated with osteoporosis diagnosis according to WHO criteria. Many review articles have already addressed this association, but only a few original research have been conducted to evaluate it, with controversial results (Cattaneo et al., 2022; Frisoli Jr et al., 2011; Calado et al., 2016). A cross-sectional investigation of 385 adults declared a significant correlation between frailty syndrome and self-reported osteoporosis (Calado et al., 2016). The other study, a case-control study on 113 older adults conducted by F. Cattaneo and colleagues, concluded that osteoporosis in frail and robust older adults was not significantly different but that the frail group had considerably lower Femoral BMD (Cattaneo et al., 2022). The correlation between femoral BMD and frailty syndrome was also significant in the cross-sectional study of Li-Kuo Liu et al. on 1839 participants>50 years old (Laskou et al., 2022). However, two additional studies detected no significant correlation between frailty and BMD. One was conducted on 287 men aged ≥50, while the other was conducted on 707 older adults of all genders aged ≥60 years (Tembo et al., 2021a; Tembo et al., 2021b). Other studies reported a significant association between concomitant sarcopenia and osteoporosis; however, there was no significant association between osteoporosis and frailty syndrome. These studies were restricted by the limited number of frail participants, specifically 17 and 33 frail participants (Frisoli Jr et al., 2011; Laskou et al., 2022).

This investigation revealed a significant and independent association between frailty syndrome and osteoporosis, following the study of Calado et al. Regarding the BMD correlation with frailty, although the correlation between femoral and lumbar T-score and frailty syndrome was significant in bivariate analysis, the correlation was not significant in the regression model when other covariates, including age, were considered. The absence of a significant and independent correlation between BMD T-scores and frailty syndrome was aligned with previous research (Tembo et al., 2021a; Tembo et al., 2021b). This data suggests that frailty syndrome and mineral density may not correlate linearly, but a particular decline in bone mineral density may be attributed to frailty syndrome. Nonetheless, this observation requires further investigations to reconcile.

These disparities can be ascribed to many additional factors. First, although the frailty syndrome criteria were similar in the aforementioned studies, the methods for osteoporosis diagnosis vary. These methods encompassed self-report diagnosis, diagnosis only based on femoral T-score, diagnosis based on both the femoral and lumbar T-scores, diagnosis based on T-score and usage of anti-osteoporosis medications including hormone replacement therapy (HRT). Hence, we diagnosed osteoporosis based on BMD of both the spine and femur, and to reduce bias, we excluded patients with a history of osteoporosis treatment, as the effect of these treatments on frailty syndrome is unknown. Moreover, since the osteoporotic fracture is also a diagnostic criterion for osteoporosis, we asked the patients for a history of osteoporotic fracture, and neither osteoporosis nor the non-osteoporosis group noted a history of osteoporotic fracture. Since self-reported data were susceptible to recall bias, we used bone mineral densitometry on every patient. Future research is recommended to contemplate osteoporotic fractures with a more reliable method. Furthermore, earlier research evaluated this correlation on a few frail participants that may not be sufficiently powered to detect the difference. This study was conducted on a greater number of frail women, as the prevalence of frailty was high in the sampling area. Moreover, it is important to acknowledge the established gender disparities in frailty syndrome; therefore, the diverse distribution of genders across various studies may be an additional explanation for the observed discrepancy (Zhang et al., 2018; Mielke et al., 2022; Gordon et al., 2017). Inclusion of single-gender population was one of the strengths of this study. Lastly, there are a great number of comorbidities that affect frailty or osteoporosis. The varying prevalence of these conditions across different studies may skew the findings. Excluding groups with a higher frequency of frailty syndrome (ESRD, HF, disability, and others), as well as drugs affecting bone metabolism, was an additional advantage we employed to diminish bias.

Various causes can justify the association between frailty syndrome and osteoporosis. Osteoporosis and frailty syndrome are both age-related disorders. Aging processes are accompanied by primary osteoporosis via these mechanisms: inflammatory processes, elevated parathyroid hormone levels, calcium and vitamin D deficiency, and osteoblast malfunction (Föger-Samwald et al., 2022). Frailty is also conceptualized as an age-related state of decreased reserves, resulting in increased vulnerability to adverse outcomes (Fried et al., 2021). Age may, therefore, contribute to the co-occurrence of these two conditions. Notwithstanding by excluding the age effect by applying the regression model, we have noticed that the relationship between frailty syndrome and osteoporosis is beyond the role of age. Sarcopenia is a condition of the muscles characterized by a loss of muscle mass and strength (Vogele

et al., 2023). This condition is linked to osteoporosis for multiple reasons, including the same risk factors, similar etiological pathways, endocrine basis, and the phenomenon of bidirectional bone-muscle crosstalk (Yu et al., 2022; He et al., 2020). Sarcopenia is also associated with frailty syndrome. Sarcopenic obesity, the co-existence of excessive adiposity and low muscle mass/function, is one of the leading causes of frailty (Hirani et al., 2017; Donini et al., 2022). Furthermore, in both the frailty syndrome and osteoporosis, hormones (testosterone, estrogen, growth hormone, and IGF—I), vitamin D, and cytokines fluctuate similarly (Rolland et al., 2008). Importantly, osteoprotegerin, a marker of robust osteoclast activity, was significantly enhanced in patients with both osteoporosis and frailty syndrome based on Fried's criteria (Valentini et al., 2019; Pandey et al., 2018). Finally, additional common characteristics in both conditions, such as weight loss, falls, decreased physical activity, depression, and diminished cognitive function, may also contribute to their association (Rolland et al., 2008).

4.2. Frailty syndrome and menopause

There was a significant correlation between menopausal age and frailty in this study. This correlation was consistent with the review study and meta-analysis conducted by Kojima et al., which claimed that the risk of frailty syndrome in women is reduced by 2 % each year that a woman experiences menopause later in life (Kojima et al., 2022). Hormonal changes were cited as a similarity between frailty syndrome and osteoporosis (Rolland et al., 2008). Hormonal changes, including decreased sex hormones, increased cortisol, and decreased IGF-1, play critical roles in the pathogenesis of both osteoporosis and frailty syndrome (Chen et al., 2014; Cannarella et al., 2019). One of these hormones that diminishes during menopause is estrogen, which plays a crucial role in maintaining bone and muscle health (Cauley, 2015; Chidi-Ogbolu and Baar, 2018). Estrogen deficiency is also closely associated with systemic chronic inflammation and diminishes the capacity to respond and adapt adequately to external mechanical and metabolic stressors (Nedergaard et al., 2013). These factors may contribute to the co-occurrence of osteoporosis and frailty in postmenopausal women. The higher prevalence of frailty in older women compared to older men may be impacted by the decrease of estrogen after menopause, as early menopause is related to frailty syndrome and because of the negative correlation between hormone therapy after menopause and frailty (Wang et al., 2022; Fried et al., 2001; Kojima et al., 2022; Kim and Lee, 2022).

4.3. Frailty syndrome and falling

Nineteen percent of older adults evaluated in this study had a history of falling twice or more. In the systematic review and meta-analysis, the prevalence of falls in older people worldwide was 26.5 % (Salari et al., 2022). In older adults, falls are one of the leading causes of death and disability. Although the chi-square test showed a significant relationship between fall and frailty syndrome in this study, according to the regression model, the history of falling did not independently predict frailty.

Given that osteoporotic persons have a higher risk of falling and that frailty is associated with osteoporosis, probably, the higher risk of falling in frail people showed by other research may have probably contributed to a higher prevalence of osteoporosis among frail individuals (Fhon et al., 2016). Further research is required to identify whether a history of falling independently correlates to frailty syndrome or is a factor linking osteoporosis with frailty syndrome.

4.4. Frailty screening

The International Conference of Frailty and Sarcopenia Research (ICFSR), recommended frailty screening for all adults 65 years or older (Dent et al., 2019b). However, there is insufficient information on how physicians adhere to this guideline. Most clinicians, excluding those with frailty interests or job roles, reported little or no training in frailty, resulting in widespread ambiguity regarding how to diagnose frailty. Furthermore, a paucity of comprehensive policies for implementing frailty screening in the healthcare setting has been reported (Liu et al., 2022; Seeley et al., 2023). On the other hand, primary care practitioners experience intense patient loads globally. A typical consultation with a primary care physician lasts from under a minute to 20 min. Since the diagnosis of frailty syndrome is clinical rather than based on diagnostic testing, and the restricted time makes it nearly impossible to construct a comprehensive diagnostic and therapy plan for geriatric disorders, a substantial portion of cases with frailty syndrome are left undiagnosed (Ruiz et al., 2020). Bone mineral densitometry is recommended as a screening for all women 65 or older (Curry et al., 2018). Due to the existence of a current screening program for osteoporosis in women older than 65 years; and regarding the fact that a T-score lower than −2.5 in either femoral neck or lumbar spine of women 60 years and older can predict frailty syndrome with a sensitivity of 86.6 % and a specificity of 76.5 %, we emphasize a greater alertness for screening all the women with the aforementioned T-score for frailty syndrome using a validated tool. If there is a need to increase sensitivity, a T-score of −2.0 is advised to boost sensitivity up to 93 %. Although the goal is to screen all women over 65 years following the ICSFR, screening of this high-risk population is even more critical and can be time-saving and cost-beneficial regardless of intensive patient loads according to the obtained sensitivity and specificity and the considerable impact of frailty syndrome on individual and public health. (Dent et al., 2019b) Consequently, we suggest primary care providers consider the crucial importance of evaluating osteoporotic women for frailty syndrome and, with impracticality, refer this group to geriatrics for evaluation.

4.5. Limitations

One significant limitation impacting the generalizability of results in this study was utilization of convenience sampling and the absence of a multicenter design. Notably, we could not assess the temporal relationship between osteoporosis and frailty syndrome because this was a cross-sectional study. To address these limitations, prospective multicenter or population-based studies are suggested. We did not enroll muscle mass and strength as a variable; however, they may affect the BMD. Finally, osteoporotic fracture is the other diagnostic criterion for osteoporosis, and self-report of this criterion is associated with recall bias; hence, we recommend considering a more accurate diagnosis tool for this criterion in future studies.

5. Conclusion

Older adults with osteoporosis are at greater risk of developing frailty syndrome; therefore, we recommend that primary care providers screen osteoporotic women for frailty syndrome and, if this is not practicable, refer this group to geriatrics for assessment. Furthermore, we encourage researchers to investigate the impact of osteoporosis prevention and early therapy on preventing and treating frailty syndrome.

CRediT authorship contribution statement

Shiva Rahimipour Anaraki: Writing – original draft, Investigation, Formal analysis. **Ali Mohammadian:** Writing – original draft, Conceptualization. **Samaneh Saghafian Larijani:** Writing – review & editing, Supervision. **Maryam Niksolat:** Writing – review & editing, Investigation, Conceptualization. **Vahid Rashedi:** Writing – review & editing, Methodology. **Milad Gholizadeh Mesgarha:** Writing – original draft.

Declaration of competing interest

Shiva Rahimipour Anaraki, Ali Mohammadian, Samaneh Saghafian Larijani, Maryam Niksolat, Vahid Rashedi and Milad Gholizadeh Mesgarha declare that they have no conflict of interest.

Data availability

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

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Consent for publication

Not applicable.

Informed consent

Informed consent was obtained from all individual participants included in the study.

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