scientific reports



OPEN

Fat mass in postmenopausal women with osteoporosis is associated with cognitive function

Dongxue Zhang^{1,3}, Zijing Zhu^{1,3}, Lu Xue¹, Yifeng Zheng¹, Xiongfeng Li¹, Miyang Xu², Xinfang Xie^{1,4⊠} & Yongli Wang^{1,4™}

Postmenopausal women undergo significant changes in endogenous hormones, which lead to reduced bone mineral density (BMD) and alterations in body composition. However, the relationship between body composition and cognitive function in this demographic has not yet been explored. This study aims to examine this relationship in postmenopausal women with osteoporosis. This survey will involve 120 postmenopausal women with osteoporosis. Dual-energy X-ray absorptiometry (DXA) will be used to assess L1-L4 BMD, fat mass (FM), trunk fat mass (TFM), fat-free mass (FFM), and appendicular skeletal muscle mass (ASMM). The relationship between body composition and cognitive function will be analyzed using t-tests and multiple linear regression. Our findings suggest that in postmenopausal women with osteoporosis, cognitive function (MMSE score) is positively correlated with body composition indicators such as FM and BMD, and positively correlated with educational level, but negatively correlated with age. FM plays a significant role in influencing cognitive function and is a crucial indicator of body composition in postmenopausal women with osteoporosis.

Keywords Body composition, postmenopausal osteoporosis, cognition function, fat mass, fat-free mass

Osteoporosis (OP) is a systemic skeletal disease characterized by decreased bone density and deterioration in bone structure, leading to reduced bone strength, increased bone fragility, and a higher risk of fractures^{1,2}. In China, the incidence rate of osteoporosis among those aged 50 and above is 19.2%, with a prevalence rate of 6.0% in males and 32.1% in females³. Postmenopausal osteoporosis (PMOP) is the most prevalent type of primary osteoporosis. Following menopause, estrogen levels drop sharply, leading to a higher production of osteoclasts relative to osteoblasts. This imbalance accelerates bone loss and disrupts the metabolic balance of bone, culminating in osteoporosis^{4,5}. Concurrently, the postmenopausal period marks a critical phase in female aging. The decline in estrogen not only affects bone health but also alters body composition, leading to increased fat accumulation, muscle loss, and reduced muscle strength. In severe cases, this can progress to sarcopenia⁶. These changes in bone structure and muscle function can cause symptoms like multi-joint pain, muscle loss, skeletal deformities, and fractures, which significantly burden postmenopausal women both physically and mentally, impacting their quality of life and leading to substantial socio-economic losses^{1,3}.

Increasing evidence suggests a correlation between OP and cognitive impairment (CI)^{7,8}. Cognitive impairment, a precursor to dementia, is marked by mild yet significant deficits in memory and/or other cognitive functions, impacting daily life activities⁹. It has emerged as a critical public health issue among the elderly. Often, low bone density and cognitive impairment occur concurrently¹⁰. For instance, Ebrahimpur et al. reported that women with low spinal bone density have a 1.83-fold increased risk of cognitive impairment (95% CI: 1.13–2.96)¹¹. Additionally, changes in body composition may influence cognitive functions¹², yet the relationship and underlying mechanisms between these factors remain unclear, particularly among postmenopausal women with osteoporosis. This study aims to explore this relationship.

Materials and methods Study population

This study was conducted on 120 postmenopausal women with osteoporosis at Huzhou Central Hospital from November 2023 to March 2024, with approval from the Medical Ethics Committee of Huzhou Central Hospital (No. 202303041-01). Each patient in this experiment provided written informed consent.

¹Huzhou Central Hospital, Affiliated Central Hospital of Huzhou University, Huzhou, China. ²Huzhou Central Hospital, Fifth School of Clinical Medicine of Zhejiang Chinese Medical University, Huzhou, China. ³Dongxue Zhang and Zijing Zhu contributed equally. ⁴Yongli Wang and Xinfang Xie contributed equally. [∞]email: xxf7281517@163.com; wyl1944@hzhospital.com

Inclusion criteria included postmenopausal women with a T-score of axial bone (lumbar spine) density \leq -2.5 or a T-score between -1.0 and -2.5 with a brittle fracture in the proximal humerus, pelvis, or distal forearm¹³.

Exclusion criteria encompassed non-natural menopause, patients who had undergone lumbar spine surgery, those with severe physical and mental illnesses (such as speech or hearing impairments, mental disorders, primary or metastatic malignant tumors) that could interfere with testing, and cases of secondary osteoporosis.

Height and weight testing methods

Height and weight were measured using the Giant Sky Ultrasonic Height and Weight Measuring Instrument (model: JT-918 C). Body mass index (BMI) was calculated using the standard formula: BMI=weight (kg) / height² (m².

Body composition testing

Dual-energy X-ray absorptiometry (DXA) is the gold standard for diagnosing osteoporosis and also serves as a non-invasive method for assessing fat, muscle, and bone density, providing more accurate results compared to bioelectrical impedance analysis for skeletal muscle measurement ^{14,15}. During the assessment, patients wore only underwear and removed all metal accessories. The DXA machine (GE Lunar Prodigy Advance) utilized two X-ray beams at different energy levels to measure fat mass (FM), trunk fat mass (TFM), fat-free mass (FFM), appendicular skeletal muscle mass (ASMM), and L1-L4 bone mineral density (BMD)¹⁶. The machine was calibrated every morning and at the end of each day for all measurements. Compared to other methods such as total body potassium (TBK), magnetic resonance imaging (MRI) or computer tomography (CT) imaging, DXA offers accuracy, simplicity, and practicality, with low radiation exposure and minimal risk. Apart from pregnancy, there are no contraindications for DXA use in clinical practice¹⁷.

Demographics and covariates

Data were collected through interviews conducted by professional researchers. The questionnaire covered age, educational level, age at menarche, age at menopause, duration of menopause, number of pregnancies, number of births, proportion of meat consumption in the diet, and cognitive function. Cognitive function was assessed using the Mini Mental State Examination (MMSE), an 11-question test that can be completed in 5–10 minutes¹⁸. A total MMSE score of 30 points indicates higher cognitive function, with a score ≥24 suggesting normal cognition¹⁹. The Chinese version of the MMSE, widely used in both clinical settings and research, has been validated for the Chinese population²⁰.

Statistical analysis

We described participant characteristics using percentages for categorical variables and means with standard deviations for continuous variables. We grouped and characterized patients with cognitive impairment and severe osteoporosis, using frequencies and percentages for categorical variables, and compared them using the chi-square test. Continuous variables were represented as mean ± standard deviation and compared using the t-test or Mann-Whitney U test, depending on normality as assessed by the Shapiro-Wilk test. We identified factors related to cognitive function scores, including L1-L4 bone density and total fat mass.

Factors associated with cognitive function and having p-values less than 0.05 were included in a multiple linear regression analysis. We determined the key factors affecting cognitive function scores through stepwise regression based on the minimum Akaike Information Criterion (AIC). The results are presented as regression coefficients with 95% confidence intervals (CI).

We stratified participants for cognitive impairment and examined the relationships between height, weight and fat-free mass (FFM) with osteoporosis. Similarly, we stratified participants with severe osteoporosis to compare the relationships between total fat mass (FM) and other related variables with cognitive function. A p-value less than 0.05 was considered statistically significant. All analyses were conducted using R software (version 4.3.1).

Results

Population characteristics

This study included 120 postmenopausal women with osteoporosis, summarized in Table 1. The average age was 66.84 ± 8.83 years, and the average duration of menopause was 17.47 ± 9.71 years. About 49% of participants had an education level of junior high school or lower. The average BMI was 21.61 ± 2.77 kg/m2, average FM was 18.08 ± 4.79 kg, average TFM was 10.09 ± 3.29 kg, average FFM was 34.63 ± 4.24 kg, and average ASMM was 13.98 ± 1.97 kg. The mean MMSE score was 23.62 ± 4.51 points, and the average L1-L4 BMD was 0.8 ± 0.12 kg/cm2. All patients had a T-score of \le -1.

Cognitive function related factors

Participants were divided into two groups based on MMSE scores: a non-cognitive impairment group (MMSE score \geq 24) and a cognitive impairment group ¹⁹. Table 2 shows the results. There were 51 individuals in the cognitive impairment group and 69 in the non-cognitive impairment group, with a cognitive impairment incidence rate of 42.5%. The average age of the non-cognitive impairment group (63.75 ± 8.24 years) was significantly lower than that of the cognitive impairment group (71.02 ± 7.89 years) (p < 0.05). The non-cognitive impairment group also showed younger ages at menarche and fewer numbers of births compared to the cognitive impairment group (p < 0.05). The average duration of menopause was shorter in the non-cognitive impairment group (14.65 ± 9.14 years) compared to the cognitive impairment group (21.27 ± 9.22 years) (p < 0.05). The non-cognitive impairment group had better nutritional management and higher educational levels than the cognitive impairment group (p < 0.05).

** • • • •	120
Variables	n=120
Age	66.84± 8.83
Educational level	
illiteracy	29(24)
primary school	30(25)
Junior high school and above	61(51)
duration of menopause	17.47± 9.71
Age of menarche	
12	5(4)
13	14(12)
14	28(23)
15	21(18)
16	18(15)
17	15(13)
18	13(11)
19	3(3)
20	3(3)
Age of menopause	49.38±3.23
Pregnancy frequency	
1	7(6)
2	34(28)
3	44(37)
4	23(19)
5	6(5)
6	4(3)
7	1(0)
8	1(0)
Production frequency	
1	52(43)
2	44(37)
3	17(14)
4	5(4)
6	2(2)
The proportion of meat in the diet	
30%below	54 (45)
30%-50%	52 (43)
50% above	14 (12)
MMSE score	23.62±4.51
Body composition	
L1-L4BMD(kg/m²)	0.80±0.12
Height(m)	1.56±0.06
Weight(kg)	52.71±7.97
BMI (kg/m2)	21.61±2.77
Fat Mass(kg)	18.08±4.79
Trunk Fat Mass(kg)	10.09±3.29
Fat-Free Mass(kg)	34.63±4.24
Appendicular Skeletal muscle Mass(kg)	13.98±1.97

Table 1. General characteristics and body composition of study participants (*n*=120).

The average L1-L4 BMD in the non-cognitive impairment group $(0.83\pm0.1~{\rm kg/cm2})$ was higher than in the cognitive impairment group $(0.76\pm0.14~{\rm kg/cm2})$ (p<0.05). The average height of the non-cognitive impairment group $(1.57\pm0.06~{\rm m})$ was also higher than that of the cognitive impairment group $(1.54\pm0.05~{\rm m})$ (p<0.05). The average FM in the non-cognitive impairment group $(18.96\pm3.99~{\rm kg})$ was higher than in the cognitive impairment group $(16.89\pm5.53~{\rm kg})$ (p<0.05). Similarly, the average TFM was higher in the non-cognitive impairment group $(10.74\pm2.79~{\rm kg})$ compared to the cognitive impairment group $(9.21\pm3.71~{\rm kg})$ (p<0.05).

However, the differences in average FFM $(34.99 \pm 4.25 \text{ kg vs. } 34.13 \pm 4.22 \text{ kg})$ and ASMM $(14.19 \pm 1.93 \text{ kg vs. } 13.69 \pm 2 \text{ kg})$ between the groups were not statistically significant (p > 0.05).

Cognitive impairment					
Variables	Total (n = 120)	Yes(n=51)	No(n=69)	p Value	
Age	66.84 ± 8.83	71.02 ± 7.89	63.75 ± 8.24	< 0.001	
Educational level				< 0.001	
illiteracy	29 (24)	25 (49)	4 (6)		
primary school	30 (25)	15 (29)	15 (22)		
Junior high school and above	61 (51)	11 (22)	50 (72)		
duration of menopause	17.47 ± 9.71	21.27 ± 9.22	14.65 ± 9.14	< 0.001	
Age of menarche				0.047	
12	5 (4)	0 (0)	5 (7)		
13	14 (12)	3 (6)	11 (16)		
14	28 (23)	9 (18)	19 (28)		
15	21 (18)	8 (16)	13 (19)		
16	18 (15)	9 (18)	9 (13)		
17	15 (12)	10 (20)	5 (7)		
18	13 (11)	8 (16)	5 (7)		
19	3 (2)	2 (4)	1 (1)		
20	3 (2)	2 (4)	1 (1)		
Age of menopause	50 (48, 51.25)	50 (48, 52)	49 (48, 51)	0.076	
Pregnancy frequency				0.119	
1	7 (6)	2 (4)	5 (7)		
2	34 (28)	12 (24)	22 (32)		
3	44 (37)	22 (43)	22 (32)		
4	23 (19)	7 (14)	16 (23)		
5	6 (5)	5 (10)	1 (1)		
6	4 (3)	1 (2)	3 (4)		
7	1 (1)	1 (2)	0 (0)		
8	1 (1)	1 (2)	0 (0)		
Production frequency				< 0.001	
1	52 (43)	11 (22)	41 (59)		
2	44 (37)	26 (51)	18 (26)		
3	17 (14)	9 (18)	8 (12)		
4	5 (4)	3 (6)	2 (3)		
6	2 (2)	2 (4)	0 (0)		
The proportion of meat in the diet				0.031	
30%below	54 (45)	30 (59)	24 (35)		
30%-50%	52 (43)	16 (31)	36 (52)		
50% above	14 (12)	5 (10)	9 (13)		
Body composition					
L1-L4BMD(kg/m²)	0.8 ± 0.12	0.76 ± 0.14	0.83 ± 0.1	0.001	
Height(m)	1.56 ± 0.06	1.54 ± 0.05	1.57 ± 0.06	0.003	
Weight(kg)	52.71 ± 7.97	51.03 ± 8.7	53.96 ± 7.21	0.046	
BMI (kg/m2)	21.61 ± 2.77	21.38 ± 3.09	21.78 ± 2.52	0.442	
Fat Mass(kg)	18.08 ± 4.79	16.89 ± 5.53	18.96 ± 3.99	0.018	
Trunk Fat Mass(kg)	10.09 ± 3.29	9.21 ± 3.71	10.74 ± 2.79	0.011	
Fat-Free Mass(kg)	34.63 ± 4.24	34.13 ± 4.22	34.99 ± 4.25	0.275	
Appendicular Skeletal muscle Mass(kg)	13.98 ± 1.97	13.69 ± 2	14.19 ± 1.93	0.169	

Table 2. Cognitive function related factors.

The relationship between cognitive function and age, educational level, L1-L4BMD, and FM Multivariate linear regression analyses revealed significant relationships between cognitive function scores and several variables. Age was negatively associated with cognitive function (β = -0.14, 95% CI [-0.22, -0.07], p < 0.001). Educational level showed a positive correlation with cognitive function (β = 2.76, 95% CI [1.13, 4.39], p < 0.001). L1-L4 BMD was also positively correlated (β = 6.12, 95% CI [0.89, 11.34], p = 0.022), as was total FM (β = 0.20, 95% CI [0.08, 0.33], p = 0.002). These findings are summarized in Table 3.

Variables	β (95% CI) *	p Value **
Age	-0.14(-0.22;-0.07)	< 0.001
Educational level	_	_
illiteracy		
primary school	2.76(1.13;4.39)	0.001
Junior high school and above	4.79(3.28;6.30)	< 0.001
L1-L4BMD(kg/m ²)	6.12(0.89;11.34)	0.022
Fat Mass(kg)	0.20(0.08;0.33)	0.002

Table 3. The relationship between cognitive function and age, educational level, L1-L4BMD, and FM. * β (95% IC): linear regression coefficient β (95% confidence interval). ** p value: significant difference if p-value < 0.05 (highlighted in bold).

Factors related to bone density

Participants were categorized into two groups based on a T-score of \leq -3: those at high risk of fracture were divided into severe osteoporosis group(T1) and osteoporosis group(T2)¹³, as shown in Table 4. The T1 group included 68 individuals, while the T2 group had 52 individuals. The average age in the T1 group was 68.88 ± 8.85 years, which was significantly higher than the average age of 64.17 ± 8.14 years in the T2 group (p < 0.05). The average duration of menopause was longer in the T1 group (19.68 ± 9.73 years) compared to the T2 group (14.58 ± 8.98 years) (p < 0.05). The average age at menarche was higher in the T1 group than in the T2 group (p < 0.05). Conversely, the education level was lower in the T1 group compared to the T2 group (p < 0.05).

In terms of body measurements, the average height in the T1 group was 1.55 ± 0.06 m, lower than the 1.58 ± 0.04 m in the T2 group (p<0.05). The average weight in the T1 group was 50.65 ± 7.45 kg, lower than the 55.4 ± 7.9 kg in the T2 group (p<0.05). The average BMI in the T1 group was 21.15 ± 2.57 kg/m2, lower than the 22.2 ± 2.94 kg/m2 in the T2 group (p<0.05). The average total FM was 17.27 ± 4.63 kg in the T1 group, lower than the 19.14 ± 4.84 kg in the T2 group (p<0.05). The average TFM was 9.41 ± 3.18 kg in the T1 group, lower than the 10.98 ± 3.23 kg in the T2 group (p<0.05). The average FFM was 33.38 ± 3.89 kg in the T1 group, lower than the 36.26 ± 4.16 kg in the T2 group (p<0.05). The average ASMM was 13.51 ± 1.94 kg in the T1 group, lower than the 14.59 ± 1.84 kg in the T2 group (p<0.05).

Severity stratification of osteoporosis, relationship between body composition and cognitive function

In the severe osteoporosis group, several body composition measures including height, weight, total fat mass, and trunk fat mass were significantly lower in the cognitive impairment subgroup compared to those without cognitive impairment (p < 0.05), as shown in Table 5.

Stratification of cognitive impairment, relationship between body composition and severity of osteoporosis

Within the cognitive impairment group, those with severe osteoporosis had lower values for height, weight, and fat-free mass compared to those with osteoporosis (p < 0.05). Besides, in the non-cognitive impairment group, fat-free mass was lower in the severe osteoporosis subgroup compared to the osteoporosis group (p < 0.05), as depicted in Fig. 1.

Discussion

We assessed the body composition and MMSE scores of 120 postmenopausal women diagnosed with osteoporosis. Our results indicated a positive correlation between cognitive function (measured by MMSE scores) and body composition indicators such as FM and BMD. Additionally, cognitive function positively correlated with education level and negatively with age among these women. Those in the cognitive impairment group were characterized by a later age of onset, more frequent childbirth, poor nutritional management, lower weight, and shorter stature. Women with severe osteoporosis after menopause exhibited lower FM, TFM, FFM, and ASMM. Factors such as older age, later menarche, lower education level and lower BMI were associated with severe osteoporosis.

There is a correlation between osteoporosis and cognitive function²¹. Research by Jiang et al. has demonstrated a communication mechanism between the bone and brain. Extracellular vesicles derived from healthy bone cells (OCY-EVs) can transfer to the brain under both physiological and pathological conditions, potentially ameliorating cognitive impairment in Alzheimer's disease²². This supports the notion that healthy bones, indicative of good bone density, are linked to higher cognitive functions, aligning with our findings.

Endogenous estradiol is known for its neuroprotective effects in models of oxidative stress, excitatory neurotoxicity, ischemia, and apoptosis, and it is associated with a reduced risk of cognitive impairment²³. Our study corroborates that postmenopausal women with osteoporosis who do not have cognitive impairment tend to have experienced earlier menarche, suggesting that early menarche may confer benefits from the neuroprotective effects of estrogen, leading to higher cognitive functioning. As postmenopausal women age and estrogen levels decline sharply, changes in body composition (bones, muscles, and fat) occur alongside a decline in cognitive function^{5,24,25}. FM, the main source of endogenous estrogen in postmenopausal women, shows a positive correlation with cognitive function in the Asian population^{26,27}. As a component of body weight, FM

osteoporosis				
Variables	Total (n = 120)	T1(n=68)	T2(n=52)	p Value
Age	66.84 ± 8.83	68.88±8.85	64.17 ± 8.14	0.003
Educational level				0.02
illiteracy	29 (24)	17 (25)	12 (23)	
primary school	30 (25)	23 (34)	7 (13)	
Junior high school and above	61 (51)	28 (41)	33 (63)	
duration of menopause	17.47 ± 9.71	19.68 ± 9.73	14.58 ± 8.98	0.004
Age of menarche				0.03
12	5 (4)	4 (6)	1 (2)	
13	14 (12)	7 (10)	7 (13)	
14	28 (23)	12 (18)	16 (31)	
15	21 (18)	7 (10)	14 (27)	
16	18 (15)	11 (16)	7 (13)	
17	15 (12)	12 (18)	3 (6)	
18	13 (11)	11 (16)	2 (4)	
19	3 (2)	2 (3)	1 (2)	
20	3 (2)	2 (3)	1 (2)	
Age of menopause	50 (48, 51.25)	49 (48, 51)	50 (48, 52)	0.251
Pregnancy frequency	(,,	(,,	(,)	0.331
1	7 (6)	3 (4)	4 (8)	
2	34 (28)	15 (22)	19 (37)	
3	44 (37)	27 (40)	17 (33)	
4	23 (19)	14 (21)	9 (17)	
5	6 (5)	3 (4)	3 (6)	
6	4(3)	4 (6)	0 (0)	
7	1(1)	1(1)	0 (0)	
8	1(1)	1 (1)	0 (0)	
Production frequency	- (-)	- (-)	- (0)	0.122
1	52 (43)	28 (41)	24 (46)	
2	44 (37)	26 (38)	18 (35)	
3	17 (14)	7 (10)	10 (19)	
4	5 (4)	5 (7)	0 (0)	
6	2 (2)	2 (3)	0 (0)	
The proportion of meat in the diet	- (-)	- (-)	- (-)	0.829
30%below	54 (45)	30 (44)	24 (46)	0.025
30%-50%	52 (43)	29 (43)	23 (44)	
50% above	14 (12)	9 (13)	5 (10)	
Body composition	. ,		,	
Height(m)	1.56 ± 0.06	1.55 ± 0.06	1.58±0.04	0.001
Weight(kg)	52.71 ± 7.97	50.65 ± 7.45	55.4±7.9	0.001
BMI (kg/m2)	21.61 ± 2.77	21.15 ± 2.57	22.2±2.94	0.039
Fat Mass(kg)	18.08 ± 4.79	17.27 ± 4.63	19.14±4.84	0.034
Trunk Fat Mass(kg)	10.00 ± 4.79	9.41 ± 3.18	10.98 ± 3.23	0.009
Fat-Free Mass(kg)	34.63 ± 4.24	33.38 ± 3.89	36.26±4.16	< 0.001
Appendicular Skeletal muscle Mass(kg)	13.98 ± 1.97	13.51 ± 1.94	14.59 ± 1.84	0.003
ripperioreniai okcietai musele iviass(kg)	13.70 ± 1.77	13.31 ± 1.74	17.57 ± 1.04	0.003

Table 4. Factors related to bone density. Abbreviations: T1, Severe osteoporosis; T2, osteoporosis.

influences the expression and release of sex hormones and molecules such as leptin, insulin, and adiponectin in adipose tissue. This leads to decreased bone turnover and resorption, an upregulation of osteoblast activity, and enhanced bone formation²⁸. These findings are consistent with our observation that higher FM is associated with better cognitive function and higher BMD in postmenopausal women with osteoporosis. Furthermore, fat is also linked to nutritional intake²⁹. Studies have indicated that women are more susceptible to malnutrition, particularly deficits in energy and protein, which are crucial factors leading to loss of physical function³⁰. Nutrition significantly impacts cognitive function in postmenopausal women with osteoporosis. In our study, those who derived 30–50% of their diet from meat exhibited better cognitive function. A nutrient-rich diet is believed to be beneficial for overall health and brain aging, potentially reducing the incidence of dementia and

	osteoporosis n = 52 (43)		p value	Severe osteoporosis n = 68 (57)		p value
	non Cognitive impairment <i>n</i> = 35 (67)	Cognitive impairment n=17 (33)		non Cognitive impairment $n = 34 (50)$	Cognitive impairment n=34 (50)	
Height(m)	1.58 ± 0.05	1.57 ± 0.04	0.472	1.56 ± 0.06	1.53 ± 0.05	0.013
Weight(kg)	55.57 ± 7.61	55.04 ± 8.7	0.822	52.29 ± 6.46	49.02 ± 8.09	0.07
BMI (kg/m2)	22.18 ± 2.72	22.26 ± 3.43	0.931	21.36 ± 2.26	20.95 ± 2.86	0.505
Fat Mass(kg)	19.25 ± 4.15	18.92 ± 6.16	0.821	18.19 (16.39, 20.63)	15.58 (13.39, 17.37)	0.002
Trunk Fat Mass(kg)	11.08 ± 2.95	10.76 ± 3.84	0.743	10.39 ± 2.6	8.43 ± 3.44	0.01
Fat-Free Mass(kg)	36.32 ± 4.34	36.13 ± 3.87	0.873	33.62 ± 3.73	33.14±4.09	0.613
Appendicular Skeletal muscle Mass(kg)	14.61 ± 1.94	14.54 ± 1.67	0.896	13.76 ± 1.85	13.27 ± 2.03	0.3

Table 5. Severity stratification of osteoporosis, relationship between body composition and cognitive function. a The relationship between fat free mass, cognitive function, and severity of osteoporosis. b The relationship between height, cognitive function, and severity of osteoporosis. c The relationship between weight, cognitive function, and severity of osteoporosis. Abbreviations: T1,Severe osteoporosis; T2,osteoporosis; CI, Cognitive impairment.

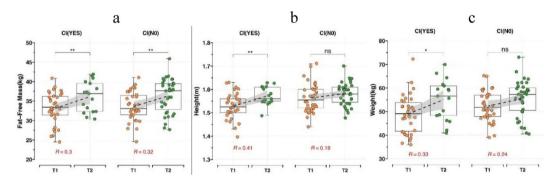


Fig. 1. Stratification of cognitive impairment, relationship between body composition and severity of osteoporosis. **a** The relationship between fat free mass, cognitive function, and severity of osteoporosis**b** The relationship between height, cognitive function, and severity of osteoporosisc The relationship between weight, cognitive function, and severity of osteoporosis Abbreviations:T1,Severe osteoporosis; T2,osteoporosis;CI, Cognitive impairment

maintaining brain health³¹. Thus, these factors may explain why higher FM is observed in postmenopausal women with osteoporosis who have better cognitive function.

Muscle wasting is a common factor influencing both osteoporosis and cognitive impairment³². In our study, the group of postmenopausal women with osteoporosis who exhibited cognitive impairment had significantly lower fat-free mass (FFM) and appendicular skeletal muscle mass (ASMM), although no differences were observed between groups. This outcome might be attributable to the fact that the participants were more engaged in physical labor, potentially leading to an increase in muscle mass. Cross-sectional studies have demonstrated that women with sarcopenia are five times more likely to develop cognitive impairment than those without sarcopenia³³. Within the components of sarcopenia, which include muscle mass and muscle strength, muscle strength is positively correlated with cognitive function and may serve as a better predictive indicator of cognitive performance³⁴. Moreover, our findings that FFM and ASMM are reduced in postmenopausal women with severe osteoporosis align with previous research³⁵. Osteoporosis and sarcopenia may share common pathophysiological pathways, including hormonal imbalances, increased inflammatory cytokine activity, nutritional changes, and physical injuries³⁶. Changes in endogenous hormones in postmenopausal women typically lead to decreases in muscle mass and bone density³⁷. Estrogen helps maintain skeletal muscle contractility and prevents osteoporosis, while androgens and testosterone promote myoblast growth²⁷. Additionally, many other tissue-specific factors released by muscles, such as insulin-like growth factor-1 (IGF-1), interleukin-6 (IL-6), and muscle growth inhibitor, can also regulate bone health³⁶. Hu et al. found that individuals with sarcopenia are 1.43 times more likely to develop mild cognitive impairment than those without sarcopenia³⁸. Sarcopenia is related to various brain phenotypes, including cortical thickness, brain volume, and white matter microstructure; the brain's sensory-motor system mediates the connection between muscle loss and cognitive features³⁹. Therefore, sarcopenia is associated with decreased cognitive function and bone density in postmenopausal women with osteoporosis.

As age increases, cognitive function typically decreases, potentially leading to dementia in severe cases⁴⁰. Research has shown a positive correlation between education level and cognitive function⁴¹. Similarly, our study

indicated that age and education level are strong predictors of cognitive function in postmenopausal women with osteoporosis. Childbirth increases the risk of cognitive decline and dementia by affecting neurodegenerative markers such as HVa, SPARE-AD volume, and SPARE-BA volume⁴². Compared to women who have not given birth, those who have given birth experience an approximate 22% decrease in estrogen levels and a shortened menstrual cycle, reflecting a decrease in cumulative estrogen exposure⁴³. In our study, postmenopausal women with osteoporosis who displayed poor cognitive function had given birth more frequently, consistent with previous findings⁴². Additionally, women in our study with poorer cognitive function exhibited significantly lower height. Height, an indicator of health and nutrition primarily influenced by genetic factors, affects individual development and is positively correlated with physical health levels, potentially impacting the cognitive function of postmenopausal women with osteoporosis^{44,45}.

Our research focuses primarily on the objective measurements of body composition and cognition in postmenopausal women with osteoporosis, which is crucial for understanding this demographic. Body composition was measured using DXA, providing more accurate data than previous studies. However, our study's limitation is that it only includes postmenopausal women with osteoporosis from Huzhou, Zhejiang Province, China. Consequently, our conclusions cannot be generalized to the entire population. To better understand the relationship between body composition and cognitive function in postmenopausal women with osteoporosis in the future, it will be necessary to expand the sample size and include additional FM-related body composition indicators, which may provide a more detailed explanation of the role of fat in cognitive function in this group.

Conclusions

FM is a crucial factor affecting cognitive function in postmenopausal women with osteoporosis. Women with postmenopausal osteoporosis who have low FM tend to exhibit decreased cognitive function and are more susceptible to cognitive dysfunction. Furthermore, low FM is associated with severe osteoporosis in this group. Therefore, FM is an important indicator of body composition in postmenopausal women with osteoporosis. In summary, monitoring FM in postmenopausal women with osteoporosis is of great significance and should be considered as a key monitoring indicator for follow-up and intervention.

Data availability

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Received: 18 July 2024; Accepted: 21 May 2025

Published online: 24 May 2025

References

- 1. Brown, J. P. Long-Term treatment of postmenopausal osteoporosis. *Endocrinol. Metab.* (Seoul). **36**, 544–552. https://doi.org/10.3803/EnM.2021.301 (2021).
- 2. Zhou, S., Tao, Z., Zhu, Y. & Tao, L. Mapping theme trends and recognizing hot spots in postmenopausal osteoporosis research: a bibliometric analysis. *PeerJ* 7, e8145. https://doi.org/10.7717/peerj.8145 (2019).
- 3. Management of osteoporosis in. postmenopausal women: the 2021 position statement of The North American Menopause Society. Menopause 28, 973–997, (2021). https://doi.org/10.1097/gme.000000000001831
- Ma, M. L. et al. Efficacy of vitamin K2 in the prevention and treatment of postmenopausal osteoporosis: A systematic review and meta-analysis of randomized controlled trials. Front. Public. Health. 10, 979649. https://doi.org/10.3389/fpubh.2022.979649 (2022).
- Yong, E. L. & Logan, S. Menopausal osteoporosis: screening, prevention and treatment. Singap. Med. J. 62, 159–166. https://doi.org/10.11622/smedj.2021036 (2021).
- Khalafi, M. et al. The effects of exercise training on body composition in postmenopausal women: a systematic review and metaanalysis. Front. Endocrinol. (Lausanne). 14, 1183765. https://doi.org/10.3389/fendo.2023.1183765 (2023).
- Zhao, Y., Chen, H., Qiu, F., He, J. & Chen, J. Cognitive impairment and risks of osteoporosis: A systematic review and metaanalysis. Arch. Gerontol. Geriatr. 106, 104879. https://doi.org/10.1016/j.archger.2022.104879 (2023).
- Amouzougan, A. et al. High prevalence of dementia in women with osteoporosis. *Joint Bone Spine*. 84, 611–614. https://doi.org/1 0.1016/j.jbspin.2016.08.002 (2017).
- Wang, Y. Y., Zhang, M., Wang, X. X., Liu, S. & Ding, H. Correlates of cognitive impairment in the elderly in China: A cross-sectional study. Front. Public. Health. 10, 973661. https://doi.org/10.3389/fpubh.2022.973661 (2022).
- Kang, H. G., Park, H. Y., Ryu, H. U. & Suk, S. H. Bone mineral loss and cognitive impairment: the PRESENT project. *Med. (Baltim)*. 97, e12755. https://doi.org/10.1097/md.000000000012755 (2018).
- Ebrahimpur, M. et al. Osteoporosis and cognitive impairment interwoven warning signs: community-based study on older adults-Bushehr elderly health (BEH) program. Arch. Osteoporos. 15, 140. https://doi.org/10.1007/s11657-020-00817-1 (2020).
- 12. Heisey, H. D., Kunik, M. E., Qualls, C., Segoviano-Escobar, M. B. & Villareal, D. T. Truncal fat and frailty are important predictors of cognitive performance among aging adults with obesity. *J. Nutr. Health Aging.* 26, 425–429. https://doi.org/10.1007/s12603-02 2-1776-x (2022).
- 13. Arceo-Mendoza, R. M. & Camacho, P. M. Postmenopausal osteoporosis: latest guidelines. *Endocrinol. Metab. Clin. North. Am.* **50**, 167–178. https://doi.org/10.1016/j.ecl.2021.03.009 (2021).
- 14. Cheng, K. Y. et al. Diagnosis of sarcopenia by evaluating skeletal muscle mass by adjusted bioimpedance analysis validated with dual-energy X-ray absorptiometry. *J. Cachexia Sarcopenia Muscle.* 12, 2163–2173. https://doi.org/10.1002/jcsm.12825 (2021).
- 15. Shevroja, E., Cafarelli, F. P., Guglielmi, G. & Hans, D. DXA parameters, trabecular bone score (TBS) and bone mineral density (BMD), in fracture risk prediction in endocrine-mediated secondary osteoporosis. *Endocrine* 74, 20–28. https://doi.org/10.1007/s 12020-021-02806-x (2021).
- 16. Achamrah, N. et al. Comparison of body composition assessment by DXA and BIA according to the body mass index: A retrospective study on 3655 measures. *PLoS One.* 13, e0200465. https://doi.org/10.1371/journal.pone.0200465 (2018).
- 17. Marra, M. et al. Assessment of body composition in health and disease using bioelectrical impedance analysis (BIA) and dual energy X-Ray absorptiometry (DXA): A critical overview. *Contrast Media Mol. Imaging.* **2019** (3548284). https://doi.org/10.1155/2019/3548284 (2019).

- 18. Folstein, M. F., Folstein, S. E. & McHugh, P. R. Mini-mental State. A practical method for grading the cognitive State.of patients for the clinician. *J. Psychiatr Res.* 12, 189–198. https://doi.org/10.1016/0022-3956(75)90026-6 (1975).
- 19. Lv, X. et al. Cognitive decline and mortality among community-dwelling Chinese older people. BMC Med. 17 https://doi.org/10.1 186/s12916-019-1295-8 (2019).
- Jia, X. et al. A comparison of the Mini-Mental state examination (MMSE) with the Montreal cognitive assessment (MoCA) for mild cognitive impairment screening in Chinese middle-aged and older population: a cross-sectional study. BMC Psychiatry. 21, 485. https://doi.org/10.1186/s12888-021-03495-6 (2021).
- 21. Xie, C., Wang, C. & Luo, H. Increased risk of osteoporosis in patients with cognitive impairment: a systematic review and meta-analysis. BMC Geriatr. 23, 797. https://doi.org/10.1186/s12877-023-04548-z (2023).
- 22. Jiang, Y. L. et al. The protective effects of Osteocyte-Derived extracellular vesicles against Alzheimer's disease diminished with aging. Adv. Sci. (Weinh). 9, e2105316. https://doi.org/10.1002/advs.202105316 (2022).
- 23. Morgan, K. N., Derby, C. A. & Gleason, C. E. Cognitive changes with reproductive aging, perimenopause, and menopause. *Obstet. Gynecol. Clin. North. Am.* 45, 751–763. https://doi.org/10.1016/j.ogc.2018.07.011 (2018).
- Ko, S. H. & Jung, Y. Energy metabolism changes and dysregulated lipid metabolism in postmenopausal women. Nutrients 13 https://doi.org/10.3390/nu13124556 (2021).
- Xi, H. et al. Reproductive factors and cognitive impairment in natural menopausal women: A cross-sectional study. Front. Endocrinol. (Lausanne). 13, 893901. https://doi.org/10.3389/fendo.2022.893901 (2022).
- Mina, T. et al. Adiposity impacts cognitive function in Asian populations: an epidemiological and Mendelian randomization study. Lancet Reg. Health West. Pac. 33, 100710. https://doi.org/10.1016/j.lanwpc.2023.100710 (2023).
- Spauwen, P. J. et al. Associations of fat and muscle tissue with cognitive status in older adults: the AGES-Reykjavik study. Age Ageing. 46, 250–257. https://doi.org/10.1093/ageing/afw219 (2017).
- 28. Fan, J., Jiang, Y., Qiang, J., Han, B. & Zhang, Q. Associations of fat mass and fat distribution with bone mineral density in Non-Obese postmenopausal Chinese women over 60 years old. *Front. Endocrinol. (Lausanne).* 13, 829867. https://doi.org/10.3389/fendo.2022.829867 (2022).
- 29. Holmes, C. J. & Racette, S. B. The utility of body composition assessment in nutrition and clinical practice: an overview of current methodology. *Nutrients* 13 https://doi.org/10.3390/nu13082493 (2021).
- 30. Jyväkorpi, S. K. et al. Relationship between frailty, nutrition, body composition, quality of life, and gender in institutionalized older people. *Aging Clin. Exp. Res.* 34, 1357–1363. https://doi.org/10.1007/s40520-022-02077-0 (2022).
- 31. Ellouze, I., Sheffler, J., Nagpal, R. & Arjmandi, B. Dietary Patterns and Alzheimer's Disease: An Updated Review Linking Nutrition to Neuroscience. *Nutrients* 15 https://doi.org/10.3390/nu15143204 (2023).
- 32. Bliuc, D. et al. Cognitive decline is associated with an accelerated rate of bone loss and increased fracture risk in women: a prospective study from the Canadian multicentre osteoporosis study. *J. Bone Min. Res.* 36, 2106–2115. https://doi.org/10.1002/jbm r.4402 (2021).
- 33. Lee, I. et al. Sarcopenia is associated with cognitive impairment and depression in elderly Korean women. *Iran. J. Public. Health.* 47, 327–334 (2018).
- 34. Sui, S. X., Williams, L. J., Holloway-Kew, K. L., Hyde, N. K. & Pasco, J. A. Skeletal muscle health and cognitive function: A narrative review. *Int. J. Mol. Sci.* 22 https://doi.org/10.3390/ijms22010255 (2020).
- 35. Lin, Y., Wang, X., Wu, R., Zhou, J. & Feng, F. Association between segmental body composition and bone mineral density in US adults: results from the NHANES (2011–2018). BMC Endocr. Disord. 23, 246. https://doi.org/10.1186/s12902-023-01506-z (2023).
- 36. Mathieu, M. et al. Association between bone mineral density and fat mass independent of lean mass and physical activity in women aged 75 or older. *Nutrients* 13 https://doi.org/10.3390/nu13061994 (2021).
- Cheng, L. & Wang, S. Correlation between bone mineral density and sarcopenia in US adults: a population-based study. J. Orthop. Surg. Res. 18 https://doi.org/10.1186/s13018-023-04034-7 (2023).
- 38. Hu, Y., Peng, W., Ren, R., Wang, Y. & Wang, G. Sarcopenia and mild cognitive impairment among elderly adults: the first longitudinal evidence from CHARLS. J. Cachexia Sarcopenia Muscle. 13, 2944–2952. https://doi.org/10.1002/jcsm.13081 (2022).
- Gurholt, T. P. et al. Linking sarcopenia, brain structure and cognitive performance: a large-scale UK biobank study. *Brain Commun.* f. fcae083. https://doi.org/10.1093/braincomms/fcae083 (2024).
- Gómez-Soria, I. et al. Cognitive stimulation and cognitive results in older adults: A systematic review and meta-analysis. Arch. Gerontol. Geriatr. 104, 104807. https://doi.org/10.1016/j.archger.2022.104807 (2023).
- 41. Lövdén, M., Fratiglioni, L., Glymour, M. M., Lindenberger, U. & Tucker-Drob, E. M. Education and cognitive functioning across the life span. *Psychol. Sci. Public. Interest.* 21, 6–41. https://doi.org/10.1177/1529100620920576 (2020).
- 42. Jung, J. H. et al. Brain atrophy, and cognitive decline. Front. Aging Neurosci. 12, 159. https://doi.org/10.3389/fnagi.2020.00159 (2020). Multiparity.
- 43. Han, S. L., Liu, D. C., Tan, C. C., Tan, L. & Xu, W. Male- and female-specific reproductive risk factors across the lifespan for dementia or cognitive decline: a systematic review and meta-analysis. *BMC Med.* 21, 457. https://doi.org/10.1186/s12916-023-031 59-0 (2023).
- Selvamani, Y. & Arokiasamy, P. Association of life course socioeconomic status and adult height with cognitive functioning of older adults in India and China. BMC Geriatr. 21, 354. https://doi.org/10.1186/s12877-021-02303-w (2021).
- 45. Amin, V. & Fletcher, J. M. What is driving the relationship between height and cognition? Evidence from the twins early development study. Econ. Hum. Biol. 47, 101174. https://doi.org/10.1016/j.ehb.2022.101174 (2022).

Author contributions

All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by DZ, ZZ, LX, YZ, XL, MX, XX, and YW. The first draft of the manuscript was written by DZ, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Funding

This study was supported by the following grants: General Medical and Health Projects in Zhejiang Province (2024KY414); General Public Welfare Application Research Project of Huzhou Science and Technology Bureau (Class B) (2023GYB65).

Declarations

Competing interests

The authors declare no competing interests.

Conflict of interest

The authors declare that there are no conflicts of interest.

Statement

This study had been approved by the Medical Ethics Committee of Huzhou Central Hospital (No. 202303041-01). And the study was performed in accordance with relevant regulations. And informed consent was obtained from all participants and/or their legal guardians.

Additional information

Correspondence and requests for materials should be addressed to X.X. or Y.W.

Reprints and permissions information is available at www.nature.com/reprints.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Open Access This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by-nc-nd/4.0/.

© The Author(s) 2025