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The Role of Bone Mineral Density Assessment in Health-Related Quality of Life in Postmenopausal Han Chinese Women Prior to Clinic Diagnosis of Osteoporosis

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1. Abstract

1.1. Purpose: Osteoporosis is a systemic skeletal disease and strongly associated with reduced quality of life (QoL). The aim of the study was to explore BMD that might serve as index of health-related QoL (HRQoL), or the relationship between bone mineral density（BMD）and HRQoL in postmenopausal Han Chinese women prior to diagnosis of osteoporosis.

1.2. Methods: QUALEFFO-41 and an optimism questionnaire (LOT-r) were used to survey the enrolled patients. The relationships between HRQoL and FN BMD were analyzed using separate hierarchical multiple regression analysis.

1.3. Results: In the hierarchical multiple regression analysis, for those without fracture: at Step 1, age, BMI and optimism accounted for 58.6% of the variance in HRQoL total scores (Fch（3, 153）=70.75, $p < 0.05$). At Step 2, the addition of FN BMD explained 5.8% of the variance over and above the age, BMI, and optimism (Fch（4, 153）= 67.30, $p < 0.05$). FN BMD accounted for significant variance in HRQoL total scores ($p = 0.000$). In those with fracture: the number of fractures was added to the analysis as a variance. A lower FN BMD was not associated with a compromised HRQoL total score ($p = 0.555$). Younger age, increased BMI, and decreased optimism negatively correlated with HRQoL in both groups with or without fracture. Conclusions According to the survey, excluding the effects of positive BMI and negative factors such as age, optimism, FN BMD shows a positive correlation to the value of HRQoL in postmenopausal women prior to a diagnosis of osteoporosis.

2. Introduction

Osteoporosis is a systemic skeletal disease characterized by reduced bone mass and micro-architectural abnormality, with a consequent increase in bone fragility and high susceptibility to fracture, particularly in the vertebral body, distal forearm, and proximal femur of postmenopausal women [1]. It is estimated that the prevalence of osteoporosis rises from one-third in people aged 50-60 years to more than 50% in people aged over 80 years. By 2050, the global number of people with osteoporosis will reach 6 million (including both males and females), three quarters of them will reside in developing countries [2,3]. With the average life span extended to 70 years, most women will spend about one-third of their lifetimes beyond the menopausal age. Besides, the proportion of postmenopausal women is rising since the aging population is expanding rapidly. Thus, the health of menopausal women will become a prime concern worldwide [4]. During the menopausal transition period, women will experience a number of bothersome

symptoms. In addition to hot flushes, headaches, sweating, fatigue, sexual dysfunction, and reduced estrogen, osteoporosis is the most prevalent disease in menopausal women, and is strongly associated with low quality of life（QoL [4]. The prevalence of osteoporosis and related fractures is higher in postmenopausal women than in men of comparable age since estrogen plays a key role in maintaining bone health. The National Osteoporosis Foundation（NOF）estimates that there are 9.1 million women with osteoporosis and an additional 26 million with reduced bone mass. This far exceeds the estimated number of same age men with osteoporosis and reduced bone mass (2.8 million and 14.4 million, respectively) [5]. In a meta-analysis evaluating the data on the epidemiology of Chinese people over 40-year age, the author found that the total prevalence of osteoporosis at an age above 40 years in China was 13.2%, and it is significantly higher among females than males: 14.2% vs. 11.8% respectively（$P < 0.05$）. The prevalence of osteoporosis increases in both men and women with age, it increases more significantly in females over 50 years of age compared with same age range males [6]. A consequence of osteoporosis is an increased risk of fractures, particularly fragility fractures that often occur with little or no apparent trauma and are often difficult to diagnose. Fragility fractures are defined as "caused by injury that would be insufficient to fracture a normal bone … the result of reduced compressive and/or torsional strength of bone" [7]. Fracture is the major clinical outcome of osteoporosis affecting mainly the vertebrae, femur, and wrist bones. Vertebral fractures（VF）may be asymptomatic in 30% of the cases and only one-third of the fractures observed radiographically require medical attention [8]. Thus, a fracture that occurs because of osteoporosis may not be detected, which means osteoporosis is all too often "silent" or without symptoms [9]. Other than non-specific back pain, the early symptoms of osteoporosis are rarely reported, and osteoporosis is rarely diagnosed prior to an initial bone fracture [10]. As osteoporosis may lead to a limitation of daily activities due to restricted mobility and pain, women with high risk of osteoporosis tend to reduce the risk of fracture by limiting their physical activities [11,12]. This restriction leads to other consequences, such as social isolation, loneliness, depression, anxiety, despairing, loss of values, and other psychological disorders [11]. HRQoL is a subset of index to reflect overall life quality, and includes domains of physical, emotional, and social well-beings [13]. As recognized by WHO in 2003, the presence of osteoporosis accompanied by a fracture significantly impairs an individual's HRQoL by greatly reducing physical activities while producing pain, social isolation, and depression [14].

Dispositional optimism is defined as a stable, trait-like personality characterized by a generally positive mood or attitude about the future with a tendency to expect favorable outcomes in life situations [15]. In different medical settings, optimistic people have been shown to have higher QoL, compared to people with low optimism levels or pessimistic people [15-17]. Osteoporosis is a systemic disease in which bone density is reduced, leading to the weakening of body skeleton and increased vulnerability to fractures [18]. A more practical definition of osteoporosis is based on BMD. The BMD of the aged individual is compared to the average BMD of same gender at age 30 and the ratios are expressed in standard deviation units, identified as "T-score". If the T-score is equal to or less than 2.5, osteoporosis may be diagnosed [1]. Data from the National Health and Nutrition Examination Surveys of 1988–1994 and 2005–2006 suggest that the prevalence of low BMD within the population has remained relatively constant since the late 1980s [19,20]. There is less certainty about whether low BMD has an additive influence on HRQoL, or whether it is a separate factor. The impact of low bone mass on HRQoL, in the presence or absence of fracture, has received little attention [21]. Wilson et al. [21] indicated that patients referred for BMD assessment before a diagnosis of osteoporosis had reduced physical component summary scores. In patients without fracture, low BMD contributed to this reduction in HRQoL in this experiment. However, whether low BMD prior to diagnosis of osteoporosis has a separate influence on HRQoL with or without fractures has not been investigated in the Han Chinese population. Thus, the objectives of the present study were to investigate the relationship between HRQoL and BMD, and to evaluate whether optimism plays a positive role in postmenopausal Han Chinese women undergoing BMD assessment prior to diagnosis of osteoporosis.

3. Methods

3.1. Subjects

The protocol of this study was approved by the Medical Ethics Committee of Xi'an Jiaotong University. All participants have completed written informed consent forms. All subjects enrolled in this cross-sectional study were randomly selected from clinic lists in the Second Affiliated Hospital of Xi'an Jiaotong University between January 2015 and December 2019. Patients were included in the data analysis if they were female, postmenopausal, over 45 years of age, had not undergone a previous dual energy X-ray absorptiometry（DXA）examination, and did not have a prior diagnosis of osteoporosis. Patients were excluded if they were receiving treatment for osteoporosis; had conditions or medications known to affect BMD such as hyperparathyroidism, renal disease or malabsorption; had suffered a stroke or a myocardial infarction in the previous year; or had a history of cancer [21]. Measurement of bone mineral density and anthropometric baseline data DXA (Lunar Expert 1313, Lunar Corp., USA) was used to assess BMD at the femur neck. BMD was expressed in g/cm2 and as peak bone mass percentage in normal subjects (T-score) depending on the software used in the device. The patients were classified into 3 groups on the basis of the BMD results of the femur neck according to World Health Organization criteria: normal (T score < -1.0 SD), osteopenia (T score -1.0 to -2.5 SD), and osteoporosis (T

score < -2.5 SD). The anthropometric baseline data of all subjects were obtained by measurements and questionnaires.

3.2. QoL Assessment

The Questionnaire of the European Foundation for Osteoporosis (QUALEFFO) is a well-known instrument to assess functionality and QoL in this population. Different versions of the tool exist: the first one had 48 items but was shortened to 41 items (QUALEFFO-41) [22]. The Quality of Life Questionnaire of the European Foundation for Osteoporosis 41 (QUALEFFO-41) was developed for the purpose of evaluating patients with osteoporotic vertebral fractures. It is a self-administered, disease-specific tool and contains 41 items divided into several subscales: pain (5 items), physical function (17 items), social function (7 items), general health perception (3 items), and mental function (9 items). Most of the items have five response options (scores range from 0 to 4 points). Exceptions are items 27, 28, and 29 with four responses (score ranges from 0 to 3 points) and items 23, 24, 25, and 26 with 3 response options (scores range from 0 to 2 points) [23]. Domain scores were calculated by summing the answer scores and submitting the sum to a linear transformation to a 100 scale, where 0 represents the best and 100 the worst QoL [24].

3.3. Optimistic Assessment

Optimism was assessed by the Chinese version of the Life Orientation Test-Revised (LOT-R) [25,26]. The LOT-R consists of 10 questions with a 6-item measure and 4 filler items assessing individual differences in generalized optimism versus pessimism. The total score ranges from 0 to 24 with high scores indicating higher levels of optimism. For indicative purposes, we analyzed optimism using cutoff values as follows: 0–13 indicates low optimism, 14–18 moderate optimism and 19–24 high optimism. Subscales of optimism and pessimism are useful both when compared against one another and combined for practical use in a clinical setting [27].

3.4. Statistical Analysis

Differences in patient characteristics between the six groups were assessed using one-way analysis of variance (ANOVA). Excluding the effects of confounding factors such as age, BMI, number of fractures, and optimism, relationships between HRQoL and FN BMD were analyzed using separate hierarchical multiple regression analysis. $P<0.05$ was considered to indicate a statistically significant difference. Data analysis was performed using SPSS Version 15.0 (IBM, Chicago, USA).

4. Results

4.1. Participants

217 postmenopausal women were divided into those who had with or without a history of fracture,and were also stratified according to World Health Organization criteria: normal (T score < -1.0 SD), osteopenia (T score -1.0 to -2.5 SD), and osteoporosis (T score < -2.5 SD),genernating six groups (Table 1). The results of one-way ANOVA showed that there were significant differences in all variables among the six groups. In contrast with osteopenia and normal FN BMD, patients with osteoporosis were older, had lower BMI, and lower optimism. There were significant differences in the number of fractures among the three FN BMD groups. Patients with osteoporosis had a higher number of fractures compared with those with osteopenia and normal FN BMD.

Table 1: Characteristics of patients attending bone mineral density assessments

	Without a history of fracture			With a history of fracture			*p* value
	Normal	Osteopenia	Osteoporosis	Normal	Osteopenia	Osteoporosis	
N	25	97	32	34	35	48	
Age, years, mean (SD)	68.24 (8.34)	68.37 (11.11)	73.56 (8.68)	67.65 (6.37)	69.51 (10.19)	76.65 (7.87)	0.010
BMI, kg/m^2, mean (SD)	20.04 (3.01)	23.43 (3.69)	27.88 (2.92)	19.20 (2.99)	23.20 (3.48)	25.14 (4.46)	0.000
Optimism, LOT-R, mean (SD)	18.48 (4.11)	15.46 (4.95)	10.47 (3.78)	14.09 (6.41)	13.71 (4.40)	12.63 (3.87)	0.001
FN BMD T score, mean (SD)	-0.59 (0.17)	-1.79 (0.29)	-2.73 (0.13)	-0.80 (0.14)	-1.85 (0.27)	-2.87 (0.16)	0.000
Number of fractures (n, %)							
One				13 (38.2)	12 (34.3)	22 (45.8)	
Two				11 (32.4)	15 (42.9)	7 (14.6)	
More than three				10 (29.4)	8 (22.9)	19 (39.6)	0.000

4.2. QUALEFFO-41 Scores

Table 2 shows the subdomain scores of QUALEFFO-41 in postmenopausal women undergoing BMD assessments (DXA) of patients in the six groups. The most significant negatively correlated factors or subdomains in this study were mental function (51.72±24.66), pain (51.61±27.49), and general health perception (50.61±21.44). When we compared the QUALEFFO-41 scores after stratifying the groups according to fracture status and FN BMD T scores. A significant difference was found for all domains at $p < 0.001$ (Table 3).

Table 2: QUALEFFO-41 scores

	Minimum	Maximum	Mean (SD)
Total score	11.11	79.09	41.28(22.15)
Pain (5)	0	100	51.61 (27.49)
Activities of daily living (4)	0	75	25.16 (24.28)
Jobs around the house (5)	0	80	27.44 (25.19)
Mobility (8)	0	81.25	33.98 (29.73)
Social function(7)	0	100	45.65 (28.57)
General health perception(3)	0	100	50.61 (21.44)
Mental function(9)	8.33	88.89	51.72 (24.66)

Table 3: QUALEFFO-41 subdomain comparison according to fracture status and FN BMD T scores

Domain	Without fracture			With fracture			p value
	Normal	osteopenia	osteoporosis	Normal	osteopenia	osteoporosis	
QUALEFFO-41 Total score	20.00(8.24)	31.16(18.07)	54.76(16.28)	49.85（30.11）	46.85(14.96)	53.70(18.29)	0.000
Pain(5)	18.00(22.50)	43.51(27.92)	57.81 (24.53)	70.59（16.09）	66.57(19.81)	56.98(20.23)	0.000
Activities of daily living(4)	7.25 (5.00)	14.69 (15.04)	33.40 (18.35)	36.21（34.47）	28.57(20.47)	39.84(28.15)	0.000
Jobs around the house(5)	0 (0)	19.12 (20.62)	46.25 (18.23)	36.32（33.96）	30.86(19.65)	37.19(22.88)	0.000
Mobility(8)	6.75 (5.31)	19.14 (24.28)	55.08 (23.42)	41.09（35.61）	42.06(25.96)	53.19(22.46)	0.000
Social function(7)	15.06 (11.53)	35.11 (24.16)	69.67 (10.58)	46.71（36.52）	48.07(23.12)	64.34(23.45)	0.000
General health perception(3)	32.33 (23.73)	46.48 (19.05)	57.03 (21.91)	60.29（25.05）	47.86(14.90)	59.38(17.33)	0.000
Mental function(9)	47.89 (9.08)	42.04 (25.08)	59.20 (25.54)	57.68（32.81）	56.27(17.14)	60.76(20.07)	0.000

4.3. The Relationship between HRQoL and FN BMD

Hierarchical multiple regression analysis was performed to evaluate the variance in HRQoL scores for those without a history of fracture could be explained by FN BMD after controlling for confounding variables (Table 4). In those without fracture, age, BMI, and optimism were entered in Step 1, followed by FN BMD. At Step 1, age, BMI and optimism accounted for 58.6% of the variance in HRQoL total scores (Fch (3, 153) = 70.75, $p < 0.05$). At Step 2, the addition of FN BMD added extra 5.8% of the variance over and above age, BMI, and optimism (Fch (4, 153) = 67.30, $p < 0.05$). FN BMD accounted for a significant variance in HRQoL total scores ($p = 0.000$). In those with fracture, the number of fractures were added to the statistical model, and the relationship between FN BMD and HRQoL total score did not reach statistical significance ($p = 0.555$). Younger age, higher BMI, and lower optimism negatively affected the levels of HRQoL in those with or without fracture (a lower score indicates a better HRQoL).

Table 4: Hierarchical regression model of physical health-related quality of life

Population	variables	R^2	ΔR^2	Beta coefficient	*t*	*p* value
Without fracture (n = 154)	Step 1	0.586	0.586*			
	Age			-0.108	-2.035	0.044
	BMI			0.121	2.202	0.029
	Optimism			-0.723	-13.122	0.000
	Step 2	0.644	0.058*			
	FN BMD			-0.310	-4.916	0.000

With fracture (n = 117)	Step1	0.635	0.635*			
	Age			-0.131	-2.204	0.030
	BMI			0.137	2.328	0.022
	Number of fractures			0.008	0.142	0.887
	Optimism			-0.799	-13.586	0.000
	Step 2	0.636	0.001			
	FN BMD			0.043	0.592	0.555

Note. Statistical significance:*p < .05

5. Discussion

In this study population, the classification of postmenopausal women attending for BMD assessments (DXA) showed significant differences among the six groups with respect to all domains of the QUALEFFO-41. Compared with osteopenia and normal FN BMD, postmenopausal women with osteoporosis showed impairments in all domains of the specific QUALEFFO-41 instrument; scoring particularly low in the mental function (51.72 ± 24.66), pain (51.61 ± 27.49), and general health perception (50.61 ± 21.44) domains. These results are similar to those of other studies using the same questionnaire and also show a worse QoL in virtually all domains evaluated, with scores predominantly more related to the clinical aspects of the diseases [28,29].

The present study is one of few studies that has investigated the relationship between FN BMD and HRQoL in those with and without bone fracture before a diagnosis of osteoporosis after controlling confounding variables. In osteoporosis, low BMD is asymptomatic and patients with or without low-grade fractures may be unaware of their conditions. By contrast, a reduced BMD may sometimes cause a decrease in QoL owing to the fear of potential new fractures [29]. It is possible that increased pain present in patients with osteoporosis even before a true fracture occurs; which is reflected in the worse bodily pain scores. This pain could be due to micro-architectural failure of the bone, which might be associated with the low BMD [30]. It is interesting to note that Dennison et al. [31] found a relationship between HRQoL and FN BMD in men but not women after controlling for other variables, such as age, social class, BMI, and co-morbidities. This is the first study to control age, BMI, and optimism during the scoring for the QUALEFFO-41 in postmenopausal Han Chinese women undergoing FN BMD assessment prior to the diagnosis of osteoporosis. After controlling for these confounding variables, we found that HRQoL is associated with FN BMD in Han Chinese women with or without previous fractures before a diagnosis of osteoporosis. Moreover, the relationship between FN BMD and HRQoL was more evident in those without a previous fracture, suggesting that it is not always the clinical fracture itself or the impact of diagnosis of osteoporosis determining this relationship. In the present study, we found that younger age negatively affected HRQoL scores in those with or without fracture. The reasons for such influence in HRQoL by relatively younger age are still unclear. Such inverse correlation between age and HRQoL was consistent with previous studies [32-35]. They are consistent with existing literature, where in frailty patients, advancing age is associated with better HRQoL [36] and the reasons for this could be that older patients have reduced life quality expectations [37]. This may indicate that because older men start with lower baseline QOL scores, they have lower recovery expectations from their diseases, or that older patients have developed strong resilience to QOL fluctuations over time [38]. In our study, increasing BMI negatively affected HRQoL in those with or without fractures. Table 1 shows that the majority of postmenopausal patients were overweight or obese. Greater morbidity and adverse effects on HRQoL might be expected in obese individuals with fracture than in non-obese people because of a greater prevalence of comorbidities, higher risk of fracture, more post-operative complications, and slower rehabilitation [39-41]. Compston et al. reported obese women with fracture undergoing a prolonged period of hospitalization for treatment with a poor recovery of functional status and worse HRQL compared with that in non-obese women. Therefore, higher BMI might be related to higher osteoporosis risk. Prevention of weight gain in postmenopausal women should be encouraged. In addition, positive correlationship were found between levels of HRQoL and optimism among the six groups. These results are similar to previous findings that optimism and locus of control are associated with general health ratings [42,43], disability [44], HRQoL [45], and recovery in many medical disorders [45-49]. The largest study investigating the relationship between optimism and HRQoL in 1529 patients with chronic diseases found that optimism was positively linked with HRQoL [50]. Excluding the effects of confounding factors such as age, BMI, and optimism, we have observed that the HRQoL total score was significantly associated with FN BMD in those without a previous fracture. It is therefore not always true that the clinical fracture itself or the impact of diagnosis of osteoporosis determine the correlation between HRQoL and FN BMD ($p < 0.05$). It is similar to the results of Wilson et al. [21]. HRQoL is worsen even before diagnosis of osteoporosis. In recent years, scientists focused on the prevention of fracture in patients with osteoporosis. Because a more practical definition of osteoporosis is based on FN BMD, we should revise the current research results. We also need to pay close attention to the impact of fractures and FN BMD status on HRQoL in the future research and practice.

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