Int J Clin Exp Med 2018;11(3):2543-2550
www.ijcem.com /ISSN:1940-5901/IJCEM0059016

Original Article

Osteoporosis screening based on body mass index, years since menopause and age among postmenopausal women in South Central China

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Received June 8, 2017; Accepted December 5, 2017; Epub March 15, 2018; Published March 30, 2018

Abstract: We aimed to screen for high risk factors for osteoporosis and provide appropriate criteria for bone mineral testing for osteoporosis screening in healthy postmenopausal women. This cross-sectional study surveyed 782 healthy postmenopausal women aged 50-77 years from South Central China by using a questionnaire. Bone mineral density was measured by dual X-ray absorptiometry. Subjects were divided into two groups according to their T-scores: osteoporosis group and non-osteoporosis group. The χ^2 test was used to compare categorical variables between the two groups, while logistic regression models were used to identify osteoporosis-related risk factors. Receiver operating characteristic (ROC) curve analysis was applied to evaluate the prognostic performance of age, years since menopause, and body mass index (BMI) in predicting osteoporosis in postmenopausal women in China. We found that age, years since menopause, BMI, history of fragility fractures, and fall history significantly differed between the two groups ($P < 0.05$). However, only BMI ($\beta = -0.479$), years since menopause ($\beta = 0.318$), and age ($\beta = 0.298$) were significantly correlated with osteoporosis after logistic regression analysis ($P < 0.05$). The optimal cutoffs for BMI, years since menopause, and age were 22.81 kg/m^2 (area under the ROC curve [AUC]: 0.624; 95% CI: 0.584-0.664), 10.05 years (AUC: 0.658; 95% CI: 0.619-0.697), and 62.45 years (AUC: 0.644; 95% CI: 0.604-0.684), respectively. The present study demonstrates that older age, longer menopause duration, lower BMI, history of fragility fractures, and fall history are risk factors for osteoporosis. Bone mineral density testing for osteoporosis screening is indicated in healthy postmenopausal women from South Central China who are aged > 62 years, went through menopause > 10 years ago, or have a BMI of < 23 kg/m^2.

Keywords: Osteoporosis, postmenopausal, screening, risk factors, cutoff point

Introduction

Osteoporosis is a systemic metabolic skeletal disease characterized by low bone mineral density (BMD), increased bone fragility and a higher incidence of fractures [1]. The prevalence rate of osteoporosis increases with age, and thus, the aging of the population makes osteoporosis a major public health problem worldwide [2]. Postmenopausal osteoporosis (PMOP) commonly occurs within 5-10 years of menopause, and is increasingly becoming an important health care challenge in women [3]. The fracture risk associated with osteoporosis severely affects the quality of life and even mortality of old people, especially, women [4]. Therefore, the early recognition and management of those at a high risk for osteoporosis will be greatly beneficial for individuals and the society.

BMD is clinically used as the best quantitative indicator for the diagnosis of osteoporosis and for predicting the risk of osteoporotic fractures. At present, T-score measurement by dual energy X-ray absorptiometry (DXA) is the internation-

Table 1. Densitometric, anthropometric and clinical data of the 782 women studied

Characteristics	Mean ± SD	Range	
		Min	Max
Age (years)	62.4±6.2	50.0	77.1
Years since menopause (years)	13.1±7.5	1	43.8
Height (cm)	153.7±5.1	138.0	168.5
Weight (kg)	55.2±7.8	30.5	86.0
BMI (kg/m^2)	23.4±3.0	14.9	34.6
Total body BMD (g/cm^2)	1.001±0.086	0.602	1.315
Lumbar$_{1-4}$ spine BMD (g/cm^2)	0.929±0.146	0.513	1.620
Femoral neck BMD (g/cm^2)	0.732±0.118	0.384	1.465
Femoral BMD (g/cm^2)	0.811±0.124	0.425	1.206

BMI, body mass index; BMD, bone mineral density.

ally recognized gold standard for the diagnosis of osteoporosis [5]. According to the diagnostic criteria recommended by the World Health Organization (WHO), osteoporosis is defined as a BMD value ≥2.5 standard deviations (SD) below the normal peak bone mass (PBM) for adults of the same gender and race (T-score ≤-2.5) [6]. Several studies have indicated that factors such as age, years since menopause, body mass index (BMI) and a history of fragility fracture are independent contributors to osteoporotic fracture risk and improve the sensitivity of BMD measurement for the identification of high-risk populations [7-9]. However, few studies have focused on the relationship between clinical risk factors and osteoporosis risk in Chinese postmenopausal women. Therefore, in an attempt to determine the risk factors associated with PMOP among Chinese women, we examined 782 healthy postmenopausal women by means of BMD measurements and questionnaires in South Central China. The aim of the present cross-sectional study is to provide a research basis for the selection of the primary method for osteoporosis screening among postmenopausal women in China.

Material and methods

Subjects

The study population comprised 782 healthy postmenopausal women from South Central China aged 50-77 years. The study subjects were recruited from community centres. Menopause was defined clinically as the absence of menstrual cycles for at least 1 year. All of the subjects were non-institutionalized women in generally good health [1]. None of them were taking medications that could have affected their bone, soft-tissue or lean-tissue metabolism. All respondents were screened using a detailed questionnaire, including smoking/drinking/caffeine consumption habits, medical history taking and physical examination. Women who smoked or consumed alcohol or caffeine were excluded [10]. Women were also excluded if they had conditions that might affect bone metabolism, such as diseases of the kidney, liver, parathyroid, and thyroid, diabetes mellitus, hyperprolactinaemia, oophorectomy, rheumatoid arthritis, ankylosing spondylitis, malabsorption syndromes, malignant tumours, haematological diseases. Women taking oral anticoagulants were also excluded, but those taking drugs for hypertension or coronary diseases were not excluded [11]. All participants provided informed consent. The study was approved by the ethics committee of the Second Xiangya Hospital of the Central South University (Changsha, China).

Methods

Body weight and height were measured in all subjects, without shoes and in light indoor clothing, to the closest 0.1 kg and 0.1 cm, respectively. BMI was calculated as the weight in kilograms divided by the square of the height in metres [1]. Total body BMD, lumbar$_{1-4}$ spine BMD and left femoral BMD were measured using a DXA fan-beam bone densitometer (Lunar Prodigy Advance, GE Healthcare, Madison, WI, USA). According to the information provided by the manufacturer, this is a standardized commercial machine which provides total, anterior-posterior spinal and femoral BMD measurements that are precise to 1%. The control spine phantom scan performed each day demonstrated long-term (> 2 years) coefficients of variation of < 0.7% [12]. Osteoporosis was defined according to the WHO definition and the BMD reference databases established by our group [10]. All participants were interviewed using a standard questionnaire to obtain clinical data, such as history of fractures, use of calcium and family history of osteoporosis [1, 10].

Table 2. Hierarchical assignment of risk factors for osteoporosis

Risk factor for osteoporosis	Hierarchical assignment					
Age (years)	≤4.99 = 1	55~59.99 = 2		60~64.99 = 3	65~69.99 = 4	≥70 = 5
Years since menopause (years)	≤4.99 = 1		5~9.99 = 2		≥10.00 = 3	
BMI (kg/m^2)	≤18.99 = 1	19~20.99 = 2		21~24.99 = 3	25~27.99 = 4	≥28 = 5
History of fragility fractures	No = 0		Fall fracture = 1		Violent fracture = 2	
Fall history	No = 0			Yes = 1		
Calcium supplementation	No = 0			Yes = 1		
Vitamin D supplementation	No = 0			Yes = 1		
Outdoor activity time (min/d)	< 30 = 1		30~60 = 2		> 60 = 3	
More than 1 year of amenorrhea before 40 years old	No = 0			Yes = 1		
Family history of osteoporosis	No = 0			Yes = 1		

BMI, body mass index.

Table 3. Comparison of risk factors between women with and without osteoporosis

Risk factor		Women without osteoporosis (%)	Women with osteoporosis (%)	*P* value
Age (years)	≤54.99	56 (11.5)	26 (8.8)	0.000
	55~59.99	196 (40.2)	57 (19.3)	
	60~64.99	104 (21.4)	73 (24.7)	
	65~69.99	82 (16.8)	74 (25.1)	
	≥70	49 (10.1)	65 (22.0)	
Years since menopause (years)	≤4.99	88 (18.1)	25 (8.5)	0.000
	5~9.99	151 (31.1)	53 (18.0)	
	≥10.00	246 (50.7)	216 (73.5)	
BMI (kg/m^2)	≤18.99	15 (3.1)	26 (8.9)	0.000
	19~20.99	62 (12.8)	57 (19.5)	
	21~24.99	252 (52.0)	156 (53.2)	
	25~27.99	108 (22.3)	41 (14.0)	
	≥28	48 (9.9)	13 (4.4)	
History of fragility fractures	No	389 (79.9)	210 (71.2)	0.019
	Fall fracture	82 (16.8)	73 (24.7)	
	Violent fracture	16 (3.3)	12 (4.1)	
Fall history	No	481 (98.8)	281 (95.3)	0.003
	Yes	6 (1.2)	14 (4.7)	
Calcium supplementation	No	156 (32.0)	87 (29.5)	0.457
	Yes	331 (68.0)	208 (70.5)	
Vitamin D supplement	No	415 (85.2)	258 (87.5)	0.466
	Yes	72 (14.8)	37 (12.5)	
Outdoor activity time (min/day)	< 30	83 (17.3)	55 (19.0)	0.351
	30~60	114 (23.7)	56 (19.3)	
	> 60	284 (59.0)	179 (61.7)	
More than a year of amenorrhea before 40 years old	No	471 (96.7)	284 (96.3)	0.742
	Yes	16 (3.3)	11 (3.7)	
Family history of osteoporosis	No	462 (94.9)	279 (94.6)	0.860
	Yes	25 (5.1)	16 (5.4)	

Statistical analysis

All statistical analyses were performed using SPSS for Windows (SPSS version 20.0; Chicago, IL, USA). All variables were distributed normally and met the criteria for normality for basic statistical analyses and for inspection of histograms and normality plots. Data were present-

Table 4. Binary logistic regression analysis evaluating risk factors for osteoporosis

Risk factor	β	*P* value	Exp (β)	95% CI	
				Lower	Upper
BMI (kg/m^2)	-0.479	0.000	0.620	0.519	0.740
Years since menopause (years)	0.318	0.040	1.374	1.015	1.861
Age (years)	0.298	0.001	1.347	1.136	1.598
History of fragility fractures	-0.339	0.149	0.712	0.449	1.129
Fall history	-0.796	0.050	0.451	1.431	11.002

Continuous variables: BMI, Years since menopause and age; Categorical variable: History of fragility fractures and Fall history. BMI: body mass index.

ed as mean ± standard deviation. According to the WHO definition and the BMD reference databases established by our group [11], postmenopausal women with T-scores of ≤2.5 SD on BMD were determined to have osteoporosis. These scores were used to divide the subjects into two groups: the osteoporosis group and the non-osteoporosis group. The χ^2 test was used to compare categorical variables between the two groups. Binary logistic regression analysis was used to determine the association of osteoporosis with age, years since menopause, BMI, history of fragility fractures, fall history, calcium supplementation, vitamin D supplementation, outdoor activity time, more than 1 year of amenorrhea before age 40 years and family history of osteoporosis. The inclusion and exclusion criteria were $P < 0.10$ and $P > 0.15$, respectively. Significant variables were entered into the regression equation. ROC curve analysis was performed to evaluate the prognostic performance of the significant variables such as age, years since menopause, and BMI in osteoporosis [13]. All significance levels were set at $P < 0.05$.

Results

The basic clinical data of the 782 women studied are shown in **Table 1**. The average age of the participants was 62.4±6.2 years (range, 50-77 years). On average, the participants had reached menopause 13.1±7.5 years ago (range, 1-43.8 years). Their BMI was 23.4±3.0 kg/m^2 (range, 14.9-34.6 kg/m^2).

The hierarchical assignment of the experimental variables (risk factors for osteoporosis) is shown in **Table 2**. The comparison of the risk factors between women with and without osteoporosis is presented in **Table 3**. The incidence of osteoporosis was significantly differed with age ($P < 0.01$), years since menopause ($P < 0.01$), BMI ($P < 0.01$), history of fragility fractures ($P < 0.05$) and fall history ($P < 0.01$). Compared to the women with osteoporosis, those without osteoporosis were younger, had reached menopause recently and had higher BMI. There were no significant differences between the two groups in terms of calcium supplementation, vitamin D supplementation, outdoor activity time, more than a year of amenorrhea before the age of 40 years and family history of osteoporosis.

The results of binary logistic regression analysis of the risk factors for osteoporosis are presented in **Table 4**. The results showed that BMI, years since menopause, age, history of fragility fractures and fall history entered the regression equation. However, only BMI, years since menopause and age were significantly correlated with the occurrence of osteoporosis ($P < 0.05$).

We plotted the ROC curves of BMI, years since menopause and age for predicting osteoporosis risk (**Figure 1A-C**). The AUCs of BMI, years since menopause and age were 0.624 (95% CI: 0.584-0.664, $P < 0.001$, sensitivity = 0.585, specificity = 0.606), 0.658 (95% CI: 0.619-0.697, $P < 0.001$, sensitivity = 0.755, specificity = 0.478) and 0.644 (95% CI: 0.604-0.684, $P < 0.001$, sensitivity = 0.593, specificity = 0.655), respectively. The optimal cutoff points for these parameters were 22.81 kg/m^2, 10.05 years and 62.45 years, respectively.

Discussion

Osteoporosis is considered a silent disease, and fragility fractures are a serious consequence of this condition. Early detection is the only available means of preventing osteoporosis. The purpose of our study is to screen high-risk populations for osteoporosis, and thereby, enable the early diagnosis of PMOP and reduce the occurrence of osteoporosis fractures. The main clinical manifestation of osteoporosis is low BMD, which is a dynamic parameter. Bone loss occurs with increase in age, and is espe-

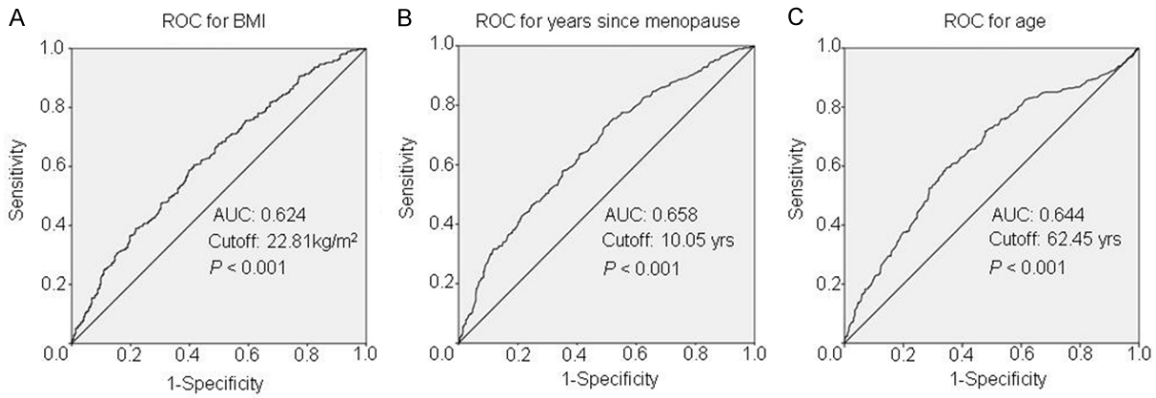

Figure 1. Receiver operating characteristic (ROC) curve for BMI (A), years since menopause (B) and age (C) according to osteoporosis. (AUC: area under the curve; BMI: body mass index; yrs: years).

cially prevalent in elderly women [14, 15]. It has been estimated that 30%-40% of the PBM is lost over a woman's lifespan [16], and the annual rate of BMD decrease can be up to 3%-5% in the early stage of PMOP [11]. Some researchers have showed that the rate of this bone loss, which significantly increases the risk of osteoporosis and fractures, can be as high as 5%-10% of the total bone mass/decade [17]. Consistent with this, our study showed that age was directly proportional to the occurrence of osteoporosis. In addition to age, years since menopause, a history of fragility fracture and fall history were positively correlated with osteoporosis in postmenopausal women, whereas BMI was negatively correlated with osteoporosis. These results are basically consistent with previous findings [18-20].

Our study also showed that there was no significant difference between postmenopausal women with and without osteoporosis with regard to calcium supplementation and family history of osteoporosis. However, many studies have indicated that calcium supplementation can increase BMD or reduce bone loss and reduce the incidence of osteoporosis [21-23]. This difference might be attributable to the fact that our questionnaire did not distinguish between calcium preparations or specify the dosage of calcium. According to the National Osteoporosis Foundation (NOF), the recommended daily intake of calcium for women aged 50 years and above is 1200 mg; this dosage is expected to maximize PBM and minimize the risk of osteoporosis in adulthood [24-26]. The calcium intake in most Asian countries falls far below this recommendation. One survey has revealed that average dietary calcium intake in Asian adults is approximately 450 mg/day [27].

The incidence of osteoporosis is related to many factors, including genetic factors. Twin studies have shown that hereditary variation accounts for 60%-80% of BMD [28-30]. A major determinant of osteoporosis is BMD, which has a heritability of 0.6%-0.85% [31]. Osteoporosis is an age-related disease. The subjects in most research studies on osteoporosis tended to be elderly people; therefore, it was difficult to clarify whether their parents had osteoporosis or not [32]. Thus far, relatively few studies have reported on a family history of osteoporosis [33]. In the present study, most of the subjects were not sure if their parents had been diagnosed with osteoporosis. This may be due to a lack of awareness of osteoporosis among the elderly in China.

At present, the prevention and treatment of osteoporosis are not very optimistic; it has been reported that the rate of osteoporosis awareness is 44.9%-62.0%, and that osteoporosis awareness is related to the level of education [34]. Moreover, a convenient and effective screening method for osteoporosis in at-risk populations is lacking. Therefore, we should promote health education and raise public awareness of osteoporosis. Frequently used screening tools for osteoporosis include the Osteoporosis Self-assessment Tool for Asians, the Fracture Risk Assessment Tool, quantitative ultrasonography and the International Osteoporosis Foundation-one-minute osteoporosis risk test. These screening methods are

based on the results of research on non-Chinese populations, and have their own limitations [35-38]. The effects of these tools in clinical practice in China is worthy of research. In our study, we used ROC curve analysis to assess three risk factors for osteoporosis: BMI, years since menopause and age. The analyses indicated that the optimal diagnostic cutoff points for these three factors were 23 kg/m^2, 10 years and 62 years, respectively.

Few studies have examined the association between clinical risk factors and the risk of PMOP in China. To our knowledge, our study is the first such study conducted in South Central China, and it serves to screen high-risk populations (Chinese postmenopausal women) for osteoporosis through BMI, years since menopause and age. Some guidelines, such as those of the NOF, US Preventive Services Task Force, American Association of Clinical Endocrinologists and American College of Preventive Medicine, recommend that women aged 65 years and older should be screened for osteoporosis [24, 39-41]. However, there is plenty of evidence that suggests that genetic factors, including racial differences, influence variations in bone mass and the occurrence of osteoporosis [28, 29, 31]. In our study, the optimal cutoff age for predicting the risk of osteoporosis was 62 years. Johnell et al. have reported that a BMI < 25 kg/m^2 predicts the risk of osteoporotic fracture [42]. In our study, the optimal BMI cutoff was 23 kg/m^2, with an accuracy of prediction of PMOP of 60.9%. Many studies have confirmed that the duration of menopause is an important factor related to bone loss and osteoporosis [43, 44], but none have provided a specific threshold. We determined that the menopause duration threshold was 10 years, with a sensitivity of 75.5% and a specificity of 47.8% in predicting osteoporosis. The above conclusions show that guidelines based on studies of European and American populations may not be applicable to the Chinese population. Further studies based on a large sample of the Chinese population are warranted to develop screening criteria for osteoporosis among high-risk populations in China.

This study has some limitations. First, our database was built using a sample from an urban population, and it might be inappropriate to extrapolate the results to rural populations. Second, the information in the questionnaire survey, for example, age at menopause and family history of osteoporosis, was provided by the respondents via recall, and their answers could not be verified. Finally, our subjects were relatively healthy postmenopausal women, and none of them had a history of smoking, alcohol or caffeine consumption, treatment with glucocorticoid drugs, etc. Women with any one of these factors are likely to have a higher risk of osteoporosis, and may require screening for osteoporosis at an earlier age. Therefore, further large-scale studies are needed in similar populations.

In conclusion, we found that older age, longer menopause duration, lower BMI, history of fragility fractures and fall history are risk factors for osteoporosis. Bone mineral testing is indicated in postmenopausal women in South Central China who are aged > 62 years, have gone through menopause > 10 years ago or have a BMI of < 23 kg/m^2. Further studies may be needed in larger populations and other urban or rural groups to confirm that the results of the present study are generally applicable.

Acknowledgements

This work was supported by grants from the National Nature Science Foundation of China [grant numbers 81000361, 81471091], the Chinese Postdoctoral Foundation [grant numbers 20090461010, 201003512], the Science Foundation of Central Higher School Foundation of China [grant number 20101220044], and the Science and Technology Project of Guangdong Province, China [grant number 2013B021800111].

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