



Vasomotor symptoms and osteoporosis in Korean postmenopausal women



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ABSTRACT

Objectives: This study examined the relationships between vasomotor symptoms (VMS), bone mineral density (BMD) and osteoporosis in postmenopausal women.

Study design: A cross-sectional study was conducted of 1390 postmenopausal Korean women aged 45–65 years who attended a routine health check-up at a single institution. Their results on the Menopause Rating Scale were used to assess VMS, and moderate, severe, and very severe VMS were combined into moderate-to-severe VMS.

Main outcome measures: The relationships of VMS with BMD and osteoporosis in the lumbar spine and femoral neck bone were analyzed by multivariate regression analyses.

Results: The mean age of all participants was 54.63 ± 4.78 years. Four hundred seventy-one (33.9%) women reported mild VMS and 344 (24.7%) reported moderate-to-severe VMS. Osteoporosis was newly diagnosed in 156 (11.2%) women. BMD levels were not significantly different among the no/mild/moderate-to-severe VMS groups, despite the significant differences in the prevalence of osteoporosis in the femoral neck bone. Women with mild VMS and those with moderate-to-severe VMS had a lower BMD than women without VMS after adjustment for age, years since menopause, years of reproductive age, BMI, insulin resistance, smoking, alcohol, steroids use, exercise, previous fracture and parental history of hip fracture. And moderate-to-severe VMS was significantly associated with the risk of osteoporosis in the femoral neck bone (OR = 2.97, 95% CI = 1.41–6.26) and in the lumbar spine (OR = 1.93, 95% CI = 1.09–3.40).

Conclusions: VMS are associated with decreased BMD, and moderate-to-severe VMS in particular are independently associated with the risk of osteoporosis in otherwise healthy postmenopausal Korean women.

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1. Introduction

Osteoporosis is a systemic skeletal disorder characterized by reduced bone mineral density (BMD), impaired bone quality, and a propensity to fractures, which are usually associated with significant morbidity and disability [1,2]. Osteoporosis and osteoporosis-related fractures are more common among postmenopausal women than premenopausal women or men, presumably because of the rapid bone loss accompanied by the loss of ovarian function in the menopausal transition [3,4]. According to the BMD data collected in the 2008–2009 Korean National Health and Nutrition Examination Survey, approximately 35.5% of Korean

women 50 years of age or older have osteoporosis [5]. In spite of such a large prevalence of the disease and the increasing number of osteoporosis-related fractures since the last decade, diagnosis rates still remain low in Korea and many cases of osteoporosis have been diagnosed after the first event of osteoporotic fracture occurred [5–7]. There should be emphasis on identifying women who are at high risk of significant bone loss and providing sensitive screening and earlier prevention of osteoporosis and its related fractures.

Vasomotor symptoms (VMS), such as hot flashes and sweating, are some of the most frequent and troublesome menopausal symptoms, and approximately half of postmenopausal Korean women experience these symptoms [8]. Although the underlying mechanisms have not yet been fully explained, declining or fluctuating estrogen circulation levels have been suggested to play a major pathogenic role in the development of VMS [9], and they are also known as key factors in the occurrence of bone

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loss during menopause [10]. Some previous epidemiologic studies have already suggested a significant association between VMS and present or future osteoporosis [11–15]. However, most of those studies used only small sample sizes and other investigations have reported conflicting results to them [16–18]. Moreover, obesity protects against postmenopausal osteoporosis, but was reported to be a risk factor for VMS in recent studies [19,20]. Thus, it is not clearly known yet whether the presence of VMS can be considered a significant risk factor for decreased BMD and osteoporosis in postmenopausal women.

We previously reported that VMS is associated with a number of metabolic components including obesity, insulin resistance and poorer lipid profiles among postmenopausal women [20]. We recently examined the association between the severity of self-reported VMS and both BMD and osteoporosis at the lumbar spine and the femoral neck bone after we adjusted for confounders in otherwise healthy postmenopausal Korean women.

2. Methods

2.1. Subjects

This cross-sectional study consisted of 2457 Korean postmenopausal women aged 45–65 years who were self-referred for a routine health check-up and who had completed BMD measurement at the Korea University Anam Hospital (Seoul, Korea) between January 2010 and December 2012. Postmenopausal status was defined as at least 12 consecutive months of amenorrhea with no other medical cause. Each participant provided written informed consent, and this study was approved by the institutional review board of the Korea University Medical Center.

The exclusion criteria were as follows: lack of information on menopausal symptoms; lack of BMD data; current hormone use; current antiresorptive drug use; current medication for diabetes mellitus or dyslipidemia; depressive mood disorders; overt thyroid disorder; surgical menopause; bilateral oophorectomy; past history of chemotherapy or pelvic radiotherapy to treat malignant disease; presence of cardiovascular disease such as prior myocardial infarction, angina, stroke, and peripheral arterial diseases; and presence of chronic diseases such as renal failure, liver cirrhosis, and current infectious diseases. Finally, 1390 postmenopausal women were included in our analysis.

2.2. Laboratory measurements

Laboratory data were collected from all women by venous blood sampling at 9:00 AM after overnight fasting. Insulin level was determined via radioimmunoassay using a commercially available kit from Biosource (Biosource Europe S.A., Nivelles, Belgium). The homeostatic model assessment insulin resistance index (HOMA-IR) was calculated using the following formula: fasting plasma glucose (mg/dL) \times fasting plasma insulin (IU/mL)/405 [21]. Fasting glucose was measured via routine clinical chemistry methods.

2.3. Bone mineral density measurement and diagnosis of osteoporosis

The BMD of the lumbar spine and left femoral neck was measured using dual-energy x-ray absorptiometry (12.6 version; Hologic, Bedford, MA, USA). Areal BMD is expressed in grams of mineral per square centimeter scanned. The mean BMD of the L1 to L4 vertebra of the lumbar spine was taken as the measure for lumbar spine BMD, and the BMD of the neck of the left femur was taken as the femoral neck BMD. The reference BMD values were determined from a group of young healthy adults of the same race and sex, and the T-score was calculated as follows: T-score = (individual

BMD – reference BMD)/reference SD [22]. We defined osteoporosis as a T-score of -2.5 or less in either the femoral neck or the lumbar spine or both, in accordance with the recommendations of the WHO [23].

2.4. Vasomotor symptoms and other definitions

To access the presence and severity of VMS (hot flashes and/or sweating) in menopausal women, we used a questionnaire based on the Menopause Rating Scale (MRS), which was developed and validated to measure the severity of menopause-related complaints [24]. Each of the eleven questions included in that questionnaire was rated from zero (no complaint) to four (extremely severe symptoms) points depending on the perceived severity of the complaints. From the results of first MRS, a trichotomous variable was created for the absence of VMS, mild VMS, or moderate-to-severe VMS, mainly because of the relatively small number of women with severe and very severe symptoms. Mild VMS was defined as an MRS score of one, and moderate-to-severe VMS was defined as scores from two to four; a score of zero was defined as the absence of VMS.

Information on current hormone use, oral glucocorticoid use, alcohol intake, physical exercise level, smoking, history of a previous fracture in adult life, and parental history of hip fracture was obtained from a questionnaire survey. Current hormone use was defined as usage of hormone replacement drugs for climacteric symptoms, or oral contraceptives at the time of the visit. Oral glucocorticoid use was defined as current usage of >5 mg of a prednisone-equivalent dose of oral glucocorticoids daily for more than 3 months. Alcohol intake was categorized according to frequency of alcohol consumed per week as follows: none or one time versus more than one time per week. Physical exercise was categorized according to the frequency of activity that lasted at least 20 min per day: none or one time versus more than one time per week. Current smoking was defined as current cigarette smoking at the time of the visit. The 10-year probability of major osteoporotic and hip fracture was calculated using the World Health Organization (WHO) Fracture Risk Assessment Tool (FRAX) algorithm, Korean model, which is available free of charge at www.shef.ac.uk/FRAX, based on the patients' clinical characteristics and femoral neck BMD.

2.5. Statistical analysis

The characteristics of the study population are described separately for each of the three groups according to the severity of VMS (none, mild, moderate-to-severe). ANOVA was used to compare differences in the mean values for the three groups, and Student *t*-test was used to compare two groups when the variable was continuous. Chi-square (χ^2) tests were used to test the independence of the categorical variables. Two multivariate linear regression models (model 1 and model 2) were constructed to evaluate the proportional association between BMD and the severity of VMS after adjusting for the following confounding factors; model 1 was adjusted for age, years since menopause, years of reproductive age, BMI, HOMA-IR, smoking, alcohol, steroids use, exercise, previous fracture and parental history of hip fracture; and model 2 was adjusted for years since menopause, years of reproductive age, HOMA-IR, exercise and FRAX score (The 10-year probability of hip fracture calculated by FRAX). The variables that overlapped with items of the FRAX algorithm were excluded in model 2. BMD of the lumbar spine and the femoral neck were log-transformed in those statistical analyses. Univariate and multivariate logistic regression analyses were performed to determine whether the VMS was independently associated with the risk of osteoporosis; model 1 and model 2 were adjusted for confounding factors as in the multivariate linear regression analysis described above. The group of women

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