Original Article

Choice of Lumbar Spine Bone Density Reference Database for Fracture Prediction in Men and Women: A Population-Based Analysis

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Abstract

The diagnosis of osteoporosis in men is controversial, although most studies demonstrate similar fracture rates for men and women with the same level of hip bone mineral density (BMD). Whether this applies to the lumbar spine is currently uncertain and has important implications with respect to choice of reference population for T-score calculation and osteoporosis diagnosis. This question was specifically addressed in the population-based Canadian Multicentre Osteoporosis Study cohort of 4745 women and 1887 men ages 50+ yr at the time of baseline lumbar spine dual energy x-ray absorptiometry. In up to 10 yr of observation, incident clinical major osteoporotic fractures occurred in 110 men (5.8%) vs 543 women (11.4%) ($p < 0.001$). Mean lumbar spine BMD in men was greater than in women, both among those with and those without incident major osteoporotic fracture ($p < 0.001$). Men were at slightly lower risk for incident major osteoporotic fracture than women for an equivalent lumbar spine BMD (age- and BMD-adjusted rate ratio 0.75, 95% confidence interval 0.60–0.93, $p = 0.008$) with similar findings after adjustment for the World Health Organization fracture risk assessment clinical risk factors or competing mortality. No significant sex difference in the BMD relationship was seen for vertebral fractures (clinical or radiographic) or for all fractures. In summary, this large population-based longitudinal cohort study found similar or lower fracture risk for men vs women after adjustment for absolute lumbar spine BMD and additional covariates. The least complicated model for describing fracture risk is therefore to use the same reference lumbar spine data for generating T-scores in men and women.

Key Words: Bone mineral density; dual energy x-ray absorptiometry; fractures; lumbar spine; sex.

Introduction

Bone mineral density (BMD) assessment with dual energy x-ray absorptiometry (DXA) is well established in the diagnosis of osteoporosis and for fracture risk assessment in

postmenopausal women *(1,2)*. The diagnosis of osteoporosis in men remains more controversial, and in a review, Khosla et al *(3)* concluded that the most appropriate definition for osteoporosis in men, in the absence of fractures, was a major unresolved issue and should be the focus of future research.

Since 2001 the International Society for Clinical Densitometry Official Position was to use young female reference data in women and young male reference data in men for T-scores until additional data could clarify the BMD-fracture risk relationship in men *(4)*. Several prospective studies have now shown that men and women with identical hip BMD have the same fracture rates if all other risk factors are the same *(5−7)*. Therefore, the World Health Organization recently has clarified diagnostic criteria for postmenopausal women by emphasizing a reference site (femoral neck) and reference population (white women ages 20−29 yr based upon the Third National Health and Nutrition Examination Survey) *(8)*.

The 2013 International Society for Clinical Densitometry Position Development Conference, after considering the new data available on the BMD-fracture risk relationship in men, recommended ''Use a uniform Caucasian (nonrace adjusted) female reference for men of all ethnic groups'' (J. Schousboe, personal communication). This recommendation was assigned a grade of ''Fair'' based upon the paucity of nonhip BMD data, and most particularly the lack of equivalent lumbar spine data, since this is one of the primary clinical assessment sites for DXA. Therefore, this question was specifically addressed in the population-based Canadian Multicentre Osteoporosis Study (CaMos) cohort, one of the first population-based cohorts to include both men and women.

Methods

Study Population

The study sample was selected from participants in an ongoing population-based longitudinal cohort study, the CaMos. We included all CaMos participants ages 50 and over at study entry for whom follow-up data and lumbar spine BMD measurements were available.

The methodological details of CaMos have been described elsewhere *(9)*. In brief, eligible participants were at least 25 yr of age at the start of the study, lived within a 50-km radius of 1 of 9 Canadian cities (St John's, Halifax, Quebec City, Toronto, Hamilton, Kingston, Saskatoon, Calgary, and Vancouver) and were able to converse in English or French (Chinese in Toronto and Vancouver only). Households were randomly selected from a list of residential phone numbers and participants were randomly selected from eligible household members using a standard protocol. Of those selected, 42% agreed to participate. Ethics approval was granted through McGill University and the appropriate ethics review boards for each participating center. All participants gave written informed consent in accordance with the Helsinki declaration.

Data Collection

Participants completed a standardized interviewer-administered questionnaire (CaMos questionnaire) at baseline, which assessed demographics, general health, nutrition, medication use, and medical history. The questionnaire was designed to capture detailed information about risk factors for fractures, including information about previous fractures, and as such assessed: all previous fractures (fracture site, date, and circumstances), family history of osteoporosis/fracture, and falls in past month. Participants had a baseline clinical assessment that included measurement of height, weight, BMD (hip and lumbar spine), and (for subjects aged 50 years and older) lateral thoracic and lumbar spine X-rays.

BMD Measurements

BMD was measured at the lumbar spine (L1-L4) and proximal femur. Seven centers used Hologic densitometers (Hologic, Bedford, MA), and 2 used GE-Lunar densitometers (GE-Lunar, Madison, WI). All Lunar measurements were converted to equivalent Hologic values by the use of standard reference formulas *(10)*. All densitometers were cross-calibrated with a European spine phantom circulated among study centers. A more detailed description of BMD quality control appears elsewhere *(11)*. To more closely match the BMD ranges for men and women, we excluded those who had BMD outside the distribution range of the opposite sex, that is, men with greater BMD than all women (N = 9), and women with lower BMD than all men (N = 17).

Fracture Assessment

Self-reported incident clinical fractures were identified by yearly postal questionnaire or at the scheduled interval for reassessment (3rd, 5th, and 10th yr after study entry). Confirmation and further information concerning the fracture was gathered with a structured interview that included date, fracture site, circumstances leading to fracture, and medical treatment. Participants who reported fractures were asked for consent to contact the treating physician or hospital for verification and for acquisition of further details. Fractures that occurred without trauma or from a fall of standing height or less were considered to be low trauma. For the current analysis, all low-trauma major osteoporotic fractures (clinical spine, hip, forearm, proximal humerus) that occurred up to the year 10 annual follow-up were included for the primary analysis. In secondary analyses, we also considered clinical spine fractures alone, any low trauma fracture or any fracture (excluding head, fingers, and toes). In individuals with spine x-rays performed at both baseline and 10 yr, we also studied the occurrence of a new vertebral fracture (grade 2 or higher) using the semiquantitative system of Genant et al *(12)*.

Statistical Methods

Simple descriptive statistics and multiple regression analyses are reported. Absolute lumbar spine BMD (g/cm^2) was used in all analyses because this is equivalent to using a common reference database for men and women. If men and women have the same fracture risk for a given level of BMD then the rate ratio should be 1; a rate ratio significantly greater than unity implies that men have greater risk for