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Original Article

Nonstandard Lumbar Region in Predicting Fracture Risk

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Abstract

Femoral neck (FN) bone mineral density (BMD) is the most commonly used skeletal site to estimate fracture risk. The role of lumbar spine (LS) BMD in fracture risk prediction is less clear due to osteophytes that spuriously increase LS BMD, particularly at lower levels. The aim of this study was to compare fracture predictive ability of upper L1–L2 BMD with standard L2–L4 BMD and assess whether the addition of either LS site could improve fracture prediction over FN BMD. This study comprised a prospective cohort of 3016 women and men over 60 yr from the Dubbo Osteoporosis Epidemiology Study followed up for occurrence of minimal trauma fractures from 1989 to 2014. Dual-energy X-ray absorptiometry was used to measure BMD at L1–L2, L2–L4, and FN at baseline. Fracture risks were estimated using Cox proportional hazards models separately for each site. Predictive performances were compared using receiver operating characteristic curve analyses. There were 565 women and 179 men with a minimal trauma fracture during a mean of 11 ± 7 yr. L1–L2 BMD *T*-score was significantly lower than L2–L4 *T*-score in both genders ($p < 0.0001$). L1–L2 and L2–L4 BMD models had a similar fracture predictive ability. LS BMD was better than FN BMD in predicting vertebral fracture risk in women [area under the curve 0.73 (95% confidence interval, 0.68–0.79) vs 0.68 (95% confidence interval, 0.62–0.74), but FN was superior for hip fractures prediction in both women and men. The addition of L1–L2 or L2–L4 to FN BMD in women increased overall and vertebral predictive power compared with FN BMD alone by 1% and 4%, respectively ($p < 0.05$). In an elderly population, L1–L2 is as good as but not better than L2–L4 site in predicting fracture risk. The addition of LS BMD to FN BMD provided a modest additional benefit in overall fracture risk. Further studies in individuals with spinal degenerative disease are needed.

Key Words: Bone mineral density; femoral neck; fracture risk prediction; lumbar spine; osteoporosis.

Introduction

Osteoporotic fracture is a common growing public health problem. The estimated number of fractures worldwide in 2000 was 8.96 million, of which 61.3% occurred in women *(1)*. With the aging population, the global burden of osteoporosis and fracture is expected to increase together with the associated morbidity, mortality *(2,3)*, and health-care costs *(1)*.

Bone mineral density (BMD) measured by dual-energy X-ray absorptiometry is the main tool to assess fracture risk *(4–6)*. It is better than total cholesterol for predicting cardiovascular disease and as good as hypertension for predicting stroke *(7)*. Clinical factors with or without BMD, including age, gender, prior fracture, and falls among others are independent contributors to fracture risk *(8,9)*.

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Femoral neck (FN) BMD is the most commonly used site for fracture risk prediction *(10,11)* because it gives similar fracture risk estimates in men and women and is not artificially elevated by osteoarthritis (OA) *(12)*. However, BMD measurements of both lumbar spine (LS) and FN have been used for osteoporosis diagnosis and therapeutic decision making *(13)*. In 1 study, a combined LS and FN BMD site approach was associated with little benefit in fracture risk prediction *(14)*, whereas in another, selecting the lowest value from LS and FN BMD did not improve fracture prediction over a single site alone *(15)*.

A major reason why LS BMD is not as good as FN BMD at fracture risk prediction is because it is often affected by OA, which spuriously elevates bone density. In Australia, 25% of women and men self-reported OA *(16)*. Thus, LS BMD becomes increasingly unreliable in the elderly *(17)*. The upper LS is less prone to these arthritic changes than the lower LS *(18)*. Thus, we hypothesized that measurement of the L1–L2 site may improve fracture risk prediction over the routinely used L2–L4 site. To our knowledge, there have not been any studies examining whether L1–L2 is a better predictor of fracture risk than L2–L4.

The aim of this study was to assess in a population of elderly women and men whether L1–L2 was (1) a better fracture risk predictor than L2–L4 and (2) whether LS BMD added additional information to FN BMD in fracture risk prediction.

Methodology

Population and Setting

The analysis was part of Dubbo Osteoporosis Epidemiology Study, the design and population of which have been described previously *(19)*. Briefly, people in the regional city of Dubbo, 400 km northwest of Sydney, Australia, were invited to participate in this ongoing population-based study in 1989. Data were collected during interviews approximately every second year. Dubbo was selected because of its stable population, relatively isolated medical care that made fracture ascertainment possible, and because the age and sex distribution of the population resembled that of the Australian population.

BMD and risk factors for osteoporosis were assessed prospectively. Informed consent was obtained from every participant, and the study was approved by St Vincent's Hospital Research Ethics Committee.

BMD Measurement

All study participants had their BMD measured (g/cm^2), according to the manufacturer's guidelines at different skeletal sites (L1, L2, L3, and L4 LS and FN). This was performed at baseline using dual-energy X-ray absorptiometry (GE LUNAR, Madison, WI, USA). The coefficient of variation with this method for BMD at our institution in normal subjects is 1.5% for the LS and 1.3% for the FN. *T*-scores were obtained using the manufacturer's reference database.

Risk Factors Assessment and Mortality

Baseline information was collected using a structured questionnaire. Information included history of falls and prior fracture, defined as fractures occurring at least 6 mo before baseline. Measurements included anthropometry (height in meters and weight in kilograms), postural stability, and quadriceps strength.

Mortality status was identified from systematic searches of funeral director lists, local newspapers, and Dubbo media reports, and verified by death certificates from the New South Wales Registry of Births, Deaths and Marriages.

Ascertainment of Fractures

All fractures were confirmed through X-ray reports from the only 2, and sometimes 3, radiological centers in Dubbo as previously described *(20)*. The circumstances surrounding each fracture were obtained by telephone interview. The first incident low trauma fracture (fall from standing height or less) was the outcome of interest. Fractures were classified as any (any first osteoporotic fracture), hip, vertebral, and non-hip non-vertebral (NHNV) fractures. Vertebral fractures identified (from X-ray) were those coming to clinical attention. No systematic screening for vertebral fractures was performed at baseline or throughout the study. Fractures occurring following more than low trauma (e.g., motor accident, sporting injuries) and fractures of the head, finger, and toe were excluded from the analysis as well as people with pathologic fractures (malignancy and Paget's disease).

Statistical Analysis

Follow-up time was calculated from the first visit date to the occurrence of the first minimal trauma fracture, death, or end of study (December 2014). Incidence rates and 95% confidence intervals (CIs) of fracture were calculated per 1000 person-years assuming a Poisson distribution. Incidence rates were gender-specific and calculated in 10-yr age groups. The risk of osteoporotic fracture was assessed using gender specific Cox proportional hazard models. Four sets of models were constructed to investigate the risk of any, hip, vertebral, and NHNV fractures. All variables, including L1–L2, L2–L4, and FN BMD, were tested in univariate and age-adjusted models. The Bayesian model averaging approach *(21)* was used to select independent predictors for different BMD models. Given that these predictors were BMD-specific, only age was included in the models for fracture performance comparison. The magnitude of fracture risk association for each continuous variable including BMD was presented as hazard ratios (HRs) per 1 standard deviation (SD) (higher/lower) and the corresponding 95% CIs. Schoenfeld residuals for each covariate in the model were plotted against time to exclude evidence for violation of the proportional hazards assumption.