Skeletal Site Bone Mineral Density Heterogeneity in Women and Men

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Abstract. The heterogeneity of skeletal bone mineral density, measured on a single dual-energy X-ray absorptiometer, was examined in a large cohort of 7050 women and 702 men referred for investigation of osteoporosis. The men were significantly older (64.8 ± 13.2 vs 60.2 ± 11.5 years) and had an increased prevalence of nontraumatic fractures (ODR: 2.18; 95% CI: 1.82–2.61). The detection rate (sensitivity) for any osteoporosis (spine or hip) in women was 87.1% and 45.1% when assessed at the anteroposterior (AP) spine and femoral neck respectively. The corresponding osteoporosis detection rate in men was 69.3% and 67.5% at the AP spine and femoral neck respectively. Age-related AP spine degenerative changes increased significantly and at a similar rate for both women and men. Misclassification, that is osteoporosis (T-score < -2.5) at one site and normal (T-score > -1) bone mass at the other, was low in both genders (<4.5%), but 3.1 (95% CI: 2.1–4.6) times more likely in women when the diagnosis was based on the femoral neck compared with the AP spine. Our findings suggest that there are significant age- and gender-related bone mineral density differences between the spine and hip skeletal sites which have to be considered if only one site is selected for investigation.

Keywords: Age-related effects; DXA; Men; Misclassification; Skeletal site heterogeneity

Introduction

Differences in bone mineral density (BMD), expressed as standardized scores related to the gender-specific young adult range (T-scores), between the lumbar spine and femoral neck have been studied by various groups [1–9]. Such investigations, however, have been almost exclusively restricted to women [2–7,9], have generally involved small sample sizes [2–5] and have not analyzed clinical factors which may directly affect the T-score difference between spine and hip. Moreover, the similar prevalence of osteoporosis (T-score < -2.5) reported at either the spine or hip [7,8] has led to a general recommendation that the hip is the preferred site for BMD measurement, since hip fracture is associated with greater morbidity and mortality and spinal BMD estimation is confounded by age-related degeneration [10]. Misclassification, that is osteoporosis at one site and normal BMD at another [6], has been reported to be more common at the spine [8], contrary to earlier findings [6,7]. To further examine these and related issues we present our results on analysis of accumulated data for 7050 women and 702 men, referred for dual-energy X-ray absorptiometry (DXA) assessment.

Materials and Methods

Women (18–94 years) and men (20–92 years) were referred by physicians for BMD measurements for the following main reasons: presence of osteoporosis risk factors, patient concerns about osteoporosis, the presence of conditions associated with rapid bone loss and monitoring response to treatment. Patients were included in the study only if they had a simultaneous spine and hip BMD measurement. Where serial DXA scans had been performed, the first scan was used. The age, weight and height were all recorded during the DXA appoint-
ment, and it was also checked that patient information, particularly that relating to any previous or present osteoporosis treatment and past fracture, had been correctly recorded on the referral form. Fractures were self-reported and were not confirmed by a radiologic report. A fracture was deemed nontraumatic if it occurred as a result of minimal force.

All BMD measurements were performed on the same Lunar DPXplus densitometer (Lunar, Madison, WI), initially using Lunar version 3.63 software which was later upgraded to DPX-IQ version 4.6b, to allow calculation of the total femur site. Original femur scans reanalyzed using DPX-IQ software showed a mean 0.7% decrease in BMD at the femoral neck [11]. An aluminum spine phantom, representing the typical density range and size of the normal human spine, is supplied by the manufacturer to monitor system bias and precision.

The Lunar Australian reference population supplied for young adults aged 20–45 years [12] was used to calculate respective $T$-scores. For women the BMD at the femoral neck and AP spine is $980 \pm 120$ and $1200 \pm 120$ mg/cm$^2$ respectively. To test for possible bias with respect to the young adult reference range, women aged 20–45 years were selected from the total cohort for analysis, excluding any with existing comorbidity, risk factors or who were being treated with anti-osteoporotic medication. The women ($n = 134$, mean age $39.8 \pm 6.2$ years) had mean $T$-scores at the femoral neck and anteroposterior (AP) spine of $-0.19$ (95% CI: $-0.38$ to $+0.003$) and $0.11$ (95% CI: $-0.13$ to $+0.35$) respectively. The respective BMD values were $957 \pm 134$ and $1210 \pm 162$ mg/cm$^2$.

For AP spine analysis, if individual L2–L4 vertebrae showed a relative increase of one $T$-score (120 mg/cm$^2$) or higher, and visual inspection of the image was consistent with a crush/compression fracture(s) or artifact interference, an alternate set of vertebrae were selected for reporting. Although reducing the number of contiguous vertebrae potentially decreases BMD precision, the impact of this error on BMD estimation, and hence classification of osteoporosis, is relatively small compared with that of including a crush fracture or artifact with a markedly raised BMD value.

Routine data analysis was performed using SPSS v6.1 (SPSS, Chicago, IL). Continuous and categorical variables were analyzed with the independent $t$-test and chi-square test respectively. Backward multiple linear regression analysis was used to investigate the relationship between dependent and independent variables. Sensitivity is the fraction of patients with an abnormal condition who have an abnormal test result. Specificity is the fraction of patients with a normal condition who have a normal test result.

**Results**

Demographics, risk factors and treatments for the female and male cohorts are shown in Table 1. Typically men were referred at an older age ($p<0.001$), and were more likely to have had a nontraumatic fracture (ODR: 2.2; 95% CI: 1.8–2.6) or to be receiving treatment with glucocorticoid therapy (ODR: 6.1; 95% CI: 5.2–7.2). Almost one-quarter of women attending for their first BMD estimation had already been prescribed hormone replacement therapy (HRT).

Table 2 summarizes the BMD-related data for all patients. Men were 1.69 (95% CI: 1.43–2.00) times more likely than women to have a $T$-score $< -2.5$ (osteoporosis).