Effect of Female Database Use for T-score Derivation in Men

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Abstract

Whether to use male or female databases to obtain T-scores in men remains controversial. This study evaluated the impact of deriving male T-scores using female databases in 350 men aged 22.8 ± 9.3 yr who were referred for clinically indicated dual-energy X-ray absorptiometry exams. Spine, femur, and nondominant radius scans were obtained in routine clinical manner using a GE Healthcare Lunar Prodigy densitometer. Analyses were performed using software version 9.30. Initially, the GE Healthcare Lunar male normative database was used to calculate T-scores. Subsequently, scans were reanalyzed using female databases; GE for the spine and radius, and NHANES III for the femur. Using the manufacturer’s male database, T-scores (mean [range]) of the L1 spine, femur neck, total femur, and .3 radius were 0.0 [–4.6 to +8.5], –1.6 [–4.3 to +2.3], –1.1 [–4.0 to +3.3], and –0.7 [–5.3 to +2.9], respectively. On reanalysis with female databases, T-scores “improved” (p < 0.0001) with a positive bias of 0.34, 0.33, 0.58, and 1.20, respectively at the above 4 sites. Using female databases, the proportion of men classified as having normal bone mass increased from 22% to 33% and those identified as osteoporotic decreased from 29% to 17%. If pharmacologic treatment were prescribed at a T-score ≤ 2.0, use of the female databases would reduce those treated for low bone mass from 46% to 32%. In conclusion, using female databases to derive male T-scores results in “improvement” of diagnostic classification for a substantial number of men with fewer being classified as having low bone mass.

Key Words: Database; DXA; T-score.

Introduction

Though osteoporosis has classically been viewed as a disease affecting women, approximately 30% of men will sustain osteoporotic fractures in their lifetime (1–3). Moreover, the consequence of osteoporotic fractures is even worse in men with a higher mortality than among women (4–6). As such, densitometric identification of men at higher risk before their sustaining a fracture, with subsequent utilization of effective treatment to reduce fracture risk, is necessary. Measurement of bone mineral density (BMD) by dual-energy X-ray absorptiometry (DXA) is an excellent tool for identification and subsequent management of such individuals (7,8). Moreover, T-scores derived using DXA are the standard for osteoporosis diagnosis (9,10). T-scores are defined as follows: (individual’s BMD – young-adult mean BMD)/SD of the young-adult normal population (11). As such, the young-adult normal reference population used (i.e., male vs. female database) impacts the T-score and consequently may affect diagnostic classification (11).

The International Society for Clinical Densitometry (ISCD) Official Position is that the WHO densitometric classification (using T-scores) is applicable to men over 50 yr of age (9). However, a recent ISCD Position Development Conference defined the international reference standard for osteoporosis as a femoral neck T-score of ≤ 2.5 using the female Caucasian NHANES III database; this might be considered as an endorsement for using a female database for men (9). Despite this, the ISCD continues to recommend use of a male normative database for T-score derivation in men of all ethnic groups. As
such, the database to use for derivation of male T-scores remains somewhat unclear and controversial (1,9,12–14).

If men and women sustain osteoporotic fractures at the same BMD value, it would indicate that the same database should be used for T-score derivation. In this regard, some studies find that both sexes sustain osteoporotic fractures at the same DXA-measured BMD (12,15). However, others find that men fracture at a higher BMD which suggests that use of a male database for T-score derivation is appropriate (16). Moreover, some studies observe that few men would be classified as “osteoporotic” using a female database (17), thus “underdiagnosis” would occur. However, the impact of changing from the currently used male databases to female databases on T-score and osteoporosis diagnosis in men using currently used databases has not been assessed. As such, the purpose of this study is to evaluate the impact of changing from male to female databases for T-score derivation on mean T-score, and BMD diagnostic classification when applying the WHO criteria, in a cohort of men referred for clinical DXA scans.

Materials and Methods

Subjects

We evaluated 350 men referred for clinically indicated DXA scans between May 2005 and October 2005 at the William S. Middleton VAMC, Madison, Wisconsin. As all identifying characteristics were removed from the clinical images before data analysis, this study was determined to be exempt from Institutional Review Board review by the University of Wisconsin Health Sciences Human Subjects Committee. Patients ranged in age from 22.8 to 93.5 yr (mean 67.5 ± 12.2). Ninety-eight percent of the subjects self-reported their race as Caucasian. Their body mass index (BMI) (kg/m²) ranged from 17.2 to 47.1 with a mean of 28.9 ± 5.8.

DXA Acquisition and Analysis

All DXA images were acquired using a GE Healthcare (Madison, WI) Lunar Prodigy densitometer. Acquisition and analyses of the lumbar spine, femur, and radius were performed in routine clinical manner with software version 9.30. Initially, the GE Healthcare Lunar male normative database was used to calculate T-scores. Subsequently, all scans were reanalyzed using the GE Healthcare female database for spine and radius, and the NHANES III female database for femur T-score derivation. The World Health Organization (WHO) diagnostic classification was applied and individuals were classified as normal (T-score ≥ −1.0), osteopenic (T-score < −1.0 to −2.5), or osteoporotic (T-score ≤ −2.5).

Statistical Analyses

Bland Altman analyses were used to compare BMD and T-scores (Analyse-it Software, Leeds, UK). The Student’s t-test was used to compare the mean T-scores between each database (Microsoft Excel). Diagnostic change was evaluated using the McNemar test with Analyse-it software (Analyse-it Software, Leeds, UK).

Results

Impact of Female Database Use on T-scores

When the scans were reanalyzed using the female databases, the BMD did not change (data not shown). However, as would be expected, the young-normal mean BMD of the female databases was lower at all sites (Table 1). Specifically, the young-normal mean BMD was 3.3%, 8.5%, 3.0%, and 11.5% lower at L1–4 spine, total femur, femur neck, and .3 radius, respectively (Fig. 1). Given this lower young-normal mean BMD, on reanalysis with female databases, T-scores “improved” (p < 0.0001) with a positive bias of 0.34, 0.58, 0.33, and 1.20 at L1–4 spine, total femur, femur neck, and .3 radius, respectively (Fig. 2A–D). Additionally, T-score correlation between male and female database calculations was high at all sites (r² ≥ 0.999, data not shown).

Impact of Female Database Use on Diagnostic Classification

Using the female databases, the proportion of men classified as having normal bone mass increased from 22% to 33% (p < 0.0001, Fig. 3A). Those classified as having osteoporosis at any single site decreased from 29% to 17% (p ≤ 0.002).

### Table 1

Mean Young Adult BMD and SDs Used for T-score Derivation

<table>
<thead>
<tr>
<th>Region</th>
<th>L1–4 spine</th>
<th>Total femur</th>
<th>Femur neck</th>
<th>.3 Radius</th>
</tr>
</thead>
<tbody>
<tr>
<td>Database</td>
<td>BMD</td>
<td>SD</td>
<td>BMD</td>
<td>SD</td>
</tr>
<tr>
<td>Male</td>
<td>1.220</td>
<td>0.12</td>
<td>1.101</td>
<td>0.14</td>
</tr>
<tr>
<td>Female</td>
<td>1.180</td>
<td>0.12</td>
<td>1.008</td>
<td>0.13</td>
</tr>
</tbody>
</table>

Abbr: BMD, bone mineral density; SD, standard deviation.

Note: The male young-adult BMD was higher at all measured sites. As such, an individual’s T-score is “better” when using the female databases. BMD data are reported in g/cm².
Additionally, fewer men ($p \leq 0.0001$) were diagnosed with osteoporosis using the spine and hip, or spine, hip, and radius, using female databases (Fig. 3B). If pharmacologic treatment was prescribed at a T-score $>0.0$ , use of the female databases would reduce those treated for low bone mass from 46% to 32% (data not shown).

**Discussion**

This report documents that use of female normative databases for T-score derivation in men leads to higher (“better”) T-scores than when male databases are used. Though this T-score improvement at the spine and hip is modest ($\sim 0.3$–$0.6$), it does substantially reduce the proportion of this male cohort classified as “osteoporotic” using the current WHO classification system.

As approximately 30% of males will sustain osteoporotic fractures in their lifetime, densitometric identification of men at risk before their sustaining a fracture is necessary (1–3). However, the normative database to use for derivation of T-scores remains controversial (1,9,12–14). Use of female normative data has been advocated based on studies indicating that men and women sustain fractures at the same DXA-measured BMD (12,15). However, it is not intuitively apparent that fractures in men and women should necessarily occur at the same DXA-measured BMD. In fact, the higher DXA-measured BMD among young men compared with young women reflects larger bone size (18,19), not greater volumetric density. In fact, peak female volumetric BMD is higher than that of men (19). Additionally, other skeletal geometric factors are present differentiating men from women, for example, hip axis length, a fracture risk factor (20,21), is higher in men (22). It is also apparent that body
morphology, and therefore innate hip padding, may differ between men and women. Finally, limited work suggests that men and women may fall differently (23). Given these skeletal and non-skeletal differences between males and females, it seems unlikely that DXA somehow precisely balances these risks such that DXA-measured BMD is identical at the time of fracture among men and women. As such, it is not surprising that the ISCD has recommended the use of a male database and that some workers find that men fracture at higher BMD than women, implying that retention of a male database is appropriate (16, 24). This study does not resolve this controversy, however it does demonstrate that if female databases are used, fewer men will be classified as having low bone mass using a T-score based system.

It could be argued that T-score-based diagnosis is of no concern given the forthcoming WHO absolute fracture risk paradigm. Although such an approach will improve selection of those at highest fracture risk and should reduce clinician reliance on a simple “use medications when the T-score is below a cutpoint” approach, it seems probable that clinicians will be more likely to prescribe, and patients more likely to accept, prescription therapy if “osteoporosis” is present. Such considerations are of practical clinical importance, as men diagnosed with low bone mass are more likely to start therapy (25). Moreover, if use of a female normative database for T-score derivation in men becomes standard practice, clinicians need to be aware that fewer men with fractures will be classified as having densitometric “osteoporosis.” It is possible that absence of a densitometric diagnosis of osteoporosis might further exacerbate the current undertreatment of men with low-trauma fracture (26).

It is of interest that use of female databases produces the least T-score alteration at the femur neck and the greatest at the .3 radius. This observation reflects the fact that the young-normal mean BMD is ~13% higher at the .3 radius, but only ~3% higher at the femur neck. As these 2 sites highly comprised cortical bone, it is not intuitive that such a difference would be anticipated. It is possible that this greater difference reflects relatively larger bone size in males or greater amounts of arm exercise in men. A limitation of this study is that only GE Healthcare Lunar instrumentation was used; whether similar T-score changes would be observed with other densitometers is not known. Additionally, this study was performed only in male veterans, however there is no a priori reason to believe that use of other male populations would produce substantially different results.

In conclusion, use of female normative databases leads to higher T-scores than obtained used male normative databases. The T-score increase is not marked at the spine or femur neck with “improvement” being in the 0.3 range. A greater impact on T-scores is observed at the .3 radius. As expected, use of female databases to derive male T-scores reduces the number of men diagnosed with osteoporosis using the current WHO classification system.

References


