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Changing from male to female bone densitometer database for T-score derivation in men: impact on bone loss diagnostic classification.

KEYWORDS: database; T-score; osteoporosis

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ABSTRACT

Objective: to evaluate the impact of changing from male to female database for T-score derivation on mean T-score, and bone mineral density diagnostic classification when applying the WHO criteria, in men.

Material and methods: 1200 men were enrolled. Lumbar spine and femur scans were obtained using a bone densitometer. Initially, the male normative database was used to calculate T-scores. Subsequently, all scans were reanalyzed using the female database for T-score derivation.

Results: when the scans were reanalyzed using the female databases, the female databases derived T-scores were lower ($p<0.0001$) and the proportion of men classified as having osteoporosis at any single site decreased from 14.8% to 11.2%. On reanalysis with female databases, T-scores increased ($p<0.0001$) with a positive bias of 0.45, 0.90, and 0.45 at L1-L4 spine, femur neck, and total hip respectively.

Conclusion: use of female databases to derive male T-scores reduces the number of men diagnosed with osteoporosis.

Introduction

Osteoporotic fracture risk is high among postmenopausal Caucasian women. It is only for this population that the World Health Organization (WHO) definition of osteoporosis—bone mineral density (BMD) more than 2.5 SDs below the young normal mean for Caucasian women (termed a T-score of –2.5)—directly applies (1). However, osteoporotic fractures are not rare in men. Men account for 33–50% of all vertebral fractures, 20–35% of all femoral fractures and 15% of all distal forearm fractures (2-5). Moreover, the consequence of osteoporotic fractures is even worse in men with a higher mortality than among women (6-9). In the other hand, it has recently been established that pharmacologic agents reduce osteoporotic fracture risk in men (10). As such, preventive efforts, which require bone mass measurement, and densitometric definition of disease prior to fracture occurrence, are necessary in men. Thus, identification of men at higher risk before their sustaining a fracture, with subsequent utilization of effective treatment to reduce fracture risk, is necessary (11).

Measurement of BMD by dual-energy X-ray absorptiometry (DXA) is an excellent tool for identification and subsequent management of such individuals (12). However, whether a male or female database should be utilized to derive T-scores for the diagnosis of osteoporosis in men is currently controversial. If men and women sustain osteoporotic fractures at the same BMD, a female database would be suitable. However, if the relationship between BMD and fracture is different between men and women, a male reference population may be more appropriate. In this regard, data exist which show that absolute fracture risk is comparable in women and men who have the same BMD level (13, 14). However, others found that men fracture at a higher BMD which suggests that use of a male database for T-score derivation is more appropriate (15, 16). Moreover, some studies observed that few men would be classified as "osteoporotic" using a female database, thus "underdiagnosis" would occur (17).

The International Society for Clinical Densitometry (ISCD) official position is that the WHO densitometric classification (using T-scores) is applicable to men aged 50 yr and older (18). 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 (18). 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 (19, 20).

We have local data about hip fractures incidence and vertebral fractures prevalence which show that osteoporotic fractures are not uncommon in Moroccan men (13, 21). However, the impact of changing from the currently used male databases to female databases on T-score and osteoporosis diagnosis in men has not been assessed. As such, the purpose of this study is to evaluate the impact of changing from male to female database 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 1200 men referred for clinically indicated DXA scans between May 2011 and September 2015 at the Military Hospital Mohammed V in Rabat, Morocco. Patients ranged in age from 20 to 90 yr (mean 50.1 ± 16.2). All subjects were Caucasians. Their body mass index (BMI) (kg/m2) ranged from 13.0 to 37.5 with a mean of 24.8 ± 3.9.

DXA Acquisition and Analysis

Bone mineral density was determined by a Lunar Prodigy Vision DXA system (Lunar Corp., Madison, WI). The DXA scans were obtained by standard procedures supplied by the manufacturer for scanning and analysis. All BMD measurements were carried out by 2 experienced technicians. Daily quality control was carried out by measurement of a Lunar phantom. At the time of the study, phantom measurements showed stable results. The phantom precision expressed as the

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coefficient of variation percentage was 0.08. Moreover, reproducibility has been assessed recently in clinical practice and showed a smallest detectable difference of 0.04 g/cm2 (spine) and 0.02 (hips) (22, 23). Patient BMD was measured at the lumbar spine (L1-L4) and at the femurs (i.e., femoral neck, trochanter, and total hip).

Initially, the Moroccan male normative database was used for T-score calculation (24): the mean (SD) values for young normal adults in the Moroccan male normative database were 1.205 g/cm2 (0.15) for lumbar spine, 1.147 g/cm2 (0.16) for femoral neck, and 1.161 g/cm2 (0.16) for total hip. Subsequently, all scans were reanalyzed using the Moroccan female database (25): the mean (SD) values for young normal adults in the Moroccan female normative database were 1.156 g/cm2 (0.12) for lumbar spine, 1.026 g/cm2 (0.12) for femoral neck, and 1.029 g/cm2 (0.11) for total hip. 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 and Altman analyses were used to compare BMD and T-scores between the two databases. The Student's t-test was used to compare the mean T-scores between each database and correlations were calculated using the spearman test. Diagnostic change was evaluated using the McNemar test. SPSS 15.0 were used for statistical analysis.

Results

In this cohort of 1200 men, the mean (SD) for age, weight, BMI and lumbar spine, femoral neck and total hip BMD were 50.1 (16.2) yr, 73.1 (12.7) kg, 24.8 (3.9) kg/m2, and 1.098 (0.17), 0.974 (0.17) and 1.006 (0.16) g/cm2 respectively (Table 1). Male and female derived T-scores were highly correlated at all sites (table 2). When the scans were reanalyzed using the female databases, and as would be expected, the young-normal mean BMD of the female databases was lower at all sites ($p<0.0001$). The mean (SD) male database derived T-scores were -0.72 (1.3), -1.06 (1.1), and -0.57 (1.1) for lumbar spine, femoral neck and total hip respectively. The mean (SD) female derived database T-scores were -0.59 (1.4), -0.62 (1.1), and -0.17 (1.2) respectively. Figure 1 shows the impact of the database change on T-scores. Fewer men ($p<0.0001$) were classified as having "osteoporosis" in all sites when female database were used (Figure 2): the proportion of men classified as having osteoporosis at any single site decreased from 14.8% to 11.2%. On reanalysis with female databases, T-scores increased ($p<0.0001$) with a positive bias of 0.45, 0.90, and 0.45 at L1-L4 spine, femur neck, and total hip respectively. Figure 3a-c shows the Bland and Altman plots and limits of agreement.

Discussion

Our study confirms that use of female normative databases for T-score derivation in men leads to higher T-scores than when male databases are used. Though this T-score improvement at the spine and hip is modest, it does substantially reduce the proportion of this male cohort classified as osteoporotic using the WHO classification system.

Approximately 30% of men will sustain osteoporotic fractures in their lifetime and it is now well established that DXA is the best method of identification of those at risk of fracture. However, the normative database to use for derivation of T-scores remains controversial. Two concepts which are not contradictory can be found in the literature. First, there is a greater relative risk of fracture per standard deviation change in BMD in women than men; and, second, the absolute risk of fracture in women and men with a given BMD level is the same.

That the relative increase in fracture risk per 1 SD decline in areal BMD (g/cm2) is greater in women than men has been suggested by a number of studies where the two sexes were assessed comparably (14, 24, 26). However, other investigators have found more comparable sex-specific relative risks for osteoporotic fractures in general (27) and for spine (28, 29) and hip fractures (14, 30, 31) in particular. Sex-specific fracture risks per 1 SD change are partly dependent upon the size of the standard deviations, and it appears that the studies which found equivalent sex-specific relative risks all used larger standard deviations for men than for women when making the calculations. The use of different standard deviations may therefore confound direct comparisons of men and women, but these relative risks can be difficult to interpret and they are not closely correlated with absolute fracture risk in any event (32).

Data also exist which show that absolute fracture risk is comparable in women and men who have the same BMD level. 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, not greater volumetric density. In fact, peak female volumetric BMD is higher than that of men (33). Moreover, men at any given level of BMD are likely to be older than comparable women, and this may help account for their equivalent fracture risk in unadjusted analyses. Indeed, the mean femoral neck BMD of women age 60–69 years is not reached in the average man until after the age of 80 years (19). This has important practical implications since many fewer men than women will experience the very low levels of bone density where fracture risk is greatest. Additionally, other skeletal geometric factors differentiate men from women, for example, hip axis length, a well-known independent fracture risk factor, is higher in men (34, 35). 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 (36).

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. 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.

Even the absolute fracture risk tool called FRAX has been developed and validated in men (37), 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 (38). Moreover, It is possible that absence of a densitometric diagnosis of osteoporosis might further exacerbate the current undertreatment of men with low-trauma fracture (39).

Conclusion:

Use of a female normative database leads to higher T-scores than obtained used male normative database. 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.

Disclosure statement

All the authors state that there is no conflict of interest related to this manuscript.

Tables :

Table 1: descriptive statistics of the study population.

	Mean	SD	Minimum	Maximum
Age (yrs)	50.1	16.2	20	90

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Weight (Kg)	73.1	12.7	40	122
Height (m)	1.71	0.07	1.50	1.96
BMI (Kg/m^2)	24.8	3.9	13.0	37.5
Lumbar spine BMD	1.098	0.177	0.404	1.702
Total hip BMD	1.006	0.161	0.463	1.703
Femoral neck BMD	0.974	0.17	0.561	1.831

Table 2: correlation between male and female derived T-scores.

	Female LS T-score	Female FN T-score	Female TH T-score
Male LS T-score	0.98	0.66	0.60
Male FN T-score	0.59	0.97	0.90
Male TH T-score	0.63	0.86	0.93

All correlations are significant at the 0.01 level.
FN: femoral neck; LS: lumbar spine; TH: total hip.

Figures:

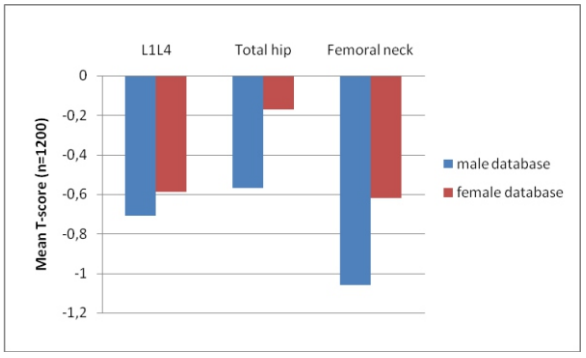


Figure 1: Effect of male and female database selection on mean T-score.

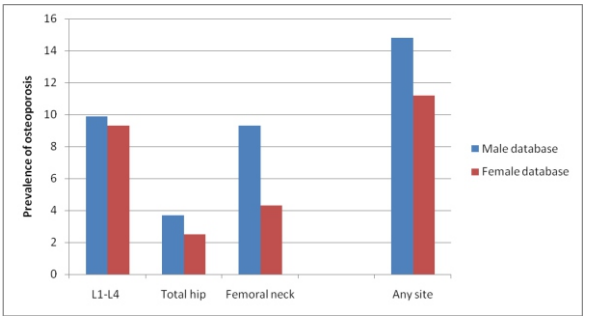
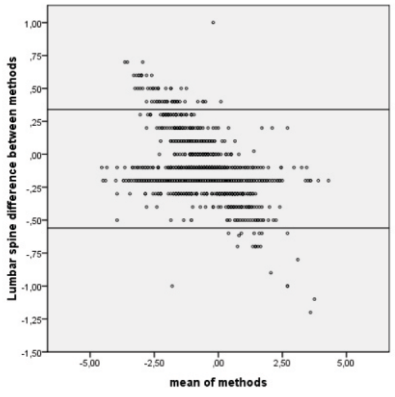
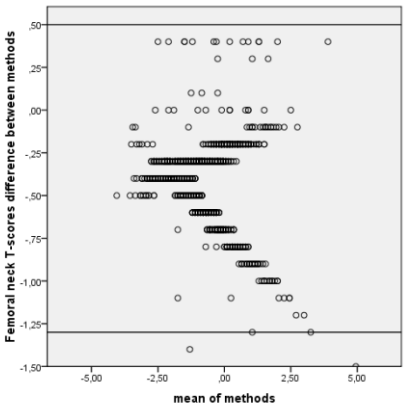


Figure 2: Impact of male and female database selection on diagnostic classification.



(a)



(b)

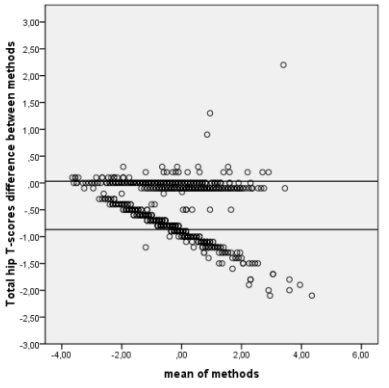


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Figure 3: Bland-Altman plots showing T-scores correlation and bias using male and female databases: (a) lumbar spine, (b) femoral neck and (c) total hip. Horizontal bars represent limits of agreement.

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