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Original Article

Dual Energy X-Ray Absorptiometry-Based Assessment of Male Patients Using Standardized Bone Density Values and a National Reference Database

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Abstract

Dual energy X-ray absorptiometry (DXA) measurements from different manufacturers provide different bone mineral density (BMD) values and derived T-scores and Z-scores. These differences result partly from technical differences in the algorithms for the determination of bone mineral content and bone area and partly from the use of different manufacturer-derived reference databases. The present study was to implement a uniform expression of BMD in all male patients by using standardized BMD (sBMD) values and referring to a newly established national male reference sample. In 8 bone densitometry centers throughout Belgium 229 young healthy men were measured on Hologic (Bedford, MA) or GE-Lunar (Madison, WI) bone densitometers. Quality control procedures were implemented and site cross-calibration performed using the European Spine Phantom. Absolute BMD values were converted to standardized values by validated formulas (sBMD). Clinically acceptable between-center differences were noted. No discrepancy was observed in terms of mean sBMD and standard deviations at the lumbar spine and proximal femur between the Belgian and the US reference populations. Region-specific sBMD thresholds for the diagnosis of male osteoporosis were calculated. The current data provide a basis to implement a nation-wide, uniform expression of BMD in male patients and allow harmonization of the BMD-based diagnosis and treatment of osteoporosis in men.

Key Words: Cross-calibration; dual energy X-ray absorptiometry (DXA); male osteoporosis; reference ranges; standardized bone mineral density.

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[a]BBC is a national nonprofit scientific organization devoted to promoting bone research and the awareness of osteoporosis—its board members are listed in Appendix A.

[b]NEMO is a Thematic Network supported by the European Commission under contract QLK6-CT-2002-00491—its participants are listed in Appendix B.

Introduction

Male osteoporosis and osteoporosis-related fragility fractures are increasingly being recognized as an important medical condition (1–3). Approximately 1 in 5 men is affected, with about 1 in every 4 or 5 hip fractures occurring in men. The total direct costs associated with male osteoporosis have been estimated at some $ 40 billion (over € 30 billion) (4). As in women, fragility fractures in men are associated with significant morbidity, functional consequences, and mortality. Excess mortality in men with osteoporosis is even higher than in women (5). Although male osteoporosis has been studied less extensively than postmenopausal osteoporosis, recent prospective data have confirmed that, among other factors, low bone mineral density (BMD), as assessed by dual energy X-ray absorptiometry (DXA), is predictive of future fracture risk in both sexes (6–8). In this regard, DXA should be an integral part of any fracture risk assessment in men. Recently, the International Society of Clinical Densitometry (ISCD) published a position paper on the use of DXA in men (9), recommending a central diagnostic role for DXA. In men over the age of 65 yr, the ISCD considered a DXA T-score below −2.5 (based on a male reference database) to be sufficient to allow the diagnosis of osteoporosis. In those under the age of 65 yr, additional risk factors for fracture should be taken into account (10,11).

One of the main problems with DXA values obtained on different devices is that these cannot be directly compared. The absolute values (g/cm^2) obtained on equipments from Hologic or Lunar are different, because of differences in calibration and bone-edge detection algorithms, and from these absolute values, T-scores will be calculated using different manufacturer-derived databases. To avoid these inconsistencies and to provide a uniform basis for patient assessment in Belgium, the Belgian Bone Club (BBC)—the Belgian national osteoporosis society—recently implemented a uniform expression of BMD in Belgian postmenopausal patients, by converting each manufacturer's absolute BMD to standardized BMD (sBMD) values and by establishing 1 single national reference range (12). In the current study, we pursued a similar approach in men, to establish uniform thresholds for the diagnosis of male osteoporosis.

Materials and Methods

Study Subjects

A total of 229 healthy young-adult men were enrolled in 8 different clinical bone densitometry centers across Belgium. All participants had to be healthy Caucasians, between 20 and 37 years of age, and provided informed consent. They were recruited partially by a population-based approach in university hospital driven studies (n = 100) and partially from hospital employees, family members, or sporadic volunteers if no population-based programs were available (n = 129). To ensure a normal "health status," the following exclusion criteria were applied: (1) a history of medical conditions known to affect BMD (including diabetes mellitus, hyperthyroidism, hyperparathyroidism, immobilization, rheumatoid arthritis, osteomalacia, gastrectomy, intestinal resection, celiac disease, anorexia nervosa, and hypogonadism), (2) any current or prior use of drugs known to affect bone metabolism (including glucocorticoids, bisphosphonates, and thyroxine), and (3) a body mass index (BMI) exceeding 38 kg/m^2. Date of birth, standing height, and weight were recorded.

BMD Measurements

BMD values (g/cm^2) were measured by DXA at the lumbar spine (ROIs: L2–L4 and L1–L4) and the proximal femur (regions of interest: femoral neck and total hip region), using devices from Hologic or GE-Lunar. In 139 men (recruited in 3 centers), BMD was measured with Hologic fan-beam scanners (2 QDR 4500As and 1 Delphi), whereas Lunar scanners were used to assess BMD in 90 men from 5 different centers (4 pencil-beam: 2 DPX-Ls, 2 DPX-NTs, and 1 fan-beam scanner: Prodigy). Posteroanterior lumbar spine and hip BMD were measured using standard procedures specified by each manufacturer for scanning and analysis. All machines were calibrated by the individual manufacturers and quality controls performed according to their standards, as described in the respective manuals of standard operating procedures. Intersite calibration differences were measured by 10 repeat measurements of a European spine phantom (ESP026; QRM, Erlangen, Germany). The in vitro coefficient of variation (CV) of the BMD was $<1\%$ on Hologic and $<2\%$ on Lunar devices.

Calculation of sBMD

Standardized BMDs were calculated using previously established cross-calibration equations (13–17), providing results in internationally accepted utilization units. To discriminate the manufacturer-specific BMD values from the sBMD values, the former values, by convention, were expressed in grams per square centimeter and the latter in milligrams per square centimeter. The formulas are given in Appendix C. These formulas resulted from regression analyses expressing the best fit between devices specific absolute BMD values in human studies confirmed by in vitro phantom measurements.

The Belgian reference sample was compared to well accepted US standards. For the lumbar spine (L2–L4/L1–L4), BMD reference values provided by the manufacturer (18,19) and for the proximal femur values (total and femoral neck), the updated data from the NHANES III survey (20) were used.

Statistical Analysis

All data were expressed as mean ± SD. Mean BMD values and thresholds were compared using Student's *t*-test. All statistical tests were 2-sided and comparisons were considered significant at a p value of 0.05 or less.