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Dual-energy X-ray Absorptiometry

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Abstract

Bone mineral density (BMD) measurement by dual-energy X-ray absorptiometry (DXA) is the most commonly used method to assess fracture risk. DXA utilizes two different energy X-rays to calculate BMD and, by comparison to a young normative database, the T-score. In 1994, the World Health Organization defined osteoporosis based on T-score, changing the paradigm of the field and forever placing DXA measurements in the center of osteoporosis diagnosis. Since then, many large studies have demonstrated the predictive value of BMD by DXA—for every standard deviation decline in BMD, there is a relative risk of 1.5–2.5 for fracture. This predictive ability is similar to how blood pressure can predict myocardial infarction.

Limitations of DXA are also important to consider. While BMD by DXA can identify those at risk, there is a significant overlap in the BMD of patients who will and will not fracture. Special considerations are also needed in men and ethnic minority groups. These groups may have different bone size, thus affecting the normative range of BMD, and/or distinct bone structure that affect the association between BMD and fractures. Finally, BMD can be affected by positioning errors or artifacts, including osteoarthritis, fracture, and jewelry. Of course, DXA has tremendous strengths as well—namely its wide availability, its low radiation exposure, and a large body of evidence that relate DXA measurements to fracture risk. For these reasons, DXA remains the cornerstone of fracture assessment now and for the foreseeable future.

Key Words: DXA; ethnicity; fracture; osteoporosis.

Bone mineral density (BMD) measurement by dual-energy X-ray absorptiometry (DXA) is the most commonly used and best studied of all methods available for fracture risk assessment. The reasons for the popularity of DXA include its wide availability, low radiation exposure, short scan times *(1)*, and large body of evidence relating DXA measurements to fracture rates *(2–7)*. Consequently, DXA results form the basis of osteoporosis diagnosis and can be used to identify those who have high risk of fracture and are most likely to benefit from pharmacologic therapy. However, although DXA remains a cornerstone of fracture risk assessment, its limitations must also be understood to use its measurements properly.

Basic Principles

BMD acquisition with DXA relies on the attenuation of X-ray beams. Below the patient, X-rays at 2 different energies are sent upward, and the attenuation of the rays is measured with sensors above. Through comparison of the attenuation at different energies, BMD can be estimated. Importantly, DXA scans are 2-dimensional projections of a 3-dimensional object, and BMD from DXA is referred to as areal BMD (for the purposes of this review, we will simply refer to areal BMD as BMD). Because it is a 2-dimensional image, it is dependent on bone size, which may explain some of the differences in BMD because of body size, gender, and ethnicity *(8)*. Although BMD measurement by DXA does not provide a true measurement of bone density, it is actually superior to 3-dimensional

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measurements in its ability to predict fractures *(9,10)*. Because a small bone fractures more easily than a large bone, areal BMD, which is influenced by size as well as true material density, will be a better predictor of fracture risk.

Like any other test, DXA scans are subject to precision and accuracy errors. Accuracy errors are largely due to the assumptions in the algorithms calculating BMD—that is, DXA assumes that soft tissue is homogeneous, whereas in reality there is heterogeneous distribution of adipose tissue in both the soft tissue and the bone marrow *(11)*. Accuracy errors have been estimated as 3%–7% *(11)*, whereas precision error is lower at 1%–2% *(12,13)*.

Classifying BMD

In 1994, the World Health Organization (WHO) defined osteoporosis, osteopenia, and normal BMD using T-scores, the number of standard deviations above or below the mean of young Caucasian women. Osteoporosis was defined as T-score of less than –2.5, osteopenia was defined as T-score between –1.0 and –2.5, and normal BMD was defined as T-score greater than –1.0 *(14)*. At the time of the report, it was not entirely clear what BMD categories T-scores of exactly –2.5 and –1.0 fell into, but these have since become commonly classified as osteoporosis and normal, respectively. Even in its report, the Study Group admitted that these cutoffs were somewhat arbitrary. However, in creating classifications based on BMD, WHO changed the paradigm of the field. Low bone mass was formally designated as a disease, even if did not produce symptoms, with treatment designed to prevent fractures. This is analogous to how we think of hypertension, an asymptomatic disease requiring treatment to prevent myocardial infarctions or strokes.

Derivation and Variability of T-scores

The T-score is at the heart of the diagnosis of osteoporosis and fracture risk assessment. Raw BMD is problematic as it varies by skeletal site and manufacturer because of differences in X-ray energy generation, region of interest placement, and bone edge detection schematics *(15)*. To simplify the interpretation of BMD and avoid the use of raw BMD, the T-score was introduced *(15)*. However, even though manufacturers uniformly began to adopt T-scores in reporting BMD, the manufacturers were using different reference databases—meaning neither the young adult mean BMD nor the standard deviation (SD) of the young adult population was identical. In fact, it was noted that different DXA manufacturers had widely different normative databases, which could lead to the same patient being classified into different BMD categories depending on the machine used *(16)*. Around the time this issue was brought to the forefront, the National Health and Nutrition Examination Survey (NHANES) III released DXA data for the hip from a representative US sample collected between 1988 and 1994 *(17,18)*. NHANES III quickly became adopted as the reference standard at the hip *(19)*. On the other hand, spine data were not available and did not appear to demonstrate the between-manufacturer discrepancies of the hip *(16,19,20)*. Subsequently, newer NHANES data from 2005 to 2008 have been released, including spine BMD. However, the International Society of Clinical Densitometry (ISCD) convened a task force on normative database in 2013 and continues to recommend the use of NHANES III for the hip and the manufacturer's databases for the spine *(19)*. There were several reasons noted by the task force, including the higher mean BMD in the newer NHANES data compared with NHANES III. If adopted, this would lower T-scores compared with NHANES III and place more patients in the osteoporosis category by BMD despite the trend of decreasing age-adjusted fracture rates in many developed nations *(19)*.

A Z-score is similar to a T-score except that it is the number of standard deviations above or below the mean of the population matched for age, gender, and ethnicity (and in some systems, weight). As detailed below, most studies examining the utility of BMD in predicting fracture risk have used relative risk (RR) per standard deviation of BMD without controlling for age, gender, and ethnicity—that is, similar to a T-score. Using Z-scores in fracture prediction is difficult, as the same raw BMD may have significantly different Z-scores depending on the age, gender, and ethnicity of the patient, even if the actual absolute fracture risk is similar. For these reasons, T-scores are used for assessment of fracture risk in adults older than 50 years, whereas Z-scores are used to assess bone mass in children or younger adults. In these populations, the background fracture risk is low, rendering T-scores relatively useless. On the other hand, Z-scores are beneficial in identifying those with low bone mass and likely bone pathology. This will be covered in-depth in Chapter 14.

Absolute and Relative Risk

Bone density measurements form an important part of assessing relative and absolute risk of fracture. First, let us address RR, as it is more intuitive. Bone density measurements have been shown to predict fracture as well as or better than blood pressure predicts myocardial infarction *(21)*. Multiple studies, including well-done meta-analyses, have examined the RRs of fracture per standard deviation decrease in BMD. Rather than list all of the original studies, we have included 2 meta-analyses, as well as an influential US study, in Table 1 *(5–7)*. Remarkably, despite including many populations of different origins, these studies have demonstrated similar RR of fracture: approximately 1.5–2.5 per SD decline in BMD. The consistency of these findings speaks to the reliability of DXA in fracture risk assessment.

As opposed to RR, the absolute risk of fracture depends on the incidence of fracture in the population. This, in turn, varies widely depending on the country of origin or ethnic background; in a study of 63 nations, the variation of hip fracture risk was greater than 10-fold *(22)*. Consequently,