REVIEW

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Assessing Fracture Risk and Effects of Osteoporosis Drugs: Bone Mineral Density and Beyond

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ABSTRACT

Although there have been numerous advances in the assessment of bone strength and fracture risk, the majority of these techniques can only be performed in research laboratories, making them largely unavailable to practicing clinicians. Prospective epidemiologic studies have identified risk factors that can be assessed within the clinic and combined with bone mineral density to allow clinicians to better identify untreated individuals at heightened risk for fracture and to make informed treatment decisions based on 10-year absolute fracture risk. This article discusses the assessment of fracture risk in clinical practice, reviews currently and soon-available bone measurement tools, and details the impacts of osteoporosis therapies on fracture risk.
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KEYWORDS: Antifracture treatment; Bone mineral density; Bone strength; Clinical risk factors; Osteoporosis

ASSESSING FRACTURE RISK WITHIN THE CLINIC

Although there are many ways of assessing bone strength and estimating fracture risk in the research laboratory, few are practical within the clinic for reasons related to time, equipment, and expertise. However, a number of assessments can be performed within the clinic to quickly provide valuable information regarding fragility fracture risk.

The measurement of bone mineral density by dual-energy x-ray absorptiometry (DXA) is the most common assessment of fracture risk. DXA-measured areal bone min-

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eral density (grams/centimeter squared) contains aspects of both bone quantity (grams of mineral) and bone size (area in centimeter squared). Despite the well-established increasing gradient of fracture risk with decreasing bone mineral density,[1] the majority of fragility fractures occur in people whose bone mineral densities are not in the osteoporotic range.[2]

In attempts to identify those individuals at a risk of fracture high enough to warrant pharmacotherapy, many algorithms have been developed that combine bone mineral density and other clinically identifiable risk factors to estimate a treatment-naïve individual's absolute fracture risk over a defined time interval. Clinical risk factors in these algorithms commonly include age, previous fragility fracture, family history of hip fracture, rheumatoid arthritis, low body mass index, cigarette smoking, excessive alcohol consumption, pharmacologic or medical causes of bone loss, and fall-related risk factors. The World Health Organization fracture risk algorithm (FRAX)[3] incorporates many of these risk factors for treatment-naïve individuals to provide a 10-year absolute fracture risk. The effects of current or previous pharmacotherapy on these risk estimates are difficult to model.

CLINICAL SIGNIFICANCE

- Fracture risk is best assessed with the combination of bone mineral density and clinical risk factors.
- History of fragility fracture significantly increases risk of future fracture.
- Bone turnover markers might provide a valuable tool for the assessment of fracture risk.
- Imaging techniques might soon provide clinicians with a "virtual biopsy" and respective strength estimate.
- Antifracture therapies significantly increase bone strength through antiresorptive or anabolic routes.

ASSESSMENT OF FRAGILITY FRACTURES

The occurrence of a fragility fracture is usually an indicator of weak bone and, at least in the context of low bone mineral density, is considered in most guidelines to warrant pharmacotherapy.[4] Personal history of fragility fracture is perhaps the most significant and clinically evident risk factor for future fracture, independent of bone mineral density.[5] Because nonvertebral fractures nearly always come to clinical attention but vertebral fractures frequently go undetected,[6] assessment techniques that identify vertebral fractures are important because those fractures act as harbingers for future vertebral and nonvertebral fractures.[7] Within the clinic, vertebral fracture presence can be estimated from measuring historical height loss (the difference between current measured height and reported lifetime maximum height) or kyphosis.[8] Vertebral fracture assessments by DXA, lateral spine x-rays, quantitative computed tomography, and magnetic resonance imaging also are available, with wide variation in cost and radiation dose. Although all of these techniques satisfactorily identify vertebral deformities, limitations to their widespread use include availability and a general unawareness as to their value and relative ease of use.

DUAL-ENERGY X-RAY ABSORPTIOMETRY-BASED ASSESSMENT

Despite limitations of DXA, bone mineral density remains the principal test for diagnosing osteoporosis. Treatment decisions for patients might be based on a 10-year absolute fracture risk assessment (World Health Organization FRAX) with country-specific treatment thresholds, rather than solely on bone mineral density values.

Assessments of both the lumbar spine and the hip bone mineral density are frequently performed. Although lumbar spine bone mineral density evaluation might provide site-specific fracture predictive value, there are few data to support the need for measuring anything other than hip bone mineral density.[9] Frequently, spine bone mineral density measurement is inaccurate because of spurious elevation by sclerotic changes.[10] Every measurement site, however, has inherent imprecision due in part to patient positioning.[11] Consequently, changes greater than the least significant change (3%-6% at lumbar spine and 4%-8% at hip) are needed to establish that a change is not simply a reflection of measurement variability.[11] Further sources of inaccuracy include improper region of interest, poor scanner quality control, and artifacts within the bone mineral density scan.[11]

It may be clinically appropriate to repeat a DXA measurement after 1 to 3 years of therapy to ensure that bone mineral density has not significantly decreased to help guide changes to therapy or mode of therapy administration. Patients with stable or improved bone mineral density, if taking their therapy, benefit from reduced fracture risk with any of the available osteoporosis medications. Although an increase in bone mineral density with therapy correlates with reduced fracture risk, a stable bone mineral density does not imply treatment failure.[12,13] Even though a loss of bone mineral density in an individual patient exceeding the least significant change may be interpreted as a treatment failure, it is possible that the therapy might have prevented a substantially larger loss in bone mineral density.

Numerous efforts have been made to obtain biomechanical strength indices from a DXA-acquired hip scan. The 2 most studied indices are hip axis length[14] and hip structural analysis,[15] both of which have demonstrated utility in independently predicting hip fracture in groups of patients. These tests require further prospective investigations to prove their usefulness in individual patients.

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