

Commentary on Current Literature

Richard A. Johnson, MD

Bone Quality—The Material and Structural Basis of Bone Strength and Fragility

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Progress in understanding the pathogenesis of bone fragility is hampered by the inaccessibility of bone for investigation. Bone densitometry is an effective, noninvasive, and quantitative method for the assessment of the risk of fracture, but structures such as the vertebral body are depicted as a two-dimensional image—the areal bone mineral density cast by the attenuation of photons by mineral during their passage through bone. Just as the shadow of the earth, cast on the moon, reveals nothing of the topology of the earth's mountain ranges, the densitometric image tells us little about the two properties that determine bone strength: its material composition and its structural design.

In this review, we define how the composition and structure of bone determine its strength, describe bone modeling and remodeling the cellular machinery responsible for constructing bone during growth and reconstructing it during adulthood, demonstrate how age-related abnormalities in these processes compromise the composition and structure of bone, and show how the mechanisms underlying the structural decay of bone offer rational approaches to the use of drugs that inhibit bone resorption and stimulate bone formation.

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This comprehensive review article, which discusses in depth the pathophysiology of bone quality, emphasizes the dynamic nature of bone. Bone is constantly going through a modeling and remodeling process that for the most part is remarkably balanced. Seeman and Delmas in this excellent review show how bone can repair itself from micro- and macrotrauma, and how significant and complex these processes are at the cellular level. The simple notion that antiresorptive agents increase bone strength by balancing this equation in favor of bone growth is dispelled. The authors detail a far greater complexity of the drug pathophysiology of antiresorptive agents and parathyroid hormone.

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Alendronate For The Treatment of Osteoporosis in Men

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Background Despite its association with disability, death, and increased medical costs, osteoporosis in men has been relatively neglected as a subject of study. There have been no large, controlled trials of treatment in men.

Methods In a two-year double-blind trial, we studied the effect of 10 mg of alendronate or placebo, given daily, on bone mineral density in 241 men (age, 31 to 87 years; mean, 63) with osteoporosis. Approximately one third had low serum free testosterone concentrations at baseline; the rest had normal concentrations. Men with other secondary causes of osteoporosis were excluded. All the men received calcium and vitamin D supplements. The main outcome measures were the percent changes in lumbar-spine, hip, and total-body bone mineral density.

Results The men who received alendronate had a mean (\pm SE) increase in bone mineral density of 7.1 ± 0.3 percent at the lumbar spine, 2.5 ± 0.4 percent at the femoral neck, and 2.0 ± 0.2 percent for the total body ($P < 0.001$ for all comparisons with baseline). In contrast, men who

received placebo had an increase in lumbar-spine bone mineral density of 1.8 ± 0.5 percent ($P < 0.001$ for the comparison with baseline) and no significant changes in femoral-neck or total-body bone mineral density. The increase in bone mineral density in the alendronate group was greater than that in the placebo group at all measurement sites ($P < 0.001$). The incidence of vertebral fractures was lower in the alendronate group than in the placebo group (0.8 percent vs 7.1 percent; $P = 0.02$). Men in the placebo group had a 2.4-mm decrease in height, as compared with a decrease of 0.6 mm in the alendronate group ($P = 0.02$). Alendronate was generally well tolerated.

Conclusions In men with osteoporosis, alendronate significantly increases spine, hip, and total-body bone mineral density and helps prevent vertebral fractures and decreases in height.

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COMMENTARY

This is one of the first randomized controlled trials of the use of alendronate (an antiresorptive drug) in the treatment of men with low bone mineral density (BMD) without secondary causes. The number of men with low testosterone levels was similar in each group. BMD increased significantly at the vertebral and hip locations in the alendronate treatment group compared with the control group. Most importantly, the incidence of vertebral fracture was reduced in the treatment group, and men in the placebo group lost 2.4 mm of vertebral height over the 2-year study period compared with only 0.6 mm with the use of alendronate. This study clearly provides the clinician with a rational basis for using alendronate in the treatment of men with low BMD, although there are currently no drug treatments approved by the US Food and Drug Administration at this point. Furthermore, it provides hope that as an aging male, I may not be doomed to “shrinking away,” at least from the perspective of my vertebral spine.