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Osteoporosis: A Therapeutic Update

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ABSTRACT

Osteoporosis is now more apparent with the aging of the population and has become a serious health problem. The end-point of osteoporosis is fracture, which has economic, social, and psychological consequences for society. Some guidelines provide recommendations for whom to screen and treat. Various risk factors are associated with osteoporosis, with many being modifiable to prevent fractures. Both nonpharmacologic and pharmacologic therapies are available to reduce fracture risk. Pharmacologic intervention is predicated on an understanding of bone turnover with predictable outcomes noted. This review provides an update on prevention, screening, and treatment modalities for osteoporosis.

Keywords: anabolic, antiresorptive, bone density, bone remodeling, fracture

INTRODUCTION

Osteoporosis is a progressive disease causing bones to become thin and fracture. It is defined by the World Health Organization as a bone mineral density (BMD) of ≥ 2.5 SD below the average value for premenopausal women (*T* score ≤ -2.5 SD) using dual-energy X-ray absorptiometry.[1] Osteoporosis is now more apparent with the aging of the population and has become a common and serious health problem facing not only postmenopausal women but also aging people of both genders. An estimated 200 million people worldwide have osteoporosis, with 44 million in the United States.[2] Fragility fractures lead to morbidity, mortality and increased financial burden on society with current studies suggesting the hospitalization cost of osteoporotic fractures exceeds that of myocardial infarct, breast cancer or stroke.[3] Bone loss is usually asymptomatic and insidious, with osteoporosis often not diagnosed until after the first fracture occurs. The major complication of osteoporosis is fragility fracture. The lifetime fracture risk for a patient with osteoporosis is as high as 40%.[1] Fragility fractures lead to morbidity, mortality, and increased financial burden on society.

Overall, the current incidence rates of hip fractures are much higher in whites than in black, Asian, or Hispanic populations, and occur much more frequently in women than men. Appropriate attention should be given to diverse subgroups of race and ethnicity. Annual fractures, specifically of the hip, are projected to continue to become more prevalent over time, and populations other than Caucasians are predicted to increasingly share the burden of this disease.[4] Information about the burden of osteoporosis and subsequent hip fractures in these subgroups is currently limited.

Osteoporosis also takes an economic toll on society. Annually, osteoporotic fractures cause > 432,000 hospital admissions, almost 2.5 million medical office visits, and about 180,000 nursing home admissions in the US. In 2005, in this country, $17 billion was spent in direct costs related to osteoporotic fractures (men accounted for 24% of this cost).[4] This is projected to increase to $25 billion by 2025.

The distal forearm (wrist), hip, and spine are the most common locations of fractures due to osteoporosis, with fractures at other sites occurring less frequently. The medical costs of hip fracture are staggering, estimated at $20 billion per year in the US and rising. Disabilities related to hip fracture may be severe and persistent. Among patients who were ambulatory before hip fracture in 1 study, 25% required long-term care.[3] Only 15% could walk across a room unaided 6 months after hip fracture,

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and nearly 25% of those > 50 years died in the first year.

SCREENING AND TREATMENT INDICATIONS

Screening Recommendations

The US Preventive Services Task Force recommends osteoporosis screening for all women aged > 65 years and for younger women who have a fracture risk greater than or equivalent to that for a 65-year-old Caucasian woman with no additional risk factors.[5] National Osteoporosis Foundation guidelines suggest diagnostic assessment with BMD in women aged > 65 years and men aged ≥ 70 years, regardless of clinical risk factors.[6] Other risk factors include a history of previous fractures, family history of osteoporosis or fragility fractures, estrogen deficiency in women, cigarette smoking, excessive alcohol use or caffeine consumption, physical immobility and lack of exercise, vitamin D deficiency, and low dietary calcium intake.

Secondary causes of osteoporosis include medication use, particularly glucocorticoids, antiseizure medications, heparin, lithium, proton pump inhibitors, or opioids. Many other diseases can also increase the risk of osteoporosis. Endocrine conditions, such as Cushing's syndrome, hyperparathyroidism, hyperthyroidism, and diabetes, as well as other medical conditions, such as malabsorption, rheumatoid arthritis, or malignancies, can all affect bone. A full list of secondary causes of osteoporosis is extensive and beyond the scope of this review.

Treatment Indications

National Osteoporosis Foundation criteria suggest that the following should be considered for treatment[6]:

- A hip or vertebral fracture, either clinical or asymptomatic.
- A *T* score on BMD testing of ≤ -2.5 at the femoral neck, total hip, or lumbar spine.
- Low bone mass (*T* score between -1 and -2.5 at the femoral neck or lumbar spine) and a 10-year probability of hip fracture of ≥ 3%, or a 10-year probability of a major osteoporosis-related fracture of ≥ 20% based on Fracture Risk Assessment Tool score (FRAX).[7,8]

TREATMENT APPROACHES BASED ON BONE PATHOPHYSIOLOGY

Bone is a dynamic organ, continuously sensing load and mechanical stresses and responding by maintaining optimal structure, mineralization, and strength. This homeostatic process occurs by bone remodeling, a process in which mature bone tissue is removed from the skeleton (bone resorption) and new bone tissue is formed (bone formation). Occurring in all bones, remodeling does not change the shape of the bone but repairs skeletal damage resulting from repeated stresses by continuously mending small areas of damage. The bone remodeling cycle consists of 2 consecutive phases: resorption and formation.[1]

The cells responsible for bone metabolism are osteoclasts, which are recruited and activated to break down bone, and osteoblasts, which build new bone. With initiation of bone remodeling, removal of bone first occurs by osteoclast recruitment and activation with subsequent bone resorption. After 2-3 weeks, osteoclast apoptosis occurs, followed by deposition of osteoid by osteoblasts. The osteoid subsequently mineralizes to form new bone (an approximately 2-month process). Bone resorption and formation are tightly linked, with the net effect being no bone gain or loss in premenopausal women.

When the balance between bone resorption and bone formation is altered, if there is more breakdown than replacement, bone loss occurs. This typically occurs in postmenopausal women and with many of the secondary causes of osteoporosis noted earlier. It follows, then, that to alter the bone remodeling cycle and improve bone density only 2 avenues are possible: either slow or stop bone resorption, or enhance bone formation (Figure 1).

NONPHARMACOLOGIC APPROACH TO MANAGEMENT

Clinicians should stress avoidance of risky physical behaviors that put the patient at risk for injury. Along with the recommendations for regular weight-bearing (walking, stair-climbing) and muscle-strengthening exercises (weight-training, yoga), cessation of smoking, decreased consumption of alcohol, and calcium and vitamin D supplementation are recommended for the general population. The average