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Osteoporosis: Good Bone Gone Bad

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As bone ages, it is affected by factors influencing its ability to repair, regenerate, and replace old bone with new bone. Whether through damage, loss of essential nutrients like calcium or vitamin D, or as a casualty of medications and diseases, bone can deteriorate in a progressive, harmful fashion affecting quality and strength. As bone density declines, osteopenia develops first. It refers to low bone mass that is not low enough to qualify as osteoporosis. Osteoporosis is a condition in which bone density and strength are reduced, leading to an increased risk of fracture. Between 9-10 million Americans have osteoporosis, most of whom are older adults. While commonly associated with women, about 2 million of the 9-10 million Americans with osteoporosis are men, but they are often not recognized as having the condition, even after a fragility fracture.

Fragility fractures of the hips, distal radius, ribs, and spine are strongly linked to osteoporosis and typically occur with minimal or no trauma. They are the final, injurious outcome of osteoporosis. These fractures often result in hospitalization and negatively affect the individual's longevity, mobility, quality of life and independence.

Over 2 million fragility fractures occur yearly in the United States. One of every 2 women over age 50, and one in 4 men will have a fracture in the course of their lifetime. The first fracture is a marker for a 6-12 fold increased risk of a subsequent fragility fracture within the next year. The high incidence of fractures and consequent increased morbidity and mortality underscores the need to identify and treat osteoporosis, to prevent or at least lower the risk for fractures. Despite these alarming statistics, osteoporosis remains underdiagnosed and undertreated.

Risk Factors

Osteoporosis risk factors include aging, smoking, heavy alcohol use, low calcium intake, small body size (BMI <20), rheumatoid arthritis, and use of certain medications.

Glucocorticoids are the most significant of these medications. Taking ≥ 7.5 mg/d of prednisone for over 6 months puts an individual at a 2-5-fold increased risk. However, any dose of prednisone increases the risk of fractures.

Primary And Secondary Osteoporosis

Primary osteoporosis develops gradually as bone loss outpaces bone formation, beginning in the fourth decade of life. Additional bone is lost by women during the perimenopausal years. As a result, women may develop osteopenia by their sixties, in contrast to men who typically manifest evidence of osteoporosis in their seventies.

Secondary causes of osteoporosis can develop at any age. In men, low testosterone and prostate cancer, especially if treated with LH antagonists, accelerate the appearance of osteoporosis. Women's risk occurs with menopause and breast cancer, particularly with the use of aromatase inhibitors. Both men and women can lose bone from hyperparathyroidism, excessive thyroid replacement, rheumatoid arthritis, chronic lung disease, diabetes, malabsorption syndromes, organ transplant, anorexia nervosa, and deficiencies of calcium and vitamin D. This list is not all-inclusive. Basic lab testing to help to identify secondary causes is shown in Table 1.

| <i>Test</i> | <i>Conditions Identified</i> |
|-----------------------------|---|
| Blood Count | Iron deficiency, B12 malabsorption |
| Chemistry Panel | Liver or renal impairment, malignancy |
| TSH | Hyperthyroidism |
| 24-hr Urine Ca ⁺ | Hypercalciuria and malabsorption |
| 25-OH Vitamin D | Vitamin D deficiency |
| In selected patients | Testing for hyperparathyroidism, multiple myeloma, and celiac disease |

TIPS FOR DEALING WITH OSTEOPOROSIS

- Ensure adequate nutrients for bone with 1200 mg calcium and 800 units vitamin D daily
- Recommend weight-bearing and muscle strengthening exercises to build and maintain bone density
- Encourage smoking cessation in those who smoke
- Screen women 65 and older for osteoporosis using DXA scan; consider screening men age 70 and older
- Institute treatment if osteoporosis is present. Treat osteopenia if fracture has occurred, or fracture risk is increased

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Continued from front page

Screening for Osteoporosis

The US Preventive Services Task Force recommends bone mineral density (BMD) screening of women aged 65 or older. The National Osteoporosis Foundation (NOF) concurs with that recommendation but also recommends screening men age 70 and older. Screening is typically performed with dual-energy x-ray absorptiometry (DXA) of the spine, hip, and femoral neck. Osteopenia is present if the BMD is 1.0 to 2.4 SD below that of a young normal population of the same gender (T score -1.0 to -2.4). Osteoporosis is present if the T score is -2.5 or less. A lateral plain film should be obtained to identify compression fractures when a person with osteopenia complains of back pain.

Predicting Fracture Risk

The Fracture Risk Assessment (FRAX) Tool, developed by the World Health Organization, calculates the 10-year probability of hip and major osteoporotic fractures in previously untreated patients. It uses additional risk factors to increase the accuracy of predicting a fragility fracture. It is useful in patients with osteopenia to determine who would benefit from treatment to prevent a fracture.

When to Treat

There are several indications for drug treatment of patients who have low BMD. They include (a) DXA T score of -2.5 or less, (b) occurrence of a fragility fracture regardless of T score, (c) osteopenia with a FRAX score indicating a >3% 10-year risk of hip fracture, or (d) FRAX score indicating a

>20% 10-year risk of a major osteoporotic fracture.

Treatment

The primary goal of treatment is preventing osteoporotic fractures. Secondary benefits are prevention of pain and maintenance of an individual's independence, which is often lost after serious osteoporosis-related fracture.

There are several classes of drugs available. Bisphosphonates are considered first-line therapy if there is no contraindication. Because long-term bisphosphonate therapy has been linked to the (rare) occurrence of atypical hip fractures, a DXA scan after 5 years of bisphosphonate therapy can be helpful to determine the need for continued treatment or treatment with another class of medication.

Note that intranasal calcitonin is no longer a recommended treatment. It does not reduce fracture incidence and is associated with a small increased risk of cancer.

Although there has been some controversy about the benefit of calcium supplementation, the NOF continues to recommend calcium and vitamin D as adjuncts to therapy, noting that many people have inadequate intake of these nutrients and that they have been shown to reduce the risk of fractures. A 25-OH vitamin D level should be obtained prior to treatment and a level below 30 ng/ml treated. Weight-bearing and strength-training exercises are beneficial for increasing BMD, although they have not been shown to reduce fracture incidence in randomized controlled trials.

| DRUG | DOSE | CONSIDERATIONS |
|-------------------|--|--|
| Bisphosphonates | | |
| • Alendronate | 70 mg weekly po | Avoid use if Cr Cl < 30 mL/min Assure adequate vitamin D intake |
| • Ibandronate | 150 mg monthly po or 3 mg q3 months IV | Correct hypocalcemia |
| • Risedronate | 35 mg weekly po | Oral agents may cause esophagitis; cannot use if unable to sit up |
| • Zoledronic Acid | 5 mg yearly IV | May rarely cause atypical femur fracture or osteonecrosis of jaw |
| Denosumab | 60 mg q6 months SC | Possible serious skin reactions May rarely cause atypical femur fracture or osteonecrosis of jaw No dose adjustment necessary in renal insufficiency |
| Teriparatide | 20 mcg daily SC | Use when high risk for fracture Limited to 2 years due to concern about causing osteosarcoma Contraindicated in patients with bone cancer or prior radiation |
| Raloxifene | 60 mg daily PO | Increased risk for venous thromboembolism |

References and Resources

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