Bone Health and Osteoporosis

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KEYWORDS

• Osteoporosis • Menopause • Fracture • Bone loss • Bone mineral density • DXA • Calcium • Vitamin D

KEY POINTS

- Osteoporosis is characterized by low bone mass and microarchitectural deterioration of bone tissue leading to an increased risk of fragility fractures.
- Central dual-energy X-ray absorptiometry measurements are the gold standard for determining bone mineral density.
- A well-balanced diet containing adequate amounts of calcium and vitamin D, exercise, and smoking cessation are important to maintaining bone health as women age.
- Pharmacologic agents should be recommended in patients at high risk for fracture.

INTRODUCTION

Osteoporosis is the most common skeletal disease in humans. It is characterized by low bone mass and microarchitectural deterioration of the bone tissue, leading to decreased bone strength and increased risk of low-energy fractures, or so-called fragility fractures. Osteoporosis affects a large number of people of both sexes and all races and its prevalence increases with age. Osteoporosis is a risk factor for fracture just as hypertension is for stroke. The most common osteoporotic-related fractures are those of the vertebrae (spine), proximal femur (hip), and distal forearm (wrist).

This article focuses on postmenopausal bone health and osteoporosis. It provides guidance for providers of health care to women on proper screening, identification of secondary causes, and appropriate treatment of osteoporosis.

PATHOPHYSIOLOGY

The skeleton is one of the largest organ systems in the body. It consists of a mineralized matrix with a small but highly active cellular fraction. Bone is formed by

Disclosure: The authors have nothing to disclose.
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Endocrinol Metab Clin N Am 44 (2015) 517–530
http://dx.doi.org/10.1016/j.ecl.2015.05.002 **endo.theclinics.com**
0889-8529/15/$ – see front matter

osteoblasts, which are derived from marrow mesenchymal cells. Osteoblasts are also important for initiating resorption. Along with the osteocytes, they release receptor activator of nuclear factor kappa B ligand (RANKL) which is essential for osteoclastogenesis. In addition to RANKL, osteoblasts produce an inhibitor of osteoclastogenesis called osteoprotegerin (OPG). OPG is a soluble receptor for RANKL that binds this ligand and prevents interaction of RANKL with its cognate receptor, receptor activator of nuclear factor kappa B. Osteoclasts are derived from hematopoietic progenitors and are highly specialized cells involved in bone resorption. The principal stimulator of osteoclast formation is RANKL.

The osteoblasts and osteoclasts are involved in bone remodeling, which is a dynamic process by which old bone is removed from the skeleton and new bone is added. Remodeling can be activated by both systemic and local factors. Changes in mechanical force can activate remodeling to improve skeletal strength and to remove and repair the bone that has undergone microdamage. Systemic hormones influencing bone remodeling include parathyroid hormone (PTH), 1,25-dihydroxyvitamin D, calcitonin, growth hormone, glucocorticoids, thyroid hormones, gonadal hormones, and cytokines. Usually this cycle is tightly coupled and the amount of new bone formed by osteoblasts is equal to the amount resorbed by osteoclasts. Bone loss occurs when this balance is altered, resulting in greater bone removal than replacement. This imbalance occurs with menopause and advanced age.[1]

During the menopausal transition, serum estradiol levels decrease by 85% to 90% and serum estrone decreases by 65% to 75% relative to premenopausal values. With the onset of menopause and the decrease in estrogen levels, the rate of bone remodeling increases by 2-fold to 4-fold. There is a greater increase in bone resorption, resulting in an imbalance in bone remodeling. The imbalance in bone resorption leads to an accelerated phase of bone loss and an efflux of skeletal-derived calcium to the extracellular fluid. These changes lead to a negative total body calcium balance, which further aggravates the skeletal losses.[2]

At menopause, women undergo rapid trabecular bone loss, which usually continues for 5 to 8 years after the cessation of menses. Initially, about 20% to 30% of the trabecular bone and 5% to 10% of the cortical bone is lost. About 8 to 10 years after menopause, a second phase of bone loss becomes predominant in which both trabecular and cortical bone are lost at equal rates. The loss of bone tissue leads to deterioration in skeletal microarchitecture and an increase in fracture risk. Later in the course of menopause, age-related bone loss and accompanying changes in the material properties of bone exacerbate the bone loss associated with estrogen deficiency.

At the cellular level the increased number and activity of osteoclasts disrupts trabecular connectivity and increases cortical porosity. Resorption pits created as part of an accelerated bone remodeling cycle are incompletely filled because osteoblastic new bone formation does not keep pace with rates of bone resorption. Reduced bone density and bone quality compromise the mechanical weight-bearing properties of the skeleton and confer a predisposition to fractures.

Even though bone loss occurs as a consequence of the decrease in estrogen levels during menopause, several other disorders can lead to accelerated bone loss regardless of age and estrogen status. These secondary causes of osteoporosis include hyperparathyroidism, vitamin D deficiency, hypercortisolism, hyperthyroidism, plasma cell dyscrasias (eg, multiple myeloma and monoclonal gammopathy of undetermined significance), inflammatory diseases (eg, rheumatoid arthritis), gastrointestinal disorders (eg, chronic liver disease, celiac disease, and inflammatory bowel disease), chronic renal disease, renal calcium losses, and drugs (eg, steroids, antiepileptics,