Indications and Outcomes of Osteoporosis and Bone Modulation Therapies

Stuart Weinerman, MD[a,*], Gianina L. Usera, MD[b]

KEYWORDS

• Bisphosphonates • Osteoporosis • Fracture • Bone mineral density • Anabolics • FRAX • Glucocorticoids

KEY POINTS

- Osteoporosis-related fractures frequently go undiagnosed and untreated.
- There are many contributing factors of osteoporosis, including menopause, drugs, age, smoking, sedentary lifestyle, and sex, among others.
- Bone mineral density testing is a useful tool for health professionals to determine the need for treatment and also as a long-term monitoring tool.
- Calcium, vitamin D, and exercise, although popularly used as treatments for low bone density, have not been found to be effective in reducing the risk of fracture.

Osteoporosis is a skeletal disorder characterized by compromised bone strength predisposing to an increased risk of fracture.[1] This article addresses the causes of osteoporosis, how to identify who is at risk for fracture, and who should be considered for medical therapy for osteoporosis.

Osteoporosis-related fractures are a major public health issue, and are therefore an important topic for all health providers. For example, a 2004 report estimated 10 million Americans above age 50 have osteoporosis, leading to approximately 1.5 million fractures per year in the United States. Lifetime incidence of osteoporosis-related fractures is approximately 1 fracture per 2 women aged 50 years and older. Despite the public perception that this is a disease only a postmenopausal woman, the incidence in men is 1 fracture per 5 men. Osteoporosis-related fractures are associated with significant morbidity and mortality. Hip fractures in older women are associated with a 15% excess mortality; men with hip fractures have an even higher mortality, estimated at 30%.[2–4]

There are multiple causes of osteoporosis. The bone is a composite material of a collagen framework strengthened by hydroxyapatite, conceptually similar to concrete supported by a steel rebar. This composite material provides both resistance to deformity but still some flexibility. Bone biology depends on a balance of new bone formation, performed by osteoblasts, and resorption of old bone by osteoclasts, which allows growth and remodeling in response to stress or fracture repair. Osteocytes are osteoblasts that become embedded in the new bone. Rates of osteoclastic and osteoblastic activity are tightly linked in normal physiology. Bone remodeling begins with a signal to resorb an area of bone in

The authors report no financial or commercial conflicts of interest to disclose.

[a] Division of Endocrinology, Diabetes and Metabolism, Hofstra North Shore-LIJ School of Medicine, 865 Northern Boulevard, Suite 203, Great Neck, NY 11021, USA; [b] Division of Endocrinology, Diabetes and Metabolism, Department of Medicine, Hofstra North Shore-LIJ School of Medicine, 865 Northern Boulevard, Suite 203, Great Neck, NY 11021, USA

* Corresponding author.

E-mail address: sweinerm@nshs.edu

Oral Maxillofacial Surg Clin N Am 27 (2015) 567–571

http://dx.doi.org/10.1016/j.coms.2015.06.009

1042-3699/15/$ – see front matter

response to fracture or new stress. The osteoblasts recruit new osteoclasts and stimulate resorption mainly through RANK-L (receptor activator for nuclear kappa beta ligand), under the influence of many of factors including sex hormones and parathyroid hormone. Osteoclasts, highly specialized cells, then resorb bone on the surface or tunneling through cortical bone. Osteoclasts form a tight seal on the bone, and then resorb the mineral with acid, and the protein matrix with proteases such as cathepsin K. The bone resorption phase lasts for approximately 3 weeks. Osteoblasts then migrate to the area and lay down new bone, first collagen matrix, which is then mineralized. Abnormalities of each phase and process of bone remodeling are represented by disease states, and are potential targets for pharmacologic therapy.

In childhood and adolescence, bone density increases as linear bone growth occurs. Peak bone density occurs slightly after linear growth stops, generally in the early 20s depending on the bone. Bone density tends to stay stable in healthy adults for several decades as long as there are normal sex steroid levels and circulation, estrogen in women and testosterone in men, and there are no other secondary risk factors such as inadequate nutrition or drugs that affect bone metabolism. Any cause of failure to achieve peak bone density will contribute to long-term risk of fractures (Box 1). Examples would include anorexia or chemotherapy in adolescence. Peak bone density appears to be genetically determined; approximately 60% of the variability between individuals appears to be familial. If peak bone density is normal, then the time or rate of bone loss later in life will contribute to the risk of fracture.

Box 1
Risk factors for osteoporosis

- History of fracture
- Low bone mass
- Fracture in first-degree relative
- Female
- Low BMI
- Advanced age
- Menopause
- Cigarette smoking
- Excessive alcohol use
- Amenorrhea
- Anorexia nervosa
- Low lifetime calcium intake
- Vitamin D deficiency
- Certain drugs
- Low testosterone
- Sedentary lifestyle
- Caucasian or Asian

The most common cause of bone loss in otherwise healthy adults is the loss of estrogen at the time of menopause, whether a surgical or natural menopause. Any other cause of estrogen deficiency will also cause bone loss. This includes drug therapy such as aromatase inhibitors for breast cancer management, or Depo—Provera for contraception. The parallel is true in men. Low testosterone at any age is a contributor to bone loss.

There are numerous secondary causes for osteoporosis, some of which affect the bone quantity (ie, density), and some of which affect the bone quality, such as microarchitecture or bone mineral properties. Numerous disease states contribute to bone loss by a variety of mechanisms. These include a systemic inflammatory mechanism such as rheumatoid arthritis, secondary hypogonadism such as seen in Klinefelter syndrome or Turner syndrome, and nutritional abnormalities especially of calcium and vitamin D such as seen in celiac disease. Endocrinopathies can also contribute to osteoporosis. Examples include hyperparathyroidism with a direct increase in bone resorption, and Cushing syndrome with the effect of excess glucocorticoids on overall bone health, especially a decrease in osteoblastic function. Less common causes of osteoporosis include genetic abnormalities of the bone such as osteogenesis imperfecta, which is a defective synthesis of the bone collagen, or mastocytosis, a disease of rapid bone loss caused by localized release of inflammatory factors.

Numerous medications can also contribute to osteoporosis, through either a direct effect on bone or indirect effects through change in sex steroid levels or vitamin D levels. The most common is chronic use of glucocorticoids such as prednisone or hydrocortisone. Drugs that decrease sex hormone levels include aromatase inhibitors in breast cancer patients and androgen deprivation therapy in prostate cancer patients. Many other drugs also interfere with bone health (Box 2).

The major public health strategy is how to identify patients who are at risk for future fracture in order to target effective therapy and reduce risk. There have been multiple recommendations from a variety of international organizations on how to identify patients, yet osteoporosis remains inadequately diagnosed and treated, especially in high-risk patients.