Osteoporosis: Diagnosis, Risk Factors, and Prevention

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Osteoporosis is one of the most prevalent metabolic bone diseases in the world and is a major public health problem. Osteoporosis consists of a heterogeneous group of syndromes in which reduction of bone mass per unit volume results in bone fragility. The increment in bone porosity causes architectural instability of the bone and increases the likelihood of fracture. In osteoporosis, the mineral-to-matrix ratio is normal, but the bone quantity is reduced. In 2005, the direct and indirect costs of osteoporosis in the United States alone were estimated to be $17 billion. In 2025, it is projected that the costs will be $25 billion, annually [1]. Much of this expense relates to hip fractures. In 15%–20% of hip fracture cases, the outcome is fatal. In osteoporotic individuals, 50% of women and 25% of men older than 50 years could have a traumatic spine fracture during their life.

Reports from Europe in 2003 indicate that variations of a gene on chromosome 20 may cause some postmenopausal women to have osteoporosis. Research studies are in progress to identify the gene in the carriers and implement preventive measures. Meanwhile, clinicians (through nonpharmacological intervention) can add quality to the years of life of osteoporotic patients with or without fractures. Nonpharmacologic intervention could be implemented alone or along with

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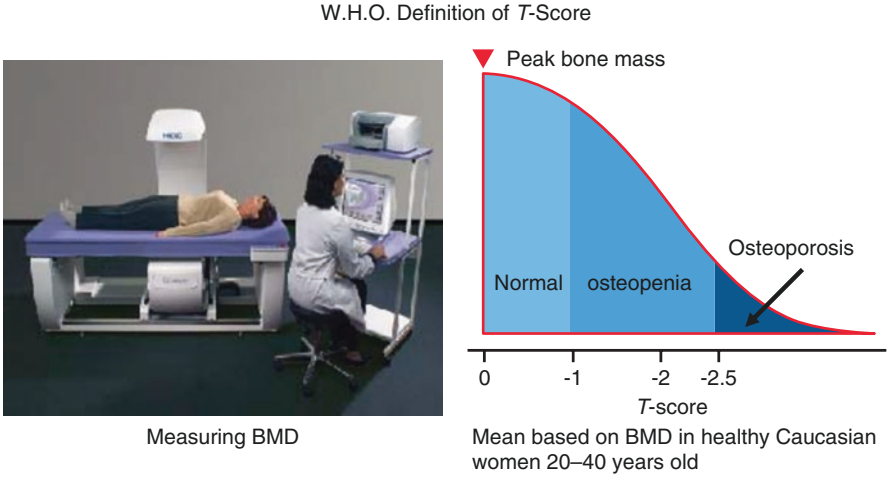

Fig. 1.1 *Left*—measuring BMD with DEXA machine; *right* normal peak bone mass and *T*-score defining osteopenia and osteoporosis

pharmacotherapy in cases of the need for pharmacotherapy. Clinical studies have shown that when pharmacotherapy is combined with the rehabilitative measures, the vertebral fracture rate is decreased [2].

Osteoporosis, a multifaceted disorder, requires a multidisciplinary approach to achieve the most successful management. The World Health Organization defines osteoporosis as bone mineral density (BMD) with a *T*-score 2.5 standard deviations below the peak mean bone mass of young healthy adults [1] (Figure 1.1). The *T*-score shows the amount of one's bone density compared with a young adult (at age 35 years) of the same gender with peak bone mass. The *Z* score is calculated in the same way, but the comparison is made with someone of the same age, sex, race, height, and weight. The *Z* score is adjusted for an individual's age, and the *T*-score is not. For example, a 75-year-old woman with a *Z* score of −1.0 is one standard deviation below the BMD of an average 75-year-old woman, but her *T*-score may be −3.0 because she is three standard deviations below the BMD of an average 35-year-old woman. Normal BMD is a *T*-score −1 or greater; osteopenia, a *T*-score between −1 and −2.5; osteoporosis, a *T*-score −2.5 or less; and severe osteoporosis, a *T*-score −2.5 or less with fracture. In the asymptomatic stage, osteoporosis is characterized simply by decreased bone mass without fracture. Osteoporosis usually is silent and becomes clinically symptomatic when the bone fractures.

Etiology and Pathogenesis

Bone remodeling is an ongoing process that allows removal of old bone and replacement with new bone tissue. Bone remodeling has five stages:

1. In activation: Osteoclastic activity is recruited.
2. In resorption: Osteoclasts make a cavity through eroding the bone.
3. Then in reversal: Osteoblasts are recruited.
4. During bone formation stage: Osteoblasts replace the cavity with new bone.
5. At the quiescence phase: Bone tissue remains dormant until the next cycle starts.

Peak adult bone mass is achieved between ages 30 and 35. High-turnover osteoporosis occurs due to an increased rate of bone remodeling and bone loss without equal bone formation; examples include disorders such as hyperparathyroidism and thyrotoxicosis. Of course, osteoporosis could be secondary to other health-related disorders (i.e., any increased or decreased rate of activation of the bone remodeling cycle could result in reduced bone formation). Loss and reduction of trabeculae result in increased bone porosity and fragility (Figure 1.2).

Trabecular (or cancellous) bone represents approximately 20% of skeletal bone mass and makes up 80% of the turnover media. The cortex makes up only 20% of the turnover media and is made of compact bone, which represents 80% of skeletal bone mass. Bone remodeling is initiated with the activation of osteoclasts for resorption. Then, resulting resorption sites are refilled by osteoblastic activities, a process called bone formation. There is no bone loss when the amount of bone resorbed equals the amount formed. After age 35 years, however, the remodeling process does not result in zero balance, and the normal process of remodeling results in bone loss [3].

When there is an increase in the rate of bone remodeling, such as in hyperparathyroidism or thyrotoxicosis, the rate of bone remodeling can increase, resulting in bone loss. Therefore, osteoporosis can occur after age 35 in a high turnover rate of the bone. The secondary causes of osteoporosis are associated with an increased rate of activation of the remodeling cycle. However, factors such as calcium intake, smoking, alcohol consumption, level of physical activity or physical exercise, and

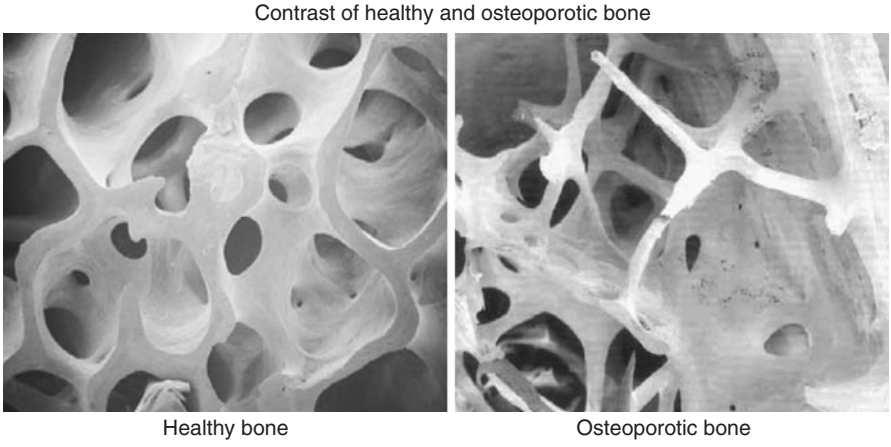

Fig. 1.2 Contrast of trabeculae in healthy and osteoporotic bone. Images by David W. Dempster, PhD, ©2005

menopause are important and could contribute to the variance in peak BMD [3]. The incidence of osteoporosis-related fractures is lower in men than in women because the diameter of vertebral bodies and long bones is greater in men at maturity, and bone loss is less (about half that of women) throughout life. In addition, women have lower muscle strength than men for support of the skeletal structures [3]. Common risk factors are reflected in Box 1.1.

Box 1.1 Common risk factors for osteoporosis

- History of fracture after age 50
- Current low bone mass
- History of fracture in a primary relative
- Female
- Small stature/thin
- Advanced age
- A family history of osteoporosis
- Estrogen deficiency as a result of menopause, especially early or surgically induced
- Low testosterone levels in men
- Anorexia nervosa
- Low lifetime calcium intake
- Vitamin D deficiency
- Use of certain medications, such as oral corticosteroids and anticonvulsants
- Presence of certain chronic medical conditions
- An inactive lifestyle
- Current cigarette smoking
- Excessive use of alcohol
- Caucasian or Asian ancestry

Modified from [1]; used with permission.

Diagnosis

Osteoporosis, in general, is a preventable disorder. Maintenance of bone mass depends on several factors, including proper level of physical activity (PA), hormones, and nutrition. Early diagnosis of low bone mass and provision of measures to prevent further bone loss are essential. The diagnosis of osteoporosis requires a thorough physical examination, including height and weight measurements, location of musculoskeletal pain, family history of osteoporosis, dietary calcium intake, level of PA, and past exercise programs. Several biochemical indices are also used in the differential diagnosis of metabolic bone disease or, in some instances, for therapeutic follow-up [4].

Biochemical markers for bone formation include calcium, phosphorus, PTH (parathyroid hormone), bone-specific alkaline phosphatase, and serum

osteocalcin. Resorption markers include 24-hour urinary calcium excretion (corrected by creatinine excretion), hydroxyproline, and pyridinium cross-links (in urine). The interpretation of these tests depends on intraindividual and interindividual variations. Also, indices of bone turnover show seasonal and circadian variations.

Radiographic findings of osteoporosis [5] consist of increased lucency of the vertebral bodies with loss of horizontal trabeculae, increased prominence of the cortical end plates, vertically oriented trabeculae, reduction in cortex thickness, and anterior wedging of vertebral bodies (Figure 1.3). The degree of wedging that indicates a true fracture varies from a 20% to 25% reduction in the anterior height relative to the posterior height of the same vertebra.

Other morphologic changes occur, such as biconcavity of vertebral bodies and complete compression fractures (reduction in both anterior and posterior heights by at least 25% compared with adjacent normal vertebrae) [5]. Bone scans and magnetic resonance imaging, if needed, can further define the cause of bone pain, such as stress fractures. Conventional radiographs may not reveal stress fractures nor reveal osteoporosis until at least 25%–30% of bone mineral has been lost. Consequently, evaluation of BMD through absorptiometry techniques is recommended [6].

The different methods for evaluation of bone mass have different levels of precision. Other available methods include photon absorptiometry (single or dual) (Figure 1.1), finger radiographic spectrometry, ultrasound densitometry, qualitative computed

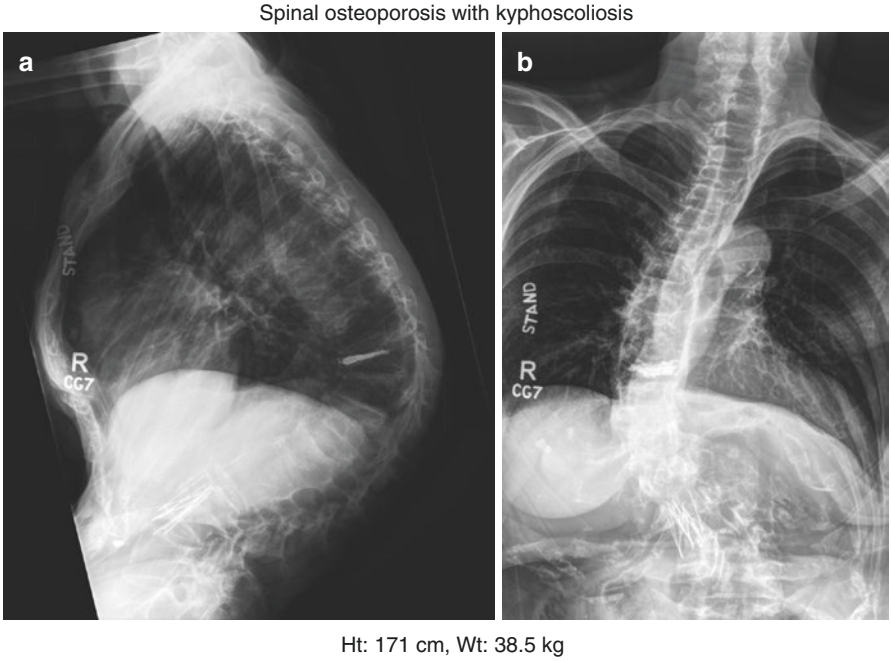

Fig. 1.3 (**a**) and (**b**) depict spinal deformities that could result from spinal osteoporosis and vertebral compression fractures

tomography, and dual-energy radiographic absorptiometry. The most commonly used technique is dual-energy radiographic absorptiometry, which has high precision and is frequently used for research and clinical evaluations to measure the BMD of the spine and hips. It is radiographically based and has a precision of approximately 1%. More

Table 1.1 Some of the diagnostic evaluations for osteoporosis

Evaluation	Details
History and physical examination	Family history of osteoporosis, type and location of pain, general dietary calcium intake, level of physical activity, height and weight
Radiographs of the chest and spine	To rule out lymphomas, rib fractures, compression fractures, etc.
Bone mineral density (spine and hip)	At menopause, every 2 years for high-risk patients, and every 5 years for low-risk patients
Complete blood cell count	To rule out anemias associated with malignancy, etc.
Chemistry group (serum calcium, phosphorus, vitamin D, parathyroid hormone, bone-specific alkaline phosphatase, osteocalcin)	To assess the level of alkaline phosphatase, which may be increased in osteomalacia, Paget's disease, bony metastasis and fracture, intestinal malabsorption, vitamin D deficiency, chronic liver disease, alcohol abuse, phenytoin (Dilantin) therapy, hypercalcemia of hyperparathyroidism, hypophosphatemia of hyperparathyroidism and osteomalacia, malabsorption, or malnutrition
Erythrocyte sedimentation rate and seroprotein electrophoresis	To determine changes indicative of multiple myeloma or other gammopathies
Total thyroxine	Increased total thyroxine concentration may be a cause of osteoporosis because of increased bone turnover
Immunoreactive parathyroid hormone	Hyperparathyroidism (accompanied by hypercalcemia)
25-Hydroxyvitamin D and 1,25-dihydroxyvitamin D3	Gastrointestinal disease, osteomalacia
Urinalysis and 24-hour urine	To check for proteinuria caused by nephrotic syndrome and for low pH resulting from renal tubular acidosis; a 24-h urine test can exclude hypercalciuria (normal calcium value in men is 25–300 mg/specimen; in women, 20–275 mg/specimen)*
Optional: bone scan, iliac crest biopsy	After tetracycline double labeling for bone histomorphometry, bone marrow biopsy may be indicated to exclude multiple myeloma and metastatic malignancy
Biochemical markers of bone turnover (Eastell)	Formation: serum osteocalcin, alkaline phosphatase (bone), procollagen type 1, C- and N-propeptides
	Resorption: serum acid phosphatase, pyridinoline, deoxypyridinoline, hydroxyproline, cross-linked telopeptides of type 1 collagen, urinary calcium, or creatinine

From [3] used with permission.
*Mayo Clinic normal values.

commonly measured is the BMD of the femoral neck, since spine bone density can be erroneously high, as in osteoarthritis of the spine [6] (Table 1.1).

Prevention

Reducing risk factors can decrease bone loss. These include positive lifestyle changes, which contribute to improvement of musculoskeletal health in general. It is suggested that the greater the bone mass at the time of menopause, the less chance for development of osteoporosis [7]. Therefore, improving muscle strength through weight-bearing exercises at a young age is beneficial [8]. Stronger back extensors and back extension-strengthening exercise could also reduce or prevent risk of vertebral fractures [9]. In addition, stronger back extensors could reduce back pain [10]. In children, stronger back extensors could decrease the risk of back pain in later years [11]. Back pain could contribute to reduced PA level and, later in adulthood, muscle and bone loss.

Proper PA plays a significant role in maintenance of musculoskeletal health. Performing strenuous flexion during a few yoga poses could result in vertebral compression and, in some cases, neck and back pain. These concerns need to be taken into consideration before prescribing an exercise program in cases of osteopenia, osteoporosis, and degenerative arthritis of the spine [12] (see Chapter 7).

Application of proper mechanical load can stimulate osteogenic activity. Axial loading of the skeleton during lifting activities at a person's job or in the care of children can be as osteogenic as mechanical-loading exercises in a gym [13].

The best preventive measures start in childhood, including proper nutrition and PA. Later in life, the level of PA plays a significant role. In women aged 30 to 40 years, BMD and muscle strength were found to be site specific. BMD of the spine was higher in women whose jobs were not sedentary [13].

One study showed a marked difference in BMD between gymnasts and volleyball players. The lower limbs are loaded differently in these two athletic activities [14]. Gymnasts had higher BMD than volleyball players, except in the pelvic bone. Swimming can improve muscle strength but not bone mass [15]. According to the theory of Frost [16, 17], a minimum threshold of mechanical loading is needed to evoke osteogenecity. This theory is referred to as that of the minimum effective strain stimulus. Lanyon [18] suggested that the greatest osteogenic effect from mechanical loading occurs when the strain is vigorous (high strain), repeated daily, short in duration, and applied to a specific bone site. There is a significant reduction of the level of PA from age 19 to 66, as shown in one study (Figure 1.4, [19]). This can contribute to age-related bone loss. Another study showed a significant correlation between the level of PA or weight-bearing involved in individual's job with BMD of the lumbar spine. Therefore, PA whether sport- or job-related could contribute to BMD ([13], Figure 1.5).

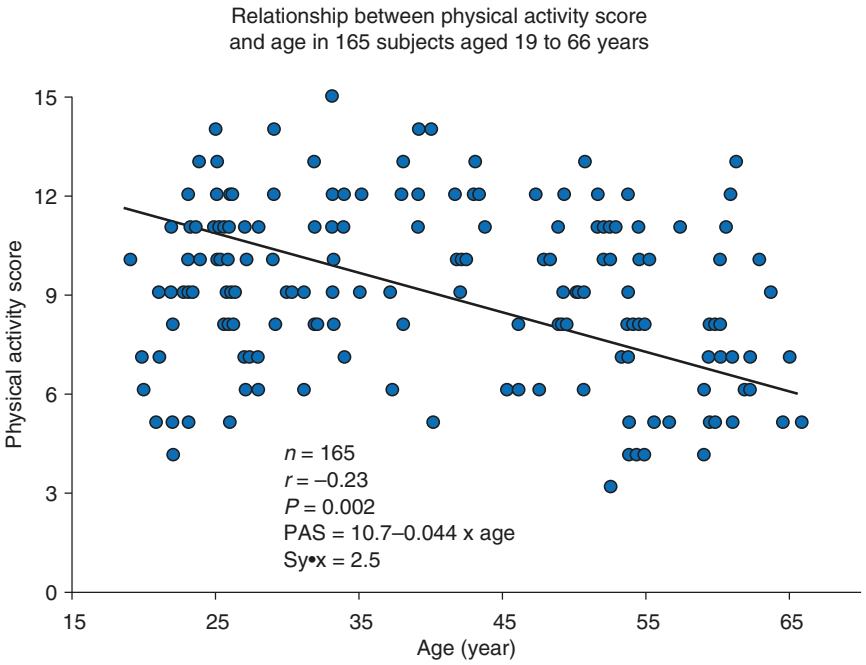

Fig. 1.4 Depicts reduction of physical activity level with increasing age in healthy population. From Sinaki M: Aging Clin Exp Res 10:249–262, 1998; used with permission.

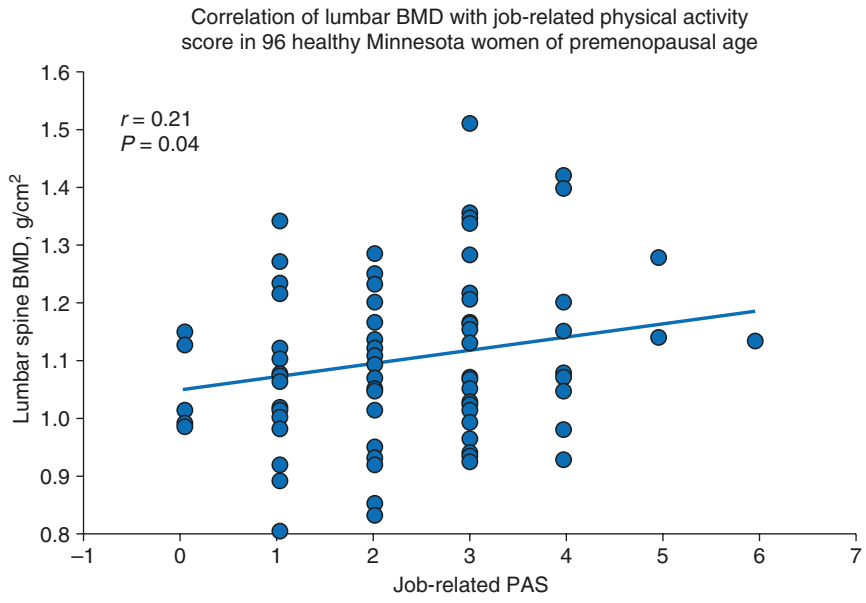

Fig. 1.5 Weight-bearing physical activity whether at job or otherwise could have positive effect on BMD of the spine. From Sinaki M, Fitzpatrick LA, Ritchie CK, Montesano A, Wahner HW. Site-Specificity of Bone Mineral Density and Muscle Strength in Women: Job-Related Physical Activity. Am J Phys Med Rehabil; 77(6):470–476, November/December, 1998; used with permission.

Maintenance of Lifelong Bone Health

Exercise is one of the factors for building and maintaining strong bones. It is well known that the risk of osteoporosis is lower for people who are active, especially for those who do weight-bearing activities at least three times a week. Exercise could also increase muscle strength and improve coordination and steadiness of gait, which helps to decrease risk of falls and situations that cause fractures.

There are different types of weight-bearing exercises with different osteogenecity effects that could be included in daily activities (e.g., walking, jogging, weight lifting, stair climbing, racquet sports, hiking, dancing). The objective of exercise needs to be defined. Compliance improves if the individual's interest is discussed prior to the recommendations. If exercise is enjoyed, it is more likely to become a habitual PA.

Healthy Bone Diet

There are a number of foods and substances that, when consumed in excess, result in excess calcium drainage from the body. These substances include caffeine and diets too high in protein from animal sources (to limit 4 oz. of meat per day would be sufficient or 0.8 g of protein per kilogram of the body weight). It is recommended by the US Department of Agriculture that all men and women over the age of 19 should get at least 0.8 g of protein per kilogram of the body weight per day (or 0.37 g per pound). This means a 130-lb woman could get 48 g of protein, such as 7 oz. of salmon.

Alcohol consumption should be limited to one drink per day (1.5 oz. of hard liquor, 12 oz. of beer, or 5 oz. of wine). Too much salt can contribute to calcium loss. To manage this concern, it is better to avoid adding extra salt to food before tasting it and reducing intake of processed foods, since they are often high in sodium.

To excrete the extra phosphates of soft drinks in urine, calcium is drawn from bones. In general, alkaline foods such as fruits, nuts, legumes, and vegetables are preferable over acidic foods such as meat, poultry, fish, dairy, eggs, grains, and alcohol. Of course, a balanced diet would take these factors into consideration.

The best source of calcium is calcium-containing foods (e.g., dairy products, leafy vegetables, nuts), but calcium supplements may also be an option. Too much calcium should be avoided, especially for patients with a history of urolithiasis. Recent studies suggest that taking high daily doses of calcium supplements (1000 mg or more) may damage the heart and have other negative health effects [20]. The type of calcium supplement and method of use is important. Calcium citrate is a highly absorbable calcium compound. It is best absorbed if taken with food. Absorption also improves if taken 500 mg at a time. Calcium ascorbate and calcium carbonate are not as easily absorbed as calcium citrate and may cause bloating. For reducing gas or constipation, increasing intake of fluids and vegetables would be of help. Vitamin D also plays a significant role in bone health. From age 18 to 70, 800 IU would be sufficient, but after 70, the amount may need to be increased to 800 IU to 1000 [21, 22].

When BMD does not improve with basic measures such as exercise, vitamin D, calcium intake, and proper nutrition, pharmacotherapy needs to be considered. There are other elemental nutrition factors that contribute to bone and muscle health and development (e.g., vitamin K and zinc), which are beyond the scope of this chapter. The authors refer the readers to the information on nutrition and maintenance of health resources.

Conclusion

Maintaining a moderate level of physical activity through a regular exercise program, combined with a balanced diet and proper calcium and vitamin D intake, is fundamental to bone and muscle health. In the case of osteoporosis and fragility, an exercise program needs to be prescribed according to the level of BMD, while being progressive and challenging. These exercises will be discussed in detail in a chapter devoted to exercise.

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