



Osteoporosis

Introduction: Osteoporosis is a disease of the bone that results from the loss of calcium and other materials from the skeleton, leaving bones with altered structure, less density, and less strength. This process results in an increased risk for fractures, which not only affects quality of life but also may result in fatal consequences.

The impact osteoporosis has on our society can hardly be overstated. Among Caucasian women over the age of 50, 17% are found to have osteoporosis, while an additional 42% can be classified as having “low bone mass” (referred to as *osteopenia*). In Caucasian men, 4% are osteoporotic, while an additional 33% are osteopenic. These figures are somewhat lower among other ethnic groups.

At present, 40% of women and 13% of men over the age of 50 are expected to sustain a fracture in their lifetime due to low bone mass. Annually, we see approximately 1.3 million fractures due to osteoporosis in the United States, and in 1995, \$13.8 billion dollars were spent on osteoporotic fractures. This amount exceeds the annual cost of treating asthma and is nearly that of the annual expense of treating heart failure. Roughly half of all women over the age of 50 who sustain a hip fracture will lose their ability to function independently, and women over the age of 65 have an approximate 25% mortality rate within one year of fracturing their hip. After menopause, a woman has a greater chance of dying from the consequences of an osteoporotic fracture than from breast, uterine, and ovarian cancer *combined*.

Features of Osteoporosis: Osteoporosis is a silent illness. It can be likened to high blood pressure or elevated cholesterol levels, neither of which cause symptoms but can result in an increased risk for heart attacks and strokes. In the same way, osteoporosis causes no symptoms until it causes complications – namely fractures.

The most common sites of osteoporotic fractures are the vertebrae of the spine, followed by the hip and the wrist. Osteoporotic fractures often occur with little to no injury. They may occur spontaneously, after a fall, or following a lifting injury.

Only 1/3 of all vertebral fractures cause symptoms and are found incidentally on x-ray studies; the remainder can be very painful. As vertebrae fracture, a loss of height commonly occurs and may result in changes in posture and the commonly described “dowager’s hump” along the upper back. Vertebral fractures only result in a mild

increase in mortality, and wrist fractures have no effect on mortality, but both have a significant impact on quality of life. Hip fractures, on the other hand, significantly impair both quality of life and survival, as mentioned above.

Risk factors for osteoporosis include female gender, Caucasian or Asian race, advanced age, slender build, low dietary intake of calcium, family history of osteoporosis, and smoking. Other factors that can adversely affect bone density include use of certain medications such as corticosteroids, hormonal imbalances (low testosterone, elevated levels of hormones from adrenal or parathyroid glands), and excessive alcohol intake. Secondary causes of osteoporosis should be sought in younger individuals or males found to have low bone mass.

Diagnosis: The most accurate and widely available method for detecting osteoporosis is known as *bone densitometry*. Techniques used for bone densitometry vary and may include quantitative computerized tomography (CT) and ultrasound, but the most commonly used modality is dual-energy x-ray absorptiometry (DEXA).

A DEXA scan is quick, painless, involves minimal radiation exposure, and yields valuable information concerning bone density and subsequent fracture risk. The spine and hip are the most common areas imaged, but certain machines have the capability of measuring bone density in the wrist or calculating a total body measurement. For the most part, however, assessing bone density of the spine and hip is sufficient to screen for osteoporosis.

Two numbers are calculated from a DEXA scan: a *T-score*, which compares bone density to young adult female averages, and a *Z-score*, which compares a patient to averages for the same age, gender, and race. It is the T-score that is used to diagnose osteoporosis. A T-score of ≤ -2.5 is classified as osteoporosis, while a score of -1.0 to -2.4 is considered osteopenia, and anything above -1.0 is normal. There are many reasons that the Z-score is less useful; for example, a “normal” bone density reading for an 80 year old female imparts a significant risk for fracture. The Z-score may be most useful when < -2.0 , which suggests that a secondary cause of low bone mass needs to be investigated.

Quantitative CT is less commonly employed and can only provide information about bone density in the spine, but this method eliminates the problem of bone spurs, which may falsely elevate bone density readings on a DEXA scan. Some DEXA machines are now equipped with software to perform lateral vertebral measurements and this too may minimize this problem. Ultrasound is performed on the heel, is very rapid, inexpensive, and can estimate fracture risks at other sites. Because ultrasound values correlate poorly with those performed at other sites, however, pursuing a formal DEXA study is usually recommended when making decisions about therapy.

Bone density measurement is recommended for: 1) all individuals with “low energy” fractures (simple falls, etc.), 2) women entering menopause with additional risk factors for osteoporosis, 3) all women over the age of 65, 4) men over the age of 70, 5)

those planning long-term steroid therapy or other medications that may cause bone loss, 6) those making decisions about whether to start therapy to prevent bone loss, and 7) monitoring the effects of therapy for low bone mass.

Plain x-rays may demonstrate evidence for prior fractures and can demonstrate bones that appear less dense, but by the time these changes are detectable by x-rays alone, a substantial amount of bone mineral has already been lost. For this reason, plain x-ray alone is a poor screening tool for osteoporosis and is not recommended.

Therapy: Treating osteoporosis involves stopping the net loss of bone mineral that is occurring. Osteoporosis occurs when more material is being taken away, or *resorbed*, from bone than what is being put into the bone. If we can slow down bone mineral being taken away (*resorption*) or increase bone mineral being added (*formation*), bone density will increase.

Decisions about the intensity of therapy are typically best made on the basis of DEXA or other bone density measurements. In an individual who is felt to be at low risk for ongoing loss of bone density and who has a T-score of >-1.0 , maintaining an adequate intake of calcium and vitamin D is sufficient. For those with relatively normal bone density or mild osteopenia who have other risk factors for osteoporosis or fractures to develop, an additional medication to help prevent future loss of bone mass is prudent. For those with a T-score of ≤ -2.0 , those with additional risk factors and a T-score of ≤ -1.5 , or those with existing fragility fractures, more aggressive treatment is indicated.

Exercise has beneficial effects on bone density by stimulating “remodeling” of bone. Low-impact activities such as walking or gentle running are preferred. Exercise has the additional benefit of improving muscle tone, which helps prevent falls.

Calcium and vitamin D supplementation is the first step in treating and preventing osteoporosis. During years of skeletal growth until peak bone mass is achieved around the age of 35, an adequate calcium intake of 1,000 mg/day and vitamin D 400 units/day is important to build strong bones. The first few years after menopause are characterized by rapid loss of bone mineral, and at that point 1,200 to 1,500 mg/day of calcium and 400 to 800 units of vitamin D are recommended. Similar recommendations are made for those taking corticosteroids and older men.

Dairy products and some orange juice preparations are good dietary sources of calcium, while carbonated beverages with high phosphate content generally result in loss of calcium from bones. Calcium supplements over the counter containing calcium carbonate or calcium citrate in combination with vitamin D provide additional protection. If added to a reasonable diet, 2 to 3 tablets of a calcium and vitamin D combination supplement are usually sufficient to provide for one’s daily needs. While some brands of calcium may attempt to claim superiority over others, it is not so much the form of calcium but the amount of calcium that is important.

Estrogen replacement therapy, given in form of pills or patches, prevents the loss of bone mineral that occurs after menopause, and when begun after the age of 65 may increase bone density by as much as 5-10%. Studies have documented lower vertebral fractures and suggested lower hip fracture rates in women taking estrogen.

Recent widely publicized data, however, has shown an increased risk of blood clots and heart attacks in women taking estrogen, particularly in those with other risk factors such as smoking. There has also been a longstanding concern about the risk of breast cancer with estrogen. When this information became available, many women stopped taking their estrogen preparations without discussing this matter with the prescribing physician. The unfortunate consequence of this decision is that bone density drops rapidly after estrogen is discontinued. Women should have a frank discussion with their doctors about the pros and cons of taking estrogen as well as alternatives to such therapy to prevent bone loss and the complications that may result if no bone protective therapy is being given.

Bisphosphonates are medications that powerfully inhibit resorption of bone. By doing so, bone density increases over time. Currently available medications in this class include alendronate (Fosamax) and risedronate (Actonel). Both of these medications may be given either once daily or once weekly in pill form, and Fosamax is also available in liquid form. Both of these agents increase bone density in both the spine and the hip, but more importantly reduce fracture risk at both of these sites by as much as 50% within 6 months of starting therapy.

Because these drugs must be well absorbed, they are taken on an empty stomach first thing in the morning, and it is recommended that no food or other medications be given until at least 30 minutes later. Some individuals experience an upset stomach or possibly even some damage to the stomach lining, which is minimized by taking these drugs with a full glass of water in the upright position. Patients with strictures in their esophagus who have difficulty swallowing pills may not be good candidates for the pill form of these medications but could still take the liquid form of Fosamax.

Raloxifene (Evista) is a medication that acts as a “selective estrogen receptor modifier,” producing the positive effects of estrogens on bone, while avoiding the negative effects of estrogen on breast tissue and possibly avoiding the increased risk of heart attacks from estrogen. Given in pill form once daily without the requirement of an empty stomach, Evista has been shown to increase bone density in both the spine and hip, but has only been shown to reduce fractures in the spine. It is possible that hip fractures are reduced as well, but studies to date may not have included enough patients to demonstrate such an effect. A small increase in blood clots may be seen with Evista, but beneficial effects are seen in cholesterol levels, and it is possible that this agent may actually *reduce* the risk of breast cancer (studies to confirm this effect are underway).

Teriparatide (Forteo) is a derivative of a hormone in the body known as parathyroid hormone (PTH). This hormone stimulates both bone formation and bone resorption, and depending on how much is present, bone density either increases or

decreases. Forteo is designed to favor bone formation, and is the only available treatment for osteoporosis that works in this way (all other medications work mostly to inhibit bone resorption). It is given in a once daily injection and while costly, assistance programs to Medicare recipients are readily available.

Forteo increases bone density in both the spine and the hip but has only been shown to reduce vertebral fractures. Moreover, this agent may become less effective when given continuously for over 2 years. While many physicians hoped that Forteo could be given in combination with bisphosphonates for additional benefit, studies have shown no more benefit when combining these therapies than when using either agent alone.

Calcitonin is also a hormone normally made by the body that blocks bone resorption. It is most commonly given in the form of a nasal spray once daily and is associated with minimal side effects. The gains in bone density seen with this agent, however, are less than what are seen with other therapies and beneficial effects are only observed in the spine. Nonetheless, vertebral fractures are reduced when using this medication long-term and it does have a role in treating osteoporosis in patients unable to take other medications.

Novel agents in development for treating osteoporosis include zoledronic acid, strontium, osteoprotegerin, and inhibitors of RANK-ligand. Zoledronic acid is an intravenous bisphosphonate similar to Fosamax and Actonel. The advantage of this therapy is that it can be given once a year and seems to have a prolonged effect on inhibiting bone resorption. Thus far, studies have yet to document a beneficial effect on reducing fractures. Strontium is a medication given orally that both increases bone formation while decreasing resorption. This agent appears to increase bone density in the spine and the hip as well as reducing vertebral fractures. Both osteoprotegerin and RANK-ligand inhibitors are in early stages of development but appear to be involved in the balance between bone formation and resorption, representing another method for reducing fractures.

Vertebroplasty and *kyphoplasty* are procedures that are now available for treating symptomatic vertebral compression fractures. Both involve the insertion of a catheter into the collapsed vertebra under x-ray guidance. With vertebroplasty, a cement-like material is injected into the vertebra to provide stability and reduce pain, while kyphoplasty involves first inflating the vertebra with a balloon before injecting with cement. Kyphoplasty has the additional benefit of improving postural changes, but is not clearly superior to vertebroplasty alone in improving outcomes. When using these methods, experienced centers are necessary, and after completion of these procedures, it is essential to pursue medical therapy to prevent future fractures.

Monitoring the effects of therapy is necessary to determine whether the medication is having its desired effect on bone density. DEXA scans performed every 1 to 2 years are usually adequate to assess whether bone density is being maintained, or hopefully increased. While important, increases in bone density explain only a fraction

of fracture reduction in patients on certain therapies (bisphosphonates, for example). Small gains in bone density may result in large reductions in fracture risk.

Because of the time needed to see a meaningful change in bone density, urine markers of “bone turnover” are available and may demonstrate positive effects within a few months of beginning osteoporosis therapy. The most common test run is a urinary ‘N-telopeptide,’ which is best collected on the second urination of the morning. This level is often elevated in those with ongoing risk for future loss of bone density but is suppressed when medications designed to inhibit resorption have their desired effect.

Because osteoporosis therapy has to be given continuously over long periods of time and does not typically result in improvement in symptoms, it is often difficult to encourage patients remain on their medications. Adherence to the plan of treatment, however, prevents complications and should result in a greater overall quality, and perhaps duration, of life.