

Osteoporosis Disease Management: What Every Orthopaedic Surgeon Should Know

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Introduction

According to recent information from the National Osteoporosis Foundation¹ and the Office of the Surgeon General², osteoporosis is a major medical problem. The disease currently affects 8 million women and 2 million men in the United States. An additional 34 million Americans have low bone mass. Each year, an estimated 1.5 million individuals in the United States experience a fragility fracture secondary to osteoporosis, resulting in an annual cost of 18 billion dollars. With the rapidly aging U.S. population, the problem of osteoporosis is now reaching epidemic proportions. There are 75 million baby boomers entering the stage in their lives when they are most at risk for osteoporosis. One-half of all women and one-third of all men will sustain a fragility fracture during their lifetime.

There is a huge cost associated with osteoporosis in terms of morbidity, mortality, and the financial impact on society. The most devastating complication of osteoporosis is a hip fracture. According to the most recent statistics published in the United States Surgeon General's 2004 report on osteoporosis, of the 325,000 patients who sustain a hip fracture each year, 25% will find it necessary to enter a nursing home, 50% will never reach their previous functional capacity, and 25% will die within the first year after the fracture³. The first-year mortality rate after a hip fracture is almost twice as high in men as it is in women (30% compared with 17%). The mortality rate associated with osteoporosis-related fractures is greater than the rates associated with breast cancer and cervical cancer combined¹⁻⁶.

Only 20% of patients who have had a previous hip fracture or other fragility fracture receive treatment for osteoporosis⁷⁻¹³. There are certainly many missed opportunities for fracture prevention¹⁴.

Pathophysiology of Osteoporosis

To achieve a significant decrease in osteoporosis-related hip fractures, it is important to understand the pathophysiology of osteoporosis as well as the risk factors that are associated with hip fractures.

Osteoporosis is characterized by low bone mass and structural deterioration of bone tissue, which leads to bone fragility

and an increased susceptibility to fractures. Bone strength is related to bone density as well as changes in the micro-architecture of bone. The micro-architecture of bone is a poorly understood concept and is currently very difficult to measure without a biopsy. A dual x-ray absorptiometry scan provides information about bone density but does not provide any information about the micro-architecture of the bone. As bone strength decreases as a result of changes in bone density and/or changes in bone micro-architecture, the risk of fracture increases¹⁵.

In both men and women of all races, bone mass increases with age until approximately thirty years of age and then begins to decrease. After menopause begins, the rapid drop in estrogen levels may lead to a 1% to 3% drop per year in bone mineral density for as long as ten years, followed by a slower loss of bone density. Men start out with a higher peak bone mass than women, and they lose bone at a slower rate than women do^{16,17}.

Bone Remodeling

Bone remodeling is a combination of resorption and formation. With osteoporosis, there is a net loss of bone as well as a change in the micro-architecture of the bone¹⁵. It is important to understand the factors that contribute to normal and abnormal remodeling of bone.

Calcium

Ninety-nine percent of the total calcium in the human body is stored in the bones. In addition to serving as a reservoir for the calcium needs of the body, stored calcium also acts as a bone strengthener. The small amount of calcium that circulates outside of bone plays a crucial role in muscle and nerve function. As serum calcium levels drop, bone resorption increases. Calcium absorption is significantly improved when the circulating levels of vitamin D are adequate².

Vitamin D

Even though it is called a vitamin, vitamin D acts more like a hormone in that it helps to increase calcium absorption and decrease calcium excretion. Vitamin D can be synthesized in the skin when the skin is exposed to ultraviolet-B rays from

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sunlight. A five to ten-minute exposure of sunlight to the unprotected arms and legs results in the production of 3000 IU of vitamin D¹⁸. Proper intake of calcium and vitamin D may decrease fracture rates by up to 25% by maintaining good bone health¹⁹. Vitamin D has been shown to decrease the types of falls that are often associated with fragility fractures²⁰.

Parathyroid Hormone

Parathyroid hormone plays a crucial role in helping to maintain calcium homeostasis. At physiologic levels, parathyroid hormone acts at the level of the osteoclast to increase bone resorption and it also acts in the gut to help assist in calcium absorption. At pharmacologic levels, parathyroid hormone stimulates osteoblasts to increase bone formation. Low vitamin-D levels may cause secondary hyperparathyroidism and a resultant increase in bone resorption².

Estrogen

Estrogen suppresses osteoclast activity in women and, surprisingly, also in men. The decrease in estrogen at the time of menopause leads to a rapid loss of bone mineral density¹⁶.

Testosterone

Testosterone helps osteoblasts to form bone. Men on medications that suppress testosterone may experience a >4% drop in bone mineral density per year²¹.

Secondary Causes of Osteoporosis

It is vital not to forget all the secondary causes of osteoporosis, such as primary hyperparathyroidism or tumors, when bone loss has been detected²².

Laboratory Tests

There is no established set of laboratory tests for the routine evaluation of osteoporosis. Prior to the initiation of treatment, however, laboratory tests can be used to identify low blood calcium levels, vitamin-D deficiencies, and renal problems.

The following common routine laboratory tests may be helpful in the diagnosis and management of osteoporosis²:

- **Serum calcium level.** This level is usually normal in patients with osteoporosis but may be elevated in patients with other bone diseases.
- **25-hydroxyvitamin-D level.** Deficiencies may lead to decreased calcium absorption. Vitamin-D deficiency is extremely common in elderly persons.
- **Complete blood-cell count.** Determination of the complete blood-cell count can be helpful in checking for secondary osteoporosis.
- **Twenty-four-hour urine calcium level.** The urine calcium level can be measured to check for hyperexcretion of calcium.
- **Parathyroid hormone level.** This level can be measured to screen for hyperparathyroidism.
- **Testosterone level.** The testosterone level can be measured to check for testosterone deficiencies in men.

- **Protein electrophoresis.** This test can aid in the identification of multiple myeloma.
- **Thyroid function tests.** The measurement of thyroid function can be helpful in screening for thyroid disease.

Risk Factors for Osteoporosis

There are modifiable and nonmodifiable risk factors for osteoporosis and fragility fractures that should be considered in all patients².

The *nonmodifiable risk factors* for osteoporosis fractures² include the following:

- **The genetic profile.** In the future, there may be a potential for treatment with gene suppression or manipulation.
- **History of fracture in a first-degree relative.** This may be related to the genetic profile.
- **Female sex.** Compared with men, women have twice the risk of sustaining a fragility fracture.
- **Advanced age.** The risk of a hip fracture doubles every five years past seventy years of age.
- **Caucasian race.** Compared with Blacks, Caucasians have twice the risk of sustaining a fragility fracture.

The *modifiable risk factors* for osteoporosis fractures² include the following:

- **Currently smoking cigarettes**
- **Low body weight** (<127 lb [57.6 kg] in women and <154 lb [69.9 kg] in men) or **low body mass index** (<20 in women and <25 in men)
- **Low calcium intake and low vitamin-D intake.** A single multivitamin tablet a day does not provide enough calcium or vitamin D.
- **Excessive alcohol intake**
- **Recurrent falls**
- **Poor physical activity**
- **Poor health or being frail**
- **Estrogen deficiency.** Early menopause or surgical menopause increases the risk of sustaining a fragility fracture.

Osteoporosis and Fracture Prevention and/or Treatment Medications

Calcium and Vitamin D

Calcium: Depending on a patient's age, the daily calcium requirement varies. For patients who are more than fifty years of age, 1200 mg of calcium per day is recommended¹.

Vitamin D: Over the past several years, the recommended daily dose of vitamin D has increased. The newest recommendations suggest that 1000 IU of vitamin D is needed daily¹.

Antiresorptive Agents

Oral bisphosphonate: Bisphosphonates are considered the mainstay of preventative prescription treatment for patients with osteoporosis. Most patients with osteoporosis now take a generic bisphosphonate medication once a week. Bisphosphonates

should be used with caution in patients with chronic kidney disease and a reduced glomerular filtration rate. Bisphosphonates are *not* recommended in women of childbearing age who are not using adequate contraception. Bisphosphonates can decrease the hip fracture rate of a patient by as much as 50%²³.

Intravenous bisphosphonates: For patients who cannot tolerate oral bisphosphonates, an alternative is an annual intravenous injection of a long-acting bisphosphonate²⁴. This usually requires a ten to fifteen-minute infusion. A recent study showed a 25% decrease in mortality in a group of hip fracture patients who were given an intravenous dose of bisphosphonate shortly after the hip fracture²⁵.

Estrogen: The U.S. Food and Drug Administration guidelines regarding estrogen state that estrogen may be considered for use in the prevention of osteoporosis but not for use in the treatment of that disease²⁶. Women taking estrogen have a 35% lower rate of fracture than women who have stopped taking estrogen^{27,28}.

Selective estrogen receptor modulators: Selective estrogen receptor modulators act on bone by binding to estrogen receptors. This type of medication should be used in women who are at low risk for thrombotic complications²⁹.

Calcitonin: Calcitonin decreases calcium mobilization from bone by decreasing osteoclastic activation. Calcitonin has also been shown to decrease the pain associated with compression fractures of the spine³⁰.

Anabolic Agents

Parathyroid hormone: Unlike the antiresorptive agents listed above, parathyroid hormone drastically stimulates the overall formation of bone. It can be taken for a period of no longer than two years because of the risk of the development of bone tumors. Parathyroid hormone should not be used in patients who are at high risk of the development of osteosarcomas, such as patients who have Paget disease or who have undergone prior bone radiation³¹.

Risk of Treatment

Bisphosphonates and Osteonecrosis of the Jaw

Osteonecrosis of the jaw (mandible) is a very rare complication in patients receiving oral and, more commonly, intravenous bisphosphonates. The risk has been estimated to be between one in 10,000 and less than one in 100,000 patient-treatment years³². The rare cases occurred mostly when an intravenous bisphosphonate medication was administered to a patient who had a metastatic tumor, was receiving chemotherapy, and recently had major dental work³³.

Bisphosphonates and Subtrochanteric Fracture

Subtrochanteric fracture is a rare complication in patients who are receiving long-term bisphosphonate treatment. The preliminary study suggests that this fracture pattern is more common in the younger and more active patients who are taking bisphosphonates. Often these patients have prodromal pain in the affected hip prior to the fracture. It is hypothesized that the lack of remodeling in the subtrochanteric region of the femur in this young and active group of patients can lead to the insufficiency fracture³⁴.

Parathyroid Hormone and Bone Tumors

In laboratory rats, osteosarcomas were found in rats that received high doses of parathyroid hormone. So far, there have been no reported cases of the development of osteosarcomas in humans who are receiving parathyroid hormone therapy³¹.

Lifestyle Changes²

Cessation of Smoking

Smoking increases the chance of sustaining a fragility fracture. All individuals who smoke should be counseled on smoking cessation.

Exercise

Exercise can increase a patient's balance and strength and decrease the chance of sustaining a fragility fracture.

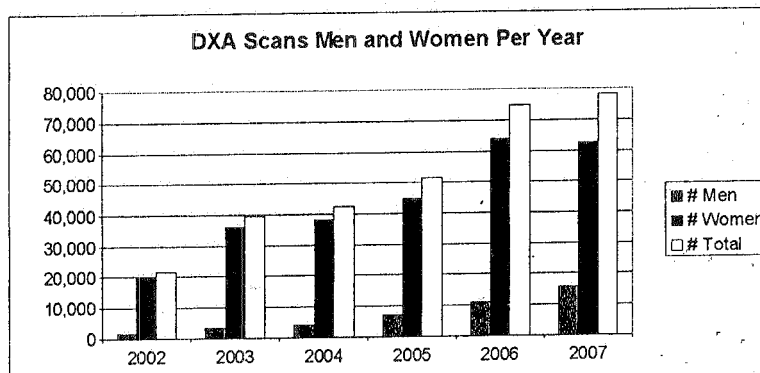


Fig. 1

Bar graph illustrating the annual number of dual x-ray absorptiometry (DXA) scans from 2002 to 2007. The overall increase was 263% (from 21,557 to 78,262), the increase in women was 213% (from 20,008 to 62,562), and the increase in men was 914% (from 1,549 to 15,700).

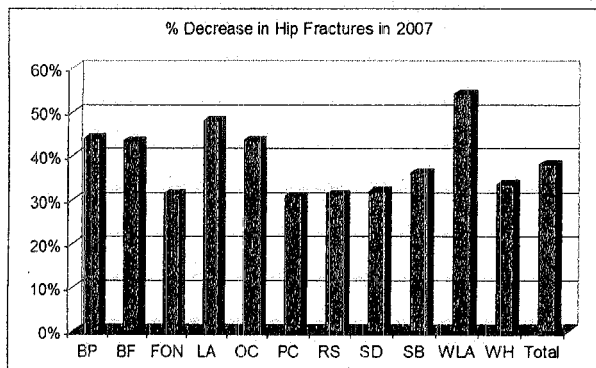


Fig. 4
Bar graph illustrating the percentage decrease in the number of hip fractures that were expected to be seen in the Kaiser SCAL system in 2007. While there was a wide variation among the medical centers in terms of the percentage decrease in hip fracture rates in 2007, the overall decrease was 38.1%. BP = Baldwin Park, BF = Bellflower, FON = Fontana, LA = Los Angeles, OC = Orange County, PC = Panorama City, RS = Riverside, SD = San Diego, SB = South Bay, WLA = West Los Angeles, and WH = Woodland Hills.

body mass index, a past prolonged use of systemic supra-physiologic glucocorticoid medication, history of rheumatoid arthritis, parental history of hip fracture, current cigarette smoking, and current alcohol intake. The decision to treat is made on the basis of whether a person's absolute fracture risk meets a predetermined intervention threshold. These thresholds may be determined by various methods, including cost-effectiveness analyses. Currently, the thresholds for treatment in the United States are a ten-year absolute hip fracture risk of 3% and a ten-year absolute fracture risk of 20% for other fragility fractures. These thresholds may change as the cost of treatment continues to decrease³⁷.

The World Health Organization fracture risk assessment calculator, FRAX, is now available online (<http://www.shef.ac.uk/FRAX>).

Knowledge That What the Orthopaedic Surgeon Does Improves Bone Health

The literature has shown that orthopaedic surgeons have not done enough to aggressively diagnose and treat osteoporosis⁷⁻¹³. It is important for orthopaedic surgeons to know that an aggressive osteoporosis disease-management program can decrease the rate of osteoporosis-related hip fractures by 25% to 50%^{15,38-40}. One such program is described below.

Background of the Kaiser Southern California Healthy Bones Program

Kaiser Southern California (Kaiser SCAL) is a health-maintenance organization in Southern California that is made up of eleven medical centers with 3.2 million members. Kaiser SCAL has an electronic medical records system that is capable of tracking dual x-ray absorptiometry scans, fragility fractures, and the medications used to treat or prevent osteoporosis. Kaiser SCAL

has a fully integrated Healthy Bones Program in place at all eleven of its medical centers. The Healthy Bones Program was established by having orthopaedic surgeons serve as champions in a large multidisciplinary team comprised of health-care providers from the following disciplines: endocrinology, family practice, internal medicine, rheumatology, gynecology, physical therapy, disease management and/or care management, radiology, and nursing education.

Materials and Methods

A prospective observational study was conducted to evaluate the effectiveness of the Healthy Bones Program on the management of osteoporotic disease in 650,000 patients in Kaiser SCAL from 2002 to 2007 inclusively. An electronic medical record system was used to collect data on these patients, including data on anti-osteoporosis medication usage, dual x-ray absorptiometry scans, and fragility fractures. For the study, we classified bisphosphonates, selective estrogen-receptor modulators, calcitonin, and parathyroid hormone as anti-osteoporosis medications. We did not include hormonal therapy, calcium, and vitamin D as anti-osteoporosis medications in our analysis, although they are helpful in the management of osteoporosis.

Source of Funding

No external funding source was used to develop or run the Healthy Bones program.

Results

Since the SCAL Healthy Bones Program was adopted, we have seen our annual dual x-ray absorptiometry scan utilization rate rise from 21,557 per year in 2002 to 78,262 per year in 2007, a 263% increase (Fig. 1). The annual dual x-ray absorptiometry scan utilization rate in men was 1549 in 2002, and it increased to 15,700 per year by 2007, a 914% increase. The annual number of patients receiving anti-osteoporosis medications rose from 33,208 per year in 2002 to 84,155 per year in 2007, a 153% increase (Fig. 2). The annual number of men who received anti-osteoporosis medications in 2002 was 2663, and that number increased to 9310 a year by 2007, a 250% increase. There was a large variation in the reduction

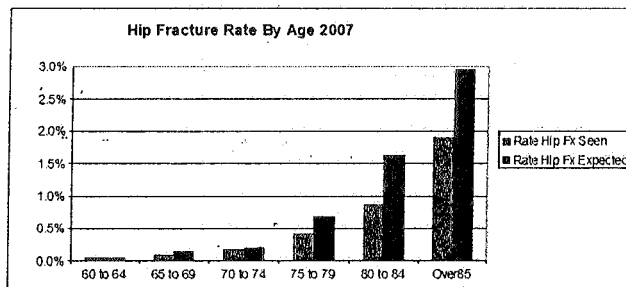


Fig. 5
Bar graph illustrating the expected and actual rates of hip fractures in the Kaiser SCAL system in 2007 according to age groups. There was an exponential increase in the hip fracture rate as age increased. Fx = fracture.

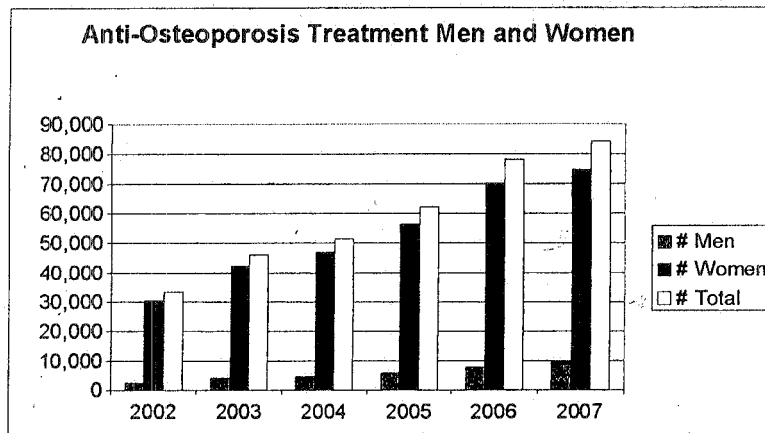


Fig. 2

Bar graph illustrating the annual anti-osteoporosis medication rates for men and women from 2002 to 2007. The overall increase was 153% (from 33,208 to 84,155), the increase in women was 145% (from 30,545 to 74,845), and the increase in men was 250% (from 2663 to 9310).

Fall Reduction Program

A fall reduction program offers individualized treatment with a concentration on specific areas, including improved strength, improved balance, proper use of a cane or walker, proper eyewear and cataract evaluation, proper footwear, and home safety.

Calculating Fracture Risk

Dual X-Ray Absorptiometry Scan and Bone Density

T-score

The World Health Organization has defined the T-score in terms of how many standard deviations the patient's bone mineral density is above or below the expected peak bone density for an average thirty-year-old of the same sex and race³⁵.

Z-score

The Z-score is defined in terms of how many standard deviations the patient's bone mineral density is above or below the expected bone mineral density for someone of the same age, sex, and race³⁵.

For every reduction in bone density by one standard deviation, the fracture risk is doubled³⁵. The World Health Organization defines osteoporosis as a bone density that is more than 2.5 standard deviations below peak bone mass³⁵.

Limitation of Dual X-Ray Absorptiometry Scans

Two important risk factors for fractures are independent of bone mineral density measurements. These factors are age and the history of a previous fracture. With aging, fracture risk rises; therefore, for any given bone-mass measurement in absolute terms, an older person will have a greater risk of sustaining a fracture. A prior fragility fracture can drastically increase a patient's risk of sustaining additional fragility fractures³⁶. Other important risk factors, such as smoking and

secondary causes of osteoporosis, also increase a patient's risk of sustaining a fracture in the future³⁷.

FRAX Risk Assessment Tool

Knowing a patient's risk factors helps in the design of a more individualized strategy for osteoporosis management and fracture prevention. The World Health Organization has developed a fracture-risk-assessment calculator known as FRAX to address the previous limitations of measuring fracture risk³⁷. This is a comprehensive tool for calculating the ten-year absolute risk of fractures.

The clinical risk factors included in the model are age, sex, fracture history, bone mineral density of the femoral neck,

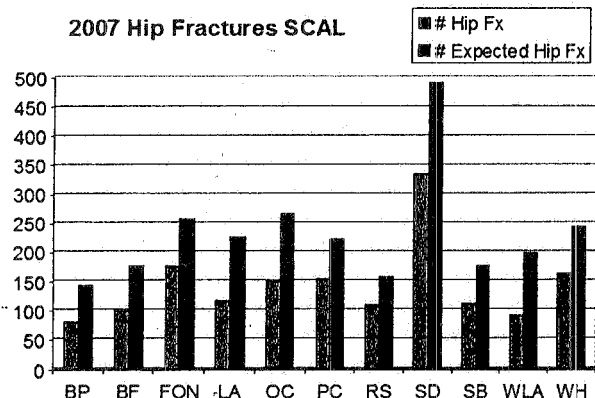


Fig. 3

Bar graph illustrating the expected and actual number of hip fractures in 2007 at our eleven medical centers in the Kaiser SCAL system. BP = Baldwin Park, BF = Bellflower, FON = Fontana, LA = Los Angeles, OC = Orange County, PC = Panorama City, RS = Riverside, SD = San Diego, SB = South Bay, WLA = West Los Angeles, and WH = Woodland Hills. Fx = fracture.

