

Osteoporosis in Men

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Osteoporosis in men is now recognized as an increasingly important public health issue. About 30 percent of hip fractures occur in men, and one in eight men older than 50 years will have an osteoporotic fracture. Because of their greater peak bone mass, men usually present with hip, vertebral body, or distal wrist fractures 10 years later than women. Hip fractures in men, however, result in a 31 percent mortality rate at one year after fracture versus a rate of 17 percent in women. Major risk factors for osteoporosis in men are glucocorticoid use for longer than six months, osteopenia seen on plain radiographs, a history of nontraumatic fracture, hypogonadism, and advancing age. Bisphosphonates and teriparatide (recombinant parathyroid hormone) have recently been approved for use in men and should be considered along with supplemental calcium and vitamin D. Increased awareness by physicians of risk factors for male osteoporosis—and early diagnosis and treatment—are needed to decrease the morbidity and mortality resulting from osteoporotic fractures. (Am Fam Physician 2003;67:1521-6. Copyright© 2003 American Academy of Family Physicians.)

Osteoporosis and osteoporosis-related fractures are usually considered conditions of postmenopausal or elderly women, but these problems also occur in men.¹⁻³ In fact, nearly 30 percent of hip fractures occur in men.⁴

Because osteoporosis is clinically silent until fractures occur, men at risk for osteoporosis and those who have the disease need to be identified. Once identified, they can be readily treated, thus possibly decreasing the morbidity and mortality that are associated with osteoporotic fractures.

See page 1413 for definitions of strength-of-evidence levels.

Pathogenesis

Osteoporosis is defined as a decrease in bone mass greater than expected for a person's sex, age, and race. Age-related osteoporosis causes loss in both trabecular and cortical bone. The presence of osteoporosis indicates an increased risk of fracture of the spine, proximal femur, or distal radius.

Men and women reach peak bone density by their early 20s.⁵ Peak bone density is heavily influenced by heredity, nutrition, hormonal effects, and environment. Thus, suboptimal bone growth related to poor nutrition or low calcium intake during childhood and adolescence is as important as bone loss related to the development of osteoporosis.⁶

Because men's bones are bigger and longer than women's, they have greater total bone mass (*Table 1*).^{3,5,7} Men and women, however, have the same trabecular number and thickness, so when values are adjusted for bone volume, men and women have similar peak bone mineral density (BMD).^{7,8}

In both men and women, age-related bone loss begins at about age 50.⁵ Acute hypogonadism at any age, such as that resulting from orchiectomy for prostate cancer, accelerates bone loss to a rate similar to that of menopausal women. The bone loss following orchiectomy is rapid for several years, then

TABLE 1
**Osteoporosis and Risk of Hip Fracture in Men and Women:
A Comparison**

Factor	Men	Women
Peak bone mass ^{5,7}	10 to 12 % greater than in women	
Lifetime risk of hip fracture at age 50 ³	6%	17.5%
Sex distribution of hip fractures worldwide ^{3,7}	30%	70.0%
U.S. incidence of hip fracture at age 65 ³	4 to 5 per 1,000	8 to 10 per 1,000
Mortality from hip fracture ⁷	31%	17.0%

Information from references 3, 5, and 7.

Epidemiology of Osteoporosis

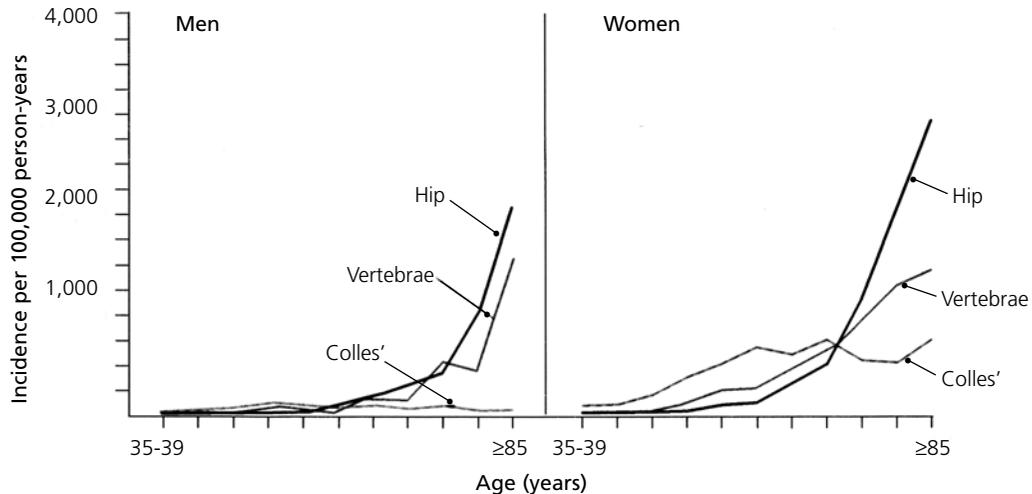


FIGURE 1. Age-specific incidence rates for hip, vertebral, and distal forearm fractures in men and women. Data are derived from the population of Rochester, Minn.

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reverts to the gradual loss that normally occurs with aging.

Epidemiology and Clinical Consequences of Aging

About 4 to 6 percent of men older than 50 have osteoporosis, and 33 to 47 percent have osteopenia (diminished bone loss not meeting diagnostic criteria for osteoporosis).¹ The prevalence of osteoporosis is 7 percent in white men, 5 percent in black men, and about 3 percent in Hispanic-American men.⁹ Data on the prevalence of osteoporosis in Asian-American men and other ethnic groups are lacking.

Because men have greater bone mass, they present with osteoporotic fracture about 10 years later than women (Figure 1).¹⁰ Thus, starting at about age 75, the incidence of hip fracture increases rapidly. Because of the predicted

growth in the number of elderly persons in this country, the number of men with hip fracture also is expected to increase dramatically.⁴

Once hip fractures occur, men have higher rates of morbidity and mortality than women. For example, men are twice as likely as women to die in a hospital after a hip fracture.⁷ Similarly, hip fracture mortality in men one year after fracture is 31 percent compared with a rate of only 17 percent in women.¹¹ This increased mortality is likely to be caused by older age at the time of fracture and the presence of comorbid conditions.¹²

In male survivors of hip fracture, more than one half have chronic pain at six months and require assistance with walking.¹³ One third of these men move to a nursing home or a relative's home.¹⁴ Morbidity includes a loss of self-esteem related to decreased independence after fracture and changed appearance related to kyphosis.

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Risk Factors for Osteoporosis

Although the development of osteoporosis in men is primarily related to aging and genetic factors, 30 to 60 percent of cases of osteoporosis are associated with one or more secondary risk factors^{6,15} (Table 2).^{3,6,7,16}

GLUCOCORTICOID THERAPY

Long-term oral glucocorticoid therapy accounts for nearly one in six cases of male osteoporosis.¹⁷ The extent of bone loss is related to the duration of therapy and the dosage of the steroid. Because of the high risk of bone loss, treatment of osteoporosis is recommended for any patient taking 5 mg or more of steroids per day

for longer than six months.¹⁸ The recommended treatment is a bisphosphonate supplemented with calcium and vitamin D.⁷

ANTICONSULSANT THERAPY

Anticonvulsant medication use, specifically phenytoin (Dilantin) and phenobarbital, may contribute to osteoporosis through multiple effects on calcium metabolism.¹⁹ Specifically, anticonvulsant drugs increase hepatic metabolism of vitamin D and 25-hydroxyvitamin D, resulting in decreased intestinal calcium absorption. Men taking phenytoin or phenobarbital also should take supplemental calcium and vitamin D and be considered for bisphosphonate or teriparatide therapy if their bone density is low.

LOW LEVELS OF ANDROGENS

Androgens are required for developing peak bone mass and maintaining bone mass. Hypogonadal young men with low testosterone levels have low bone density; testosterone replacement therapy increases bone density in this group.²⁰ Testosterone levels gradually decline with advancing age, but low levels in elderly men have not been found to correlate with low bone density.²¹ Furthermore, administering testosterone to elderly men may cause undesirable side effects related to increased prostate size and may even promote the development of occult prostate cancer.

LOW LEVELS OF ESTROGEN

Few physicians are aware that declining estradiol levels in men are more strongly correlated with decreasing bone density than are declining testosterone levels.²¹⁻²³ Currently, however, no treatment has been recommended for men with low estradiol levels.

TOBACCO AND ALCOHOL USE

In all societies, tobacco use and excessive alcohol consumption are more prevalent in men than in women, and both are independently associated with an increased incidence of osteoporotic fractures.²⁴ Tobacco-related bone loss is linked to smoking duration and quantity. The mechanism may be a combination of decreased body weight, decreased calcium absorption, decreased estradiol levels, and a direct toxic effect on bone metabolism.

Alcohol in modest amounts may have a protective effect on bone density, but sustained high consumption causes bone loss.²⁵ It is likely that alcohol has a direct toxic effect on osteoblastic function. Excessive alcohol consumption is

also often associated with poor nutrition and decreased physical activity, both of which are associated with bone loss. Further studies are needed to determine the quantity of alcohol above which the protective effect ceases and bone loss occurs.

OTHER RISK FACTORS

Table 2^{3,6,7,16} lists other risk factors for male osteoporosis. The more risk factors a man has, the greater his risk of fractures. Even with extensive evaluation for a specific cause, no cause or risk factor can be identified in about 40 percent of men with osteoporosis.^{3,19}

Male Osteoporosis Presentation and Screening

Osteoporosis in men commonly presents with vertebral body fracture or hip fracture, whereas in women it is often diagnosed by routine bone density screening. However, osteoporosis can be identified in men before fractures occur.

TABLE 2
Risk Factors for Osteoporosis in Men

High-risk causes

History of nontraumatic fracture (hip, vertebrae, or wrist)
Osteopenia seen on plain radiograph
Glucocorticoid use of 5 mg or more per day for longer than six months
Hypogonadism (glucocorticoid-induced or following orchiectomy)
Hyperparathyroidism

Medium-risk causes

Anticonvulsant drug use (phenytoin or phenobarbital)
Excess alcohol consumption
Tobacco use
Rheumatoid or other inflammatory arthritis
Multiple myeloma or lymphoma
Hypothyroidism or hyperthyroidism
Conditions associated with increased risk of falling (nursing home residence, prior fall, gait disorder, dementia, or hemiparesis)
Family history of osteoporosis

Infrequent causes

Cushing's disease
Chronic liver or kidney disease
Low body mass index
Pernicious anemia
Gastric resection

Information from references 3, 6, 7, and 16.

Men with asymptomatic vertebral body fractures can be identified during routine office visits when serial measurements of height show a loss of more than 1.5 inches or when the distal ribs touch the pelvic brim.

No professional organization has published consensus guidelines for osteoporosis screening in men, although experts in the field of osteoporosis have made recommendations.^{7,26} First, men with any of the following conditions should be considered for formal osteoporosis testing: any history of nontraumatic fracture, particularly of the hip, vertebral body, or distal wrist; radiographic evidence of osteopenia (because 30 to 50 percent of bone mass must be lost before evidence of loss is seen on a plain radiograph); long-term glucocorticoid use; hypogonadism; hyperparathyroidism; and other risk factors for osteoporosis, including disease states, medications affecting bone metabolism, or gait disorder. Second, physicians might consider routinely screening men aged 70 or older, because this is the age when fracture rates increase most rapidly.^{7,26}

Men with asymptomatic vertebral body fractures, who are at substantially increased risk of future fractures, can be identified during routine office visits using serial measurements of height. A man with a loss of height exceeding 1.5 inches or whose distal ribs touch the pelvic brim should

TABLE 3
Radiographic Diagnosis of Osteoporosis

Type of device	Radiation exposure	Cost	Use in monitoring therapy
DEXA	Low	Moderate	Accepted
Quantitative US of heel	None	Low	Not accepted
Quantitative CT	High	High	Not accepted

DEXA = dual-energy x-ray absorptiometry; US = ultrasonography; CT = computed tomography.

Adapted with permission from Bonnick SL. *Bone densitometry in clinical practice: application and interpretation*. Totowa, N.J.: Humana, 1998.

TABLE 4
Laboratory Evaluation for Osteoporosis in Men

Initial screening*	Additional tests†
Complete blood cell count	Serum protein electrophoresis to screen for multiple myeloma
Calcium	24-hour urine collection to rule out hypocalciuria or hypercalciuria
Phosphorus	Estradiol level‡
Alkaline phosphatase	Parathyroid hormone to screen for hyperparathyroidism
Kidney and liver function tests	
Vitamin D (25-hydroxyvitamin D)	
Thyroid-stimulating hormone level	
Total testosterone	

*—Recommended to determine cause in men diagnosed with osteoporosis.

†—Consider further testing when initial screening does not yield a definitive cause.

‡—If level is low, it is likely to be contributing to osteoporosis, but no treatment is available.

Information from references 3 and 16.

be considered for thoracic and lumbar spine radiographs to look for vertebral fractures.

Screening measures include diagnostic radiologic studies using dual-energy x-ray absorptiometry of the hip and spine, heel ultrasonography, or quantitative computed tomography (Table 3).²⁷ The World Health Organization's criteria for the densitometric diagnosis of osteoporosis strictly apply only to white postmenopausal women. However, in men, declining BMD and T scores (the comparison with peak BMD adjusted for sex and race) correlate with an increased risk of hip and other fractures similar to that occurring in women.

At present, no uniformly agreed-on T score has been established to define the densitometric diagnosis of osteoporosis in men. Men with T scores that are 2 to 2.5 standard deviations below the reference mean are at substantially increased risk of fracture and should probably be given treatment.²⁶ This decision depends not only on the bone density but also on other risks for fracture, such as those listed in Table 2.^{3,6,7,16}

Once osteoporosis is diagnosed, the cause should be determined, if possible, to identify the various risk factors and medical conditions listed earlier. The search for risk fac-

tors should include review of the history and physical examination findings plus a laboratory evaluation. Routine laboratory tests include complete blood cell count, liver and kidney panels, and measurement of calcium, phosphorus, alkaline phosphatase, thyroid-stimulating hormone level, and total testosterone levels (Table 4).^{3,16} If the cause remains unclear, further evaluation should be considered, particularly serum electrophoresis, to exclude multiple myeloma.

Treatment

Treatment should include discussing the long-term risks of osteoporosis with the patient and reviewing the recommendations on calcium and vitamin D intake. Calcium intake should be 1,000 to 1,500 mg per day, and vitamin D intake should be 400 to 800 IU per day (Table 5).^{6,7} Calcium supplementation is important because only 50 to 60 percent of older adults meet recommendations for calcium intake.⁶

Older adults also have decreased vitamin D levels because skin synthesis, oral intake, and gastrointestinal absorption are diminished. Skin synthesis of vitamin D decreases because older patients tend to remain indoors and incur less exposure to sunlight.

Other treatment includes regular weight-bearing exercise and the avoidance of tobacco and excess alcohol. In randomized clinical trials, regular exercise has been shown to decrease the risk of falls by 25 percent, although no evidence exists to show that exercise prevents fracture.⁶ [Evidence level C (consensus/expert guidelines)]

BISPHOSPHONATES

Treatment with bisphosphonates should be strongly considered soon after osteoporosis is diagnosed. Alendronate (Fosamax), which has been approved for the treatment of male osteoporosis, has been shown to increase BMD.²⁸ [Evidence level A, randomized controlled trial] In this trial, men treated with alendronate showed a trend toward fracture reduction, but the reduction was not statistically significant. Risedronate (Actonel) is an alternative treatment for men taking long-term glucocorticoid therapy; it has been shown to increase BMD in men.²⁹ Although the use of intravenous bisphosphonates has not been studied in men, these agents also may be considered.

OTHER TREATMENTS

A recombinant parathyroid hormone, teriparatide (Forteo), an anabolic agent, has recently been approved for the

In randomized clinical trials, regular exercise was shown to decrease the risk of falls by 25 percent, although no evidence exists to show that exercise prevents fracture.

treatment of osteoporosis in men and postmenopausal women who are at high risk for fracture. In men with primary or hypogonadal osteoporosis, teriparatide in a dosage of 20 mcg per day, administered subcutaneously, increased BMD, with a mean percentage change from baseline to end point of 5.9 percent at the lumbar spine ($P < 0.001$) and 1.5 percent at the femoral neck ($P < 0.05$).³⁰ Contraindications include hyperparathyroidism, Paget's disease of bone, osteomalacia, end-stage renal disease, primary or metastatic bone cancer, active nephrolithiasis, or unexplained elevation of serum calcium or alkaline phosphatase levels before initiation of therapy. Because the safety and efficacy of teriparatide have not been evaluated

TABLE 5
Treatment of Osteoporosis in Men

Medications and supplements

Calcium, 1,000 to 1,500 mg per day

Vitamin D, 400 to 800 IU per day

Bisphosphonates

Alendronate (Fosamax), 10 mg per day or 70 mg per week, at a cost of \$62 to \$66.50 per month*

Risedronate (Actonel), 5 mg per day, at a cost of \$67 per month*

Teriparatide (Forteo), 20 mcg per day, at a cost of \$560 per month*

Other

Physical therapy evaluation and instruction for cane or walker use

Regular exercise to increase muscle tone, improve balance

Occupational therapy to assess home fall risk

Avoidance of tobacco and excess alcohol

Decrease fall risk—review of medications, especially antihypertensive agents

*—Estimated cost to the pharmacist based on average wholesale prices for one month of therapy in Red book. Montvale, N.J.: Medical Economics Data, 2002. Cost to the patient will be higher, depending on prescription filling fee.

Information from references 6 and 7.

beyond two years of treatment, use of the drug for more than two years is not recommended.

Other options to consider are thiazides in patients who require diuretics. Thiazides decrease urinary calcium loss, possibly preserving bone density and, if used for longer than 10 years, have been associated with a reduction in hip fracture.³¹ Hip protectors, consisting of an undergarment with pads over the greater trochanters, have been shown to prevent hip fractures in frail elderly men. Fewer than 50 percent of patients use hip protectors on a long-term basis.³²

The prevention of further falls and fractures after an initial fracture is important. All patients benefit from an evaluation by a physical therapist and counseling about increasing muscle strength, improving coordination, and using adaptive equipment.

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