

OSTEOPOROSIS IN MEN

Osteoporosis is a significant threat to aging bone in men. 30% of hip fractures occur in men; during initial hospitalization and the first year after fracture, the mortality rate is twice that of women.

Nevertheless, osteoporosis in men is grossly under diagnosed and undertreated.

The most frequent factors associated with osteoporosis in men are age >75 years, low baseline body mass index ($<24 \text{ kg/m}^2$), weight loss >5% over 4 years, current smoking, and physical inactivity.

Osteoporosis in men is either secondary to a primary disease or is idiopathic. It exhibits a bimodal age distribution, with peaks at age 50 years (secondary disease) and at age 70 years (idiopathic). Prevention and early detection currently are the best forms of management. Alone or in combination, calcium, vitamin D, bisphosphonates, and human parathyroid hormone are all effective management options.

In the acute setting of fragility fracture, the orthopaedic surgeon is key in identifying patients at risk because the surgeon provides primary care and may initiate prophylactic measures to prevent future fractures.

Evaluated according to race, the prevalence of osteoporosis in the United States is highest in Caucasian men (7%), followed by African-American men (5%) and Hispanic men (3%). The World Health Organization definition of osteoporosis is a T-score of at least 2.5 standard deviations below the mean bone mineral density (BMD) of young men (age 30 years). Although this standard was developed for women, it is currently being used in diagnosing osteoporosis in men. However, controversy exists as to whether the use of a standard developed for women accurately reflects the measure of BMD loss necessary for diagnosis of osteoporosis in men.

Comparison of Osteoporosis and Fracture Occurrence in Men and Women

| Factor | Men | Women |
|---|--|--|
| Lifetime risk of osteoporosis ⁷ | 13%-25% | 50% |
| Usual presentation | Fragility fracture, back pain, loss of height | Asymptomatic via DXA scan |
| Onset of osteoporosis ⁷ | 10 years later than in women; bimodal prevalence (at ages 50 and 70 years) | Prevalence skewed toward later years |
| Prevalence of osteopenia after age 50 years ^{7,15} | 33%-47% | 50% |
| Prevalence of osteoporosis after age 50 years ¹⁵ | 3%-6% | 13%-18% |
| Causes of osteoporosis | 50% idiopathic, 50% secondary | Most idiopathic |
| Peak bone mass | 10% greater than in women | — |
| Lifetime risk of hip fracture at age 50 years ¹⁶ | 6% | 17% |
| Incidence of hip fracture after age 65 years ¹⁶ | 5/1,000 | 10/1,000 |
| Mortality within 1 year after hip fracture ¹⁷ | 31% | 17% |
| Number of patients receiving treatment for osteoporosis 1-5 years after fragility fracture ¹ | 27% | 71% |
| Prevalence of osteoporotic spine fracture | After age 50 years, 5% ¹¹ | By age 60 years, 11.6%; by age 90 years, 51.7% ¹⁸ |

As many as 85% of all hip fractures and 90% of all vertebral fractures in men are attributed to osteoporosis. Unlike the usual situation in women, however, osteoporosis in men typically is undiagnosed until the patient sustains a fragility fracture. Because men start with a higher peak BMD, they begin to experience fragility fractures 10 years later than the age at which women do (ie, 75 years). Thus, at ap-

proximately age 85 years, absolute BMD in a man generally is the same as that of a woman who began to sustain fragility fractures at approximately age 75 years. This is true for hip, vertebral, and distal radius fractures.

The economic costs of fragility fracture are high, for the individual patient as well as to the health care system in general. It is estimated that \$2.5 billion is spent annually in the United States in caring for men with osteoporotic fractures. More hospital days are used to care for men with osteoporotic fractures than those with prostate cancer.

Men Vs Women

- I Men accumulate more bone mass during development.
- II Unlike women, men do not experience the same abrupt hormone decline that women do at approximately age 50 years; rather, men experience a slow, steady decline in testosterone and bioavailable estrogen.
- III Men historically have had shorter life spans than women and therefore have had less time to develop fragility fractures.

With increased life expectancy, however, more men are now living long enough to develop osteoporosity. Finally, although both men and women with age lose cancellous bone at peripheral sites, men begin with greater bone mass; thus, over their lifetimes, women lose more central trabecular bone and cortical bone than do men.

Risk Factors for the Development of Osteoporosis in Men

Excessive alcohol use (>7 oz/wk)

Tobacco use

Sedentary lifestyle

Low body mass index

Low calcium and vitamin D intake Medication

Anticonvulsants Oral glucocorticoids Cyclosporin Methotrexate Heparin

Age Family history of fragility fractures Prostate cancer with luteinizing hormone–releasing hormone analogue use

Secondary Osteoporosis

It is more common for men than women to develop osteoporosis secondary to an underlying disease or metabolic derangement. At least 50% of the causes of osteoporosis in men are ascribed to other diseases. These include genetic disorders, drug-induced bone loss, malabsorptive diseases, and endocrine disorders. Of these, the most frequent causes of secondary osteoporosis in men are excessive alcohol consumption, corticosteroid therapy, and hypogonadism.

Genetic Causes

The genes predisposing men to osteoporosis have not yet been identified. Several genetic disorders, including homocystinuria, Marfan syndrome, and osteogenesis imperfecta, are known to cause osteoporosis and osteopenia.

Corticosteroid Therapy

Although multiple drugs are associated with osteoporosis and fragility fracture, chronic corticosteroid use (>5 mg/day for 6 months) is most commonly implicated. Potent inhaled corticosteroids also may affect bone health. The negative effects of corticosteroids are mediated via several mechanisms. They inhibit intestinal calcium absorption with resultant secondary hyperparathyroidism. This leads to increased osteoclast activity and bone turnover in combination with decreased osteoblast activity. Corticosteroids also suppress sex hormone production at the gonads and through the pituitary gonadotropin pathway.

Hypogonadism

Testosterone deficiency, secondary to endocrine abnormality or pharmacologic suppression for prostate cancer, leads to decreased peak bone mass before puberty and bone loss after puberty. It is unclear whether this is the result of increased bone resorption or of decreased bone formation. Stanley et al reported a 6.5-fold increase in hip fracture in hypogonadal men.

Idiopathic Osteoporosis

Primary, or idiopathic, osteoporosis is generally attributed to aging, although in actuality the exact cause is unknown.

Presentation

Often, men are first diagnosed with osteoporosis in association with a fracture. This need not be the case, however, if physicians remain cognizant of the man at risk for osteoporosis. Any man with a history of low-energy fracture to the hip, spine, or distal radius; radiographic osteopenia; chronic

corticosteroid use; primary or secondary hypogonadism; chronically low body mass index; acute weight loss; or any of the other medication or lifestyle risks previously discussed should be considered for BMD screening. Even men with none of these factors but with height loss >1.5 inches should be tested because they may have asymptomatic vertebral fractures. Given that osteoporosis is greatest for men aged 70 years and older, physicians should consider routine screening at that age.

Treatment Prevention

1. Prevention is the rule.
2. Encouraged to engage in weight-bearing sports exercise to maximize peak bone mass before puberty.
3. In adulthood, men require calcium 1,000 mg/day to 1,500 mg/day and vitamin D 400 IU/day to 800 IU/ day.
4. Alcohol intake must be limited to <60 g/day (four cans of beer or 2 oz of liquor), and tobacco use should be avoided.

Medical Treatment

In general, however, treatment should be considered in the patient with a fragility fracture or in the presence of low BMD plus age >55 years and one risk factor, or age >65 years with no risk factors. When osteoporosis is secondary to another primary disease, addressing the osteoporosis by treating the underlying cause.

Bisphosphonates

Two bisphosphonates currently are approved for use in men with osteoporosis: alendronate and risedronate.

Alendronate was the first antiresorptive therapy approved for use in men and is an effective treatment for both primary and secondary osteoporosis.

Recently, Ringe suggested that the treatment group had a 60% reduction in new vertebral fractures and less height loss and back pain than did the control group.

Currently, bisphosphonates are the first line of treatment in men with osteoporosis. They are well tolerated, relatively inexpensive, and effective. In men unable to take bisphosphonates, human parathyroid hormone (PTH) may be considered.

Human Parathyroid Hormone

PTH, or teriparatide, was recently approved by the US Food and Drug Administration at a dose of 20 µg/ day for treatment of osteoporosis. The drug increases bone formation by stimulating osteoblast differentiation, function, and survival. This anabolic agent has been shown to increase BMD.

Summary

Recognition is the main hurdle to the effective treatment of osteoporosis in men and subsequent prevention of fragility fractures. The consequences of low BMD in men can be greater than those seen in elderly women, yet osteoporosis in men remains underdiagnosed and under-treated. The pattern of osteoporosis in men has two age peaks, with secondary osteoporosis presenting at approximately age 50 years and primary osteoporosis at approximately age 70 years. Many of the risk factors for osteoporosis, including activity level, low body weight, smoking, alcohol use, and corticosteroid use, can be modified with proper patient education. When treatment is initiated, men must take calcium, vitamin D, and, when necessary, antiresorptive therapy. With heightened awareness, the orthopaedic surgeon not only can identify the men at risk for fragility fracture and act preemptively but also ensure that the patient who presents with fragility fracture is effectively treated with medical intervention.

Osteoporosis in Men

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