

- Review the etiology and pathophysiology of osteoporosis in men
- Outline the risk factors and primary and secondary causes of osteoporosis in men
- Discuss the elements of the history, physical assessment, and diagnostic workup
- Describe the prevention and treatment options for men with osteoporosis

Osteoporosis in men: How to treat this condition in the atypical patient

Prevention and treatment guidelines for osteoporosis frequently overlook that the disease can affect men. In fact, men fare much worse than women after a fracture.

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Commonly considered a women's health issue, osteoporosis is increasingly being recognized as a significant cause of morbidity and mortality in men.^{1,2} In 2002, more than 14 million men had osteoporosis or *osteopenia*, defined as low bone mass. This number is expected to increase to 17 million in 2010 and to more than 20 million in 2020.³ Although the prevalence of osteoporosis is lower in men than in women, one-third of all hip fractures occur in men and mortality and morbidity rates are higher in men than in women.⁴ Specifically, men are twice as likely as women to die in the hospital after sustaining a hip fracture.⁵ Furthermore, 31% of men die within 1 year of fracture, compared to only 17% of women.⁶

ETIOLOGY AND PATHOPHYSIOLOGY

The term *osteoporosis* was coined in the early 1820s, and by the 20th century it was included in the English medical vocabulary. *Osteoporosis* means porous bone and, after many years of research, the term and clinical definition have remained constant. Osteoporosis is a systemic skeletal disorder characterized by low bone mass and microarchitectural deterioration, leading to increased bone fragility and risk of fracture.⁷

Peak bone mass is attained by age 20 years in both men and women; however, men achieve greater peak bone mass and at least 8% to 10% greater bone mineral density (BMD) compared to women.^{8,9} After age 30 years, BMD is maintained through a process known as *resorption and remodeling*, defined as the continuous breakdown and reformation of bone. Resorption is facilitated by *osteoclasts*, and bone reformation is facilitated by *osteoblasts*. In older adults or in adults

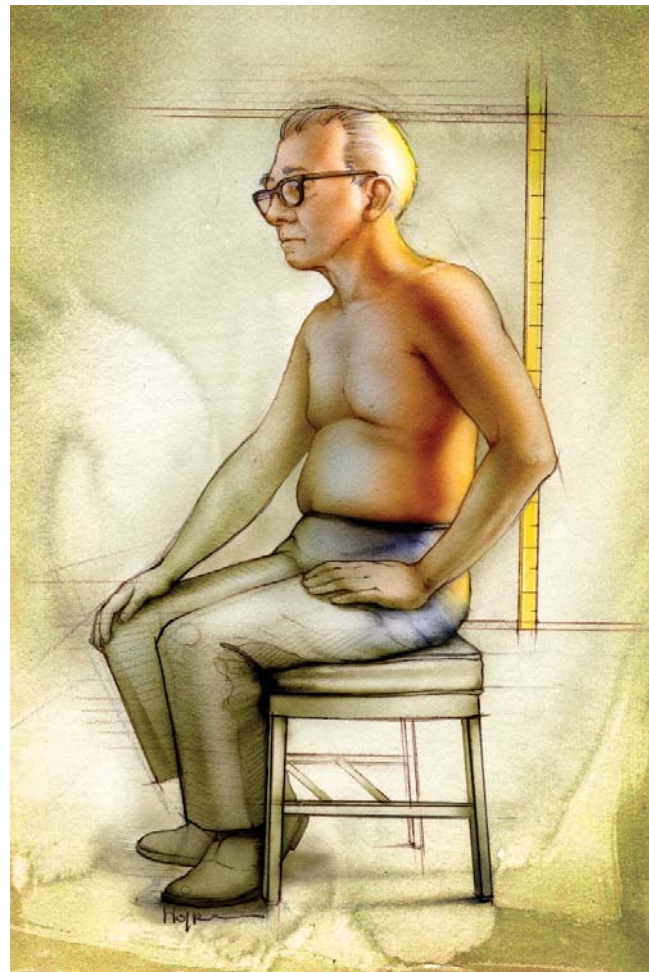


FIGURE 1. Crown-to-rump height measurement

Here and on the cover: Bonnie Hofkin

with risk factors that decrease the rate of bone remodeling, this process becomes inefficient; less bone is formed than is resorbed, leading to high bone turnover, subsequent bone fragility, and, ultimately, fracture.

RISK FACTORS AND CAUSES

Risk factors for osteoporosis development in men can be multifactorial³ (see Table 1). Cigarette smoking has been associated with lower bone density and decreased cortical thickness in men.¹⁰ Mechanisms of bone loss are a combination of decreased body weight, reduced calcium absorption, and lower estradiol levels, as well as duration and quantity of tobacco use.¹¹ The lifetime risk of vertebral and hip fractures for men who use tobacco increases by 32% and 40%, respectively.¹²⁻¹⁴ Less physical activity and lower body weight have been also associated with lower BMD.^{15,16}

Causes of osteoporosis in men are divided into two categories: primary and secondary. *Primary causes* usually occur in men older than 70 years and are related to increased age or are idiopathic in origin. *Secondary causes* include certain lifestyle practices; drug therapy; hypercalciuria; severe renal or liver disease; organ transplantation; and chronic diseases such as chronic obstructive pulmonary disease (COPD), inflammatory bowel disease, and rheumatoid arthritis.¹⁴ The most common secondary causes are hypogonadism, glucocorticoid use, and alcoholism.¹⁷ Secondary causes occur more frequently in men younger than 70 years.

Hypogonadism refers to a decrease in testosterone as a result of testicular disease (*primary hypogonadism*) or a disease of the pituitary or hypothalamus systems (*secondary hypogonadism*). Testosterone works in tandem with estrogen, the hormone responsible for regulating bone resorption. Reduced available testosterone leads to a decrease in testosterone conversion to estradiol. Lower estrogen levels lead to increased bone resorption and, subsequently, lower BMD. Although serum testosterone levels decrease with age, this imbalance can also be seen in men who are receiving androgen suppression therapy.¹⁸

Glucocorticoids have an adverse effect on the skeletal structure in that they cause excessive bone resorption and impaired bone formation.¹⁹ These drugs are commonly prescribed for asthma, COPD, and autoimmune diseases. The

risk of a fracture in men taking glucocorticoids is almost double that of men not on glucocorticoid therapy.^{20,21}

Alcohol affects bone density by suppressing new bone formation and stimulating bone resorption.²² Alcohol consumption in modest amounts may have a protective effect on bone density.¹¹ Moderate alcohol intake (1-3 glasses of wine per day) is associated with an increase in trochanteric BMD.²³ However, alcohol abuse decreases BMD in men through multiple mechanisms: reduced serum free testosterone, nutri-

“Osteoporosis often manifests in men as a low-trauma fracture or as an incidental finding of osteopenia on radiography.”

tion deficiencies, decreased physical activity, and a toxic effect on osteoblasts.^{11,24,25} Researchers have found no evidence of men regaining BMD lost through alcohol abuse after abstinence is achieved.^{24,25}

Additional causes of osteoporosis in men are primary hyperparathyroidism, excessive thyroid hormone, multiple myeloma, and other malignancies. When all identifiable causes of osteoporosis have been ruled out, a diagnosis of idiopathic osteoporosis is made.

HISTORY AND PHYSICAL EXAMINATION

Early identification of men at risk for osteoporosis or those with established disease can often be challenging. Many times the disease is asymptomatic in men, manifesting as a low-trauma fracture or as an incidental finding of osteopenia on radiography.²⁶

Low-trauma fractures can be seen in the wrists, hips, ribs, pelvis, humerus, or, most commonly, in the middle and lower thoracic and upper lumbar regions of the vertebral column.²⁷ Patients with vertebral compression fractures may experience no symptoms at all or may present with a history of back pain radiating to the flanks that began suddenly after sneezing, bending, or light lifting. Patients often attribute

KEY POINTS

- Men are twice as likely as women to die in the hospital after sustaining a hip fracture. Furthermore, 31% of men die within 1 year of fracture, compared to only 17% of women.
- Primary causes of osteoporosis usually occur in men older than 70 years and are related to increased age or are idiopathic in origin. The most common secondary causes are hypogonadism, glucocorticoid use, and alcoholism.
- Many times the disease is asymptomatic in men, manifesting as either low-trauma fractures or as an incidental finding of osteopenia on radiography.
- A cause for osteoporosis should be determined when the disease is diagnosed because secondary causes are common in men. Nonpharmacologic and pharmacologic treatment options are used either as a single entity or in combination, based on the patient's history and bone mineral density results.

COMPETENCIES

●●●● Medical knowledge

● Interpersonal & communication skills

●●●● Patient care

● Professionalism

●●● Practice-based learning and improvement

● Systems-based practice

their pain to normal aging or strain and do not seek treatment. Thus, back pain is chronic and subsides over a period of weeks to months, recurring when a new fracture occurs. Patients with vertebral compression fractures may lose height and develop spinal deformities such as dorsal kyphosis and cervical lordosis, also known as a *dowager's hump*.²⁷ Because of the ambiguous presentation and difficult diagnosis, clinicians must obtain a thorough history and perform a comprehensive physical examination on patients with suspected osteopenia or osteoporosis, keeping in mind the risk factors that lead to osteoporosis in men.

Obtaining a thorough medical history is an important first step when osteoporosis is suspected. The history should focus on nontraumatic fractures or osteopenia seen on radiography and a family history of fractures, osteoporosis, or height loss in a first-degree relative. Further, patients should be carefully questioned regarding factors that contribute to the risk of osteoporosis, including medications, adult illnesses, alcohol and tobacco use, diet, and exercise choices.

The physical examination should include height measurements; a history of height loss can be documented if previous measurements are known. Because height loss is caused by vertebral fractures, hip-to-heel length remains constant. Thus, the most accurate clinical assessment of vertebral height loss is obtained by measuring crown-to-rump height with the patient seated on a firm stool (see Figure 1, page 25). Consistently using this method of assessing height can help document vertebral height loss over time. A loss of more than 1.5 inches should prompt further evaluation.²⁷ The patient's frame, overall muscle mass, and any spinal deformities should be noted. In addition, the clinician should note any vertebral pain or tenderness to the touch, assess range of motion in the joints, and test overall muscle strength. Finally, if indicated by the patient's history, clinicians should complete full heart, lung, abdominal, and genital examinations.

DIAGNOSTIC WORKUP AND TREATMENT

BMD measurement at the hip or spine using dual-energy x-ray absorptiometry (DEXA) is considered the gold standard for diagnosing osteoporosis.^{1,2,14,26} The risk of fracture doubles for each 1 standard deviation (SD) decrease in bone mass at the spine, hip, or wrist.²⁸ Currently, there are no consensus guidelines for when to perform DEXA in men.^{1,2,14,26} However, the International Society for Clinical Densitometry recommends obtaining BMD measurements in men aged 70 years or older who have a history of fragility fractures, a disease or condition associated with low bone mass or bone loss, or are taking medications associated with low bone mass or bone loss. Also, DEXA is recommended for men who are potential candidates for pharmacologic therapy and/or to monitor the effects of long-term treatments on bone mass.²⁹

DEXA results are reported in g/cm², as well as T-score and Z-score measurements. T-score refers to the number of SDs from the mean BMD in normal sex-matched adults at age 20

TABLE 1. Risk factors for osteoporosis in men

Age >70 y
Chronic disease that affects the kidneys, lungs, stomach, or intestines and alters hormone levels
First-degree relative with osteoporosis, height loss, or forward curvature of the spine
Lifestyle habits
<ul style="list-style-type: none"> • Excessive alcohol consumption • Inadequate physical exercise • Low calcium intake • Tobacco use
Low body mass index
Prolonged exposure to certain medications
<ul style="list-style-type: none"> • Aluminum-containing antacids • Anticonvulsants • Certain cancer treatments • Corticosteroids used to treat asthma or arthritis
Undiagnosed low levels of testosterone
White race
Data from National Osteoporosis Foundation. ³

years or at peak bone mass. Z-score refers to the number of SDs from the mean BMD of a normal age- and sex-matched reference population.²⁶ Diagnostic criteria for osteoporosis in men, however, continue to be controversial. Therefore, the criteria for postmenopausal women are used to diagnose osteoporosis/osteopenia in men (see Table 2, page 28).^{7,12}

A cause for osteoporosis should be determined when the disease is diagnosed because secondary causes are common in men. Laboratory tests that rule out the presence of treatable causes of osteoporosis include measures of alkaline phosphatase, BUN, CBC, liver function, parathyroid hormone, serum and urine protein electrophoresis, serum calcium and phosphorus, serum creatinine, serum total or free testosterone, thyroid-stimulating hormone, 24-hour urinary free cortisol, and 24-hour urine concentrations of calcium and phosphorus.¹⁴ Nonpharmacologic therapies and pharmacologic treatment options are used either as a single entity or in combination, based on the patient's history and BMD measurement.

NONPHARMACOLOGIC OPTIONS

Nonpharmacologic treatment options center on lifestyle and dietary modifications such as smoking cessation, decreasing alcohol consumption, increasing weight-bearing exercises, utilizing fall prevention strategies, and maintaining adequate calcium and vitamin D intake.^{1,12,18,26} Patients who smoke tobacco should be advised to quit and offered assistance as needed. Alcohol consumption should be limited to no more than two servings per day.¹⁴

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Physical activity Adequate physical activity reduces the risk of fragility fractures and falls by increasing muscle tone, improving balance, and possibly also prompting beneficial bone remodeling. The National Osteoporosis Foundation (NOF) endorses lifelong physical activity that focuses on weight-bearing exercises such as walking, jogging, tai chi, stair climbing, dancing, and tennis.³⁰ Recommendations include performing weight-bearing exercises at least 3 days a week for 30 to 45 minutes. To avoid injury, patients should be instructed on proper form and technique. Patients should avoid movements that involve twisting the spine or bending forward from the waist with straight legs, such as toe touches.³¹

Calcium and vitamin D An adequate intake of calcium is the cornerstone of osteoporosis prevention and treatment. The combination of calcium and vitamin D has been shown to increase BMD and reduce fracture risk.³² Inadequate intake of these nutrients is linked to increased bone loss and fractures.³³ The recommended daily intake of calcium ranges from 1,200 mg/d for men older than 50 years to 1,500 mg/d for those older than 65 years.³⁰ Calcium carbonate is cost effective, contains the highest elemental content of calcium, and is widely available in a variety of formulations. However, calcium carbonate requires an acidic environment for best absorption; therefore it should be taken with food. In comparison, calcium citrate does not require an acidic environment and may cause less bloating and constipation in the elderly.

Adequate intake of vitamin D ensures absorption of dietary calcium. Vitamin D is not widely available in natural food sources; it is primarily found in fish oils, fortified milk and juice, cereals, and egg yolks. The NOF recommends 400 IU/d for adults younger than 50 years; 800 IU/d is recommended for patients 50 years or older in whom vitamin D absorption may be reduced, malnourished patients, patients that are housebound or institutionalized, and patients receiving long-term anticonvulsant or glucocorticoid therapy.^{30,34} The two major OTC vitamin D preparations are ergocalciferol (vitamin D₂) and cholecalciferol (vitamin D₃). Calcitriol (1, 25-dihydroxyvitamin D) is available by prescription and is used to manage patients with hypocalcemia and metabolic bone disease; the supplement is also used to treat secondary osteoporosis.³⁵

TABLE 2. WHO diagnostic categories of bone status

Classification	T-score
Normal	>-1.0
Osteopenia	<-1 and >-2.5
Osteoporosis	<-2.5
Severe osteoporosis	<-2.5 or below plus fractures

Key: WHO, World Health Organization.

Adapted with permission from World Health Organization. *Prevention and Management of Osteoporosis*. Geneva, Switzerland: World Health Organization; 2003. WHO Technical Report Series 921.

PHARMACOLOGIC OPTIONS

Testosterone therapy stimulates osteoblast activity while inhibiting osteoclast activity. In men with decreased testosterone levels, replacement therapy helps increase BMD. Whether men with normal testosterone levels will benefit from this treatment is still unclear.³⁶ Testosterone treatment can be administered via daily application of one or two 5-mg transdermal patches or 50 mg of 1% testosterone topical gel; 100 to 150 mg testosterone, IM, every 2 weeks is another treatment option. Prior to the start of treatment, prostate specific antigen (PSA) levels should be checked. A man with an elevated PSA level or a history of prostate cancer should not receive testosterone therapy.

“Ninety percent of hip fractures, one-third of vertebral fractures, and almost all distal forearm fractures result from a fall.”

Bisphosphonates decrease bone resorption. The bisphosphonates that are FDA-approved for osteoporosis in men are alendronate and risedronate. In a randomized trial, alendronate, 10 mg/d, significantly increased spine and hip mineral densities;³⁷ the recommended dose is 10 mg/d or 70 mg/wk. In men receiving moderate-to-high dose corticosteroid therapy, risedronate, 5 mg, was shown to increase BMD and decrease vertebral fractures;³⁸ the recommended dose is 5 mg/d or 35 mg/wk. A third bisphosphonate, ibandronate, is not indicated for use in male patients because recommended dosages are still undetermined.

One rare side effect of bisphosphonate therapy is osteonecrosis of the jaw. Most cases were seen in men with cancer who received IV bisphosphonate therapy. However, osteonecrosis has also been documented in postmenopausal women taking these agents. Therefore, any major dental surgery should be completed prior to starting bisphosphonate treatment.³⁹

Parathyroid hormone (PTH) stimulates bone formation by increasing the amount and activity of osteoblasts. Teriparatide is used to treat idiopathic or hypogonadal osteoporosis; it is also administered to patients at increased risk of fracture. A 30-week study compared three treatment regimens: PTH, 40 mcg/d SC injection; alendronate, 10 mg/d; and alendronate, 10 mg/d, plus PTH, 40 mcg/d SC injection, beginning at week 7. At the completion of the study, the PTH treatment group had a greater increase in BMD in the femoral neck and lumbar spine than the other two groups.⁴⁰ The recommended dose of teriparatide is 20 mcg/d. Total duration of therapy should be 2 years, and calcium levels should be monitored. PTH should also be reserved for men with severe cases of osteoporosis because of its high cost and the need for injections. In addition, a

risk of osteosarcoma was seen in laboratory rats administered high dosages. PTH is contraindicated in persons with bone cancer or hypercalcemia.

FALL PREVENTION

Ninety percent of hip fractures, one-third of vertebral fractures, and almost all distal forearm fractures result from a fall.³¹ The reasons why patients fall are numerous and include environmental factors, such as loose throw rugs, as well as medical conditions, such as poor vision.³¹ Patients who have fallen should undergo a detailed medical, occupational, and home risk assessment to determine if modifications are needed.

The American Association of Clinical Endocrinologists Osteoporosis Task Force offers a number of recommendations.³⁴ Fall prevention strategies for the home include anchoring rugs; minimizing clutter; removing loose wires; using nonskid mats; installing handrails in bathrooms, halls, and along stairways; and adequately illuminating hallways, stairwells, and entrances.

Medical interventions focus on identifying and treating sensory defects, neurologic diseases, and arthritis; all of which can contribute to the frequency of falls. The patient's medications should be reviewed. Drugs that have sedative effects can slow down reflexes, diminish coordination, and impair the patient's ability to break the impact of a fall; therefore, the dosages of these drugs may need to be adjusted. Gait and balance training minimizes the risk of falls. Patients should also be encouraged to wear sturdy, low-heeled shoes.³⁴

CONCLUSION

The screening guidelines for many other disease processes have greatly advanced; however, the recommendations for screening and diagnosing osteoporosis in men have remained stagnant. Therefore, clinicians must step up their awareness of the risk factors for osteoporosis in men. A thorough history and physical examination is needed to determine if the male patient is at risk for osteoporosis and, when warranted, he should be referred for further diagnostic testing. JAAPA

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DRUGS MENTIONED

Alendronate (Fosamax)
Ibandronate (Boniva)
Risedronate (Actonel)
Teriparatide (Forteo)
Testosterone

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