Osteoporosis in Older Adults

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KEYWORDS

• Osteoporosis • Postmenopausal osteoporosis • Older adults

KEY POINTS

- Osteoporosis-related fractures of the hip, vertebra, and pelvis are a common cause of morbidity and mortality in older adults.
- All healthy adults should be counseled about measures to prevent osteoporosis, including adequate calcium and vitamin D intake, participating in weight-bearing exercise, and avoiding tobacco and excess alcohol consumption.
- Women should be screened for osteoporosis beginning at age 65. Screening for osteoporosis in men should be considered when risk factors are present. Appropriate screening intervals are controversial.
- Women and men with osteoporosis should be offered pharmacologic therapy. Choice of therapy should be based on safety, cost, convenience, and other patient-related factors. Bisphosphonates are often first-line therapy based on efficacy, safety, and cost.

DEFINITION

Osteoporosis is a disease characterized by low bone mass and disruption of bone architecture, resulting in compromised bone strength and increased fracture risk. Osteoporosis is also considered a silent disease, as there are commonly no symptoms until the first fracture occurs.

The World Health Organization defines osteoporosis using bone mineral density (BMD) and T score. T score represents a standard deviation (SD) that calculates how much a result varies from the average or mean bone mineral density of a healthy young adult. A T score of 0 means that BMD is equal to the norm for a healthy young adult. The more SDs below 0, indicated as negative numbers, the lower the BMD and higher the risk of fracture. Osteoporosis is defined as a T score of <-2.5. Osteopenia, or low bone density, is defined as a T score of -1.0 to -2.5 (**Table 1**).

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Table 1
T score criteria for normal range, osteopenic range, and osteoporotic range

Normal	Bone density is within 1 SD (T score +1 to −1) of the young adult mean
Osteopenia	Bone density is 1–2.5 SDs below the young adult mean (T score −1 to −2.5)
Osteoporosis	Bone density is 2.5 SDs or more below the young adult mean (T score <−2.5)

PREVALENCE

Worldwide variation in the incidence and prevalence of osteoporosis is difficult to determine because of problems with underdiagnosis. The best way to compare osteoporosis in different population groups is by looking at the fracture rates in older individuals. As osteoporosis is not a life-threatening condition, data from developing countries are scarce. Worldwide, osteoporosis causes more than 8.9 million fractures annually, resulting in an osteoporotic fracture every 3 seconds.[1] Osteoporosis is estimated to affect 200 million women worldwide:

Approximately one-tenth of women aged 60
One-fifth of women aged 70
Two-fifths of women aged 80
Two-thirds of women aged 90[2]

One in 3 women over age 50 years will experience osteoporotic fractures, as will 1 in 5 men aged over 50 years.[3]

Data from the 2005 to 2010 National Health and Nutrition Examination Survey (NHANES) suggested that in the United States, 16.2% of adults aged 65 and over had osteoporosis at the lumbar spine or femur neck. The age-adjusted prevalence of osteoporosis at either skeletal site was higher among women (24.8%) than men (5.6%). The unadjusted prevalence was higher among adults aged 80 and over (25.7%) than for adults aged 65 to 79 (12.8%). The age-adjusted prevalence of osteoporosis was highest among Mexican American adults (24.9%), followed by non-Hispanic white adults (15.7%), and was lowest among non-Hispanic black adults (10.3%). Asian ethnicity was not included in the data.[4]

NHANES also found that 48.3% of adults aged 65 and over had osteopenia or low bone density at the lumbar spine or femur neck. Women had a higher age-adjusted prevalence of low bone mass at either skeletal site (52.3%) than men (44.0%). Adults aged 80 years and over had a higher unadjusted prevalence of low bone mass (52.7%) than adults aged 65 to 79 years (46.7%). Non-Hispanic black adults had the lowest age-adjusted prevalence of low bone mass (36.7%), while non-Hispanic white and Mexican American adults had similar age-adjusted prevalence of low bone mass (49.4% and 47.3%, respectively).[4]

RISK FACTORS

Risk factor for osteoporosis can be characterized as potentially modifiable and non-modifiable and are listed in **Table 2**. Some common risk factors are discussed in more detail.

Diet

A healthy diet in childhood is an important contributor to peak bone mass, and maintaining a healthy diet can help reduce bone loss in later life. Adequate dietary protein, calcium, vitamin D, fruits, and vegetables have a positive influence on bone health,

Table 2
Osteoporosis risk factors

Gender	Women are at higher risk than men
Age	Risk increases with age
Ethnicity	African Americans are at lower risk than Asians, Hispanics, and non-Hispanic whites
Family history	Osteoporosis in first-degree relatives increases risk
Body size	Small, thin-framed people are more at risk
Sex hormones	Amenorrhea Menopause and premature ovarian failure Hypogonadisim in men Thyrotoxicosis Panhypopituitarism Hyperprolactinemia
Body weight disorders	Body mass index <17 Anorexia nervosa Malabsorptive bariatric surgery
Calcium and vitamin D	A lifetime diet low in calcium and vitamin D is a risk factor for osteoporosis
Medications	Anticonvulsants Glucocorticoids (>5 mg/d of prednisone or equivalent for =>3 mo), GnRH antagonist/agonist, SSRIs, thiazolidinediones, aromatase inhibitors
Lifestyle	An inactive lifestyle or extended bed rest/immobilization
Cigarette smoking	Increased risk with consumption
Alcohol	Increased risk with excessive intake
Comorbid illness	Hypercalciuria Osteogenesis imperfecta Homocystinuria Hemochromatosis Glycogen storage disease Cystic fibrosis Celiac disease Cushing syndrome Inflammatory bowel disease Diabetes mellitus

while a high caloric diet has been associated with lower bone mass and higher rates of fracture.[5]

Alcohol Use and Smoking

A meta-analysis based on 18 prospective cohort studies revealed a nonlinear association between alcohol consumption and the risk of hip fracture. Light alcohol consumption (0.01–12.5 g/d) appears to be associated with a slightly reduced risk of fracture, whereas heavy alcohol consumption (>50 g/d) is associated with an increased hip fracture risk.[6]

Cigarette smoking is a risk factor for osteoporosis. Smoking causes reduction in circulating levels of 1,25-dihydroxyvitamin D and parathyroid hormone (PTH). Smokers have small but significant reductions in bone mineral density when compared with nonsmokers.[7]

Glucocorticoids

Glucocorticoid (GC)-induced osteoporosis is the most common secondary cause of osteoporosis. It is estimated that 3% of the population 50 years of age and older has used GCs, and this percentage increases to 5.2% in 80 years of age and older.[8] Thirty percent of patients with long-term GC use (>6 months) develop osteoporosis.[9] Bone loss is more pronounced in the trabecular bone, predominantly in the spine and ribs.[10] The increase in fracture risk is dose dependent, and the effect is at least partially reversible once the GC is discontinued.

Diabetes Mellitus

Type 1 diabetes mellitus is associated with low BMD, and the risk increases with the duration of disease. Data from Health Survey done in Norway showed a significant increase in hip fracture rates among females with type 1 diabetes (relative risk 6.9, confidence interval 2.2–21.6) compared with nondiabetic female patients. The mechanism of bone loss in unknown.[11]

Type 2 diabetes mellitus was earlier believed to cause increased BMD. These reports were primarily based on the concept of BMD and not from prospective controlled trials. Patients with generally larger body size and relatively high bone mass have higher fracture rates. Bone quality changes are related to microvascular events common in diabetes. A large prospective study of older women obtained from the Study of Osteoporotic Fractures, confirmed that female patients with type 2 diabetes experience higher fracture rates in regions of the hip, humerus, and foot compared with nondiabetic female patients.[12]

OSTEOPOROSIS COMPLICATIONS

Bone fractures are the most serious complication of osteoporosis. Fractures can occur at any bone site, but are most common in the hip and vertebrae. Fractures may lead to chronic pain, disability, depression, nursing home stay, reduced quality of life, and increased mortality. Pain from fracture is often the first presenting symptom of osteoporosis. Because of weakened architecture of vertebral bone, minor fractures over time can cause compression fracture. It can also lead to a condition called kyphosis, sometimes called dowager's hump. Vertebral fractures are the most prevalent osteoporotic fractures and are paradoxically the most underdiagnosed. Vertebral fractures are the predictors of future fracture risk; the probability is fivefold for subsequent vertebral fractures and twofold to threefold for fractures at other sites.[13]

Hip fractures occur usually after a fall. Hip fractures are associated with 15% to 20% increased mortality rate within 1 year, with a higher mortality rate in men than in women, followed by a 2.5-fold increased risk of future fractures. Approximately 20% to 50% hip fracture patients require long-term nursing home care and suffer from decreased quality of life, social isolation, depression, and loss of self-esteem.[13]

Multiple vertebral thoracic fractures may result in restrictive lung disease and worsened pulmonary function in women with pre-existing lung disease. Lumbar fractures may decrease the volumes between the ribs to the pelvis, alter abdominal anatomy, crowd internal organs (particularly the gastrointestinal [GI] system, causing GI complaints such as premature satiety, reduced appetite, abdominal pain, constipation, and distention); further, back pain (acute and chronic), prolonged disability, poor self-image, social isolation, depression, and positional restriction are other problems created by compression fractures in addition to increased mortality.[14]

NONPHARMACOLOGIC MEASURES FOR PREVENTION AND TREATMENT OF OSTEOPOROSIS

Once peak bone mass has been attained (ie, in middle and late middle age), the goal of prevention is to reduce the rate of bone loss. Prevention strategies include nutrition, exercise, and lifestyle factors.

Nutrition strategies include adequate calcium and vitamin D intake. The recommended calcium intake for postmenopausal women and men over age 70 is 1200 mg/d[15] Most adults do not require calcium supplementation. The US Preventive Services Task Force concluded that evidence was insufficient to recommend calcium supplementation for primary prevention (USPSTF).[16] The recommended intake of vitamin D is 600 to 800 IU daily, which can be difficult to achieve by diet alone.[17,18] Many older adults, particularly those with low dietary intake or those who are at risk of vitamin D deficiency (eg, homebound patients) benefit from supplementation. Screening for vitamin D deficiency is not recommended routinely in asymptomatic adults, but may be considered in patients at high risk for vitamin D deficiency. Although the ideal serum level of vitamin D is controversial, some experts recommend supplementation with a target serum level of 25-OH vitamin D above 20 to 30 ng/mL.[18]

Providers should recommend exercise to patients for multiple health benefits. Weight-bearing and/or resistance activity on most or all days of the week can help maintain muscle mass and BMD. Structured exercise and balance programs (eg, tai chi) can help reduce falls.[18,19]

All patients should be advised to eliminate or minimize the potentially reversible risk factors that have been discussed previously.

All older adults, but particularly older adults with osteoporosis, should be counseled in fall prevention strategies, including exercise, particularly strength and balance training, reduction or elimination of sedative-hypnotic medications, and environmental modifications.[15,18,19]

FRACTURE RISK ASSESSMENT TOOL

Risk assessment is most commonly conducted using the Fracture Risk Assessment Tool (FRAX), which is a tool that helps predict a patient's 10-year risk of hip or other major osteoporotic fracture. It has been validated for untreated patients aged 40 to 90 years in multiple countries and for multiple ethnicities. It can be accessed at www.sheffield.ac.uk/FRAX. Limitations of FRAX include that it is limited to only 4 ethnicities in the United States (Caucasian, Black, Hispanic, and Asian) and lack of validation in treated patients.[20,21]

SCREENING FOR OSTEOPOROSIS

The US Preventive Service Task Force and other societies recommend screening for osteoporosis in all women aged 65 and older.[15,18,19,22] Screening should be conducted at the hip and spine using dual energy-x-ray absorptiometry (DXA). Some guidelines recommend screening younger women with osteoporosis risk factors, but there is no consensus on how to optimally manage osteoporosis in this age group. Men should not be routinely screened for osteoporosis; however, they should be evaluated with DXA if they have risk factors for osteoporosis (eg, hypogonadism, androgen deprivation therapy, long-term glucocorticoid therapy, or celiac disease), loss of height, or fragility fractures.[15,18,19]

Screening intervals are controversial. One study suggested a screen interval of 10 to 15 years for older women with baseline T scores of >-1.5, 5 years for those with

moderate osteopenia (T score < −1.5 and >>-2.0) and 1 year for those with advanced osteopenia (T score <−2.0 and >−2.5), but this is not a consensus recommendation.[23] When to stop screening is also controversial.[15] It is reasonable to discontinue screening if treatment would not be considered based on comorbidities or patient preferences, or if life expectancy is so short (ie, less than 1–2 years) that the patient would be unlikely to benefit from treatment.

DIAGNOSIS

The diagnosis of osteoporosis can be made in the presence of a fragility fracture, particularly at the spine, hip, wrist, humerus, rib, or pelvis without measurement of BMD can also be made in the presence of a T score of no more than 2.5 SDs at any site based on measurement by DXA. Several professional organizations also support making the diagnosis when the 10- year probability of a major osteoporotic fracture is greater than 20% or the 10 year probability of hip fracture is greater than 3%.[15,18,19]

Most experts recommend laboratory evaluation with a complete blood count, a chemistry panel that includes calcium, phosphorous, and alkaline phosphatase, and a 25-hydoxyvitamin D level. Further evaluation is indicated when there is suspicion for hyperthyroidism, celiac disease, multiple myeloma, hypogonadism, or hyperparathyroidism.[15,18,19]

TREATMENT

All men and women who meet the criteria for the diagnosis of osteoporosis should be counseled about nonpharmacologic preventive measures including exercise, diet, smoking cessation, and reduction of fall risk.[15,18,19]

Pharmacologic Treatment

Both women and men with osteoporosis should be offered pharmacologic treatment, although the evidence for benefit is stronger in women than in men. **Table 3** summarizes commonly used agents, dosing guidelines, adverse effects and precautions. Some guidelines recommend treating women with osteopenia with a 10-year probability of hip fracture of greater than or equal to 3% or a 10-year probability of any major osteoporosis related fracture of greater than or equal to 20%, while other guidelines suggest used a shared decision making framework in these situations based on patient preferences, risk profile, benefits, harms, and costs of medications. Reduction in fracture risk with pharmacologic therapy has only been demonstrated with diagnosis based on DXA in the osteoporotic range or with previous fragility fracture, not when a risk assessment tool such as FRAX is used.[15,18,19,24]

Evidence is insufficient to determine the comparative effectiveness of different pharmacologic agents for the treatment of osteoporosis; therefore, choice of therapy should be based on safety, cost, convenience, and other patient-related factors (see **Table 1**).[24]

The antiresorptive agents include bisphosphonates, denosumab, selective estrogen receptor modulators (SERMs), and estrogen/progestin therapy. Anabolic agents include the parathyroid hormone/parathyroid related protein analogs teriparatide and abaloparatide and the monoclonal antibody romosozumab.

Bisphosphonates

The bisphosphonates (risedronate, alendronate, ibandronate, and zoledronic acid) are effective therapies for established osteoporosis. To ensure optimal absorption, the

Table 3
Most commonly used osteoporosis drugs

	Efficacy of Fracture Reduction	Usual Dosing	Adverse Effects, Cost, Other Considerations
	Hip (H) Vertebral (V) Nonvertebral (NV)		
Bisphosphonates			As a class, osteonecrosis of jaw (rare) As a class, atypical fracture (rare, increased with longer duration of use)
Alendronate	H, V, NV	70 mg orally weekly	GI symptoms Generic is <$100/mo
Risedronate	H, V, NV	35 mg orally weekly 5 mg orally daily	GI symptoms $100–$200/mo
Zoledronic Acid	H, V, NV	5 mg intravenously yearly	Arthralgias, myalgias, headache, hypocalcemia, atrial fibrillation Generic <$100/mo
Ibandronate	V	150 mg orally monthly	Usually avoided because of lack of evidence of evidence for hip and nonvertebral fractures GI symptoms, cramps, myalgias $100–$200/mo
Other Antiresorptive Agents			
Denosumab	H, V, NV	60 mg subcutaneously every 6 months	Mild upper GI symptoms, rash, infections Increased risk of vertebral fractures after d/c Jaw osteonecrosis of jaw (rare) Atypical fracture (rare, increased with longer duration of use) $200–$300/mo

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Table 3
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	Efficacy of Fracture Reduction	Usual Dosing	Adverse Effects, Cost, Other Considerations
Raloxifine	V	60 mg orally daily	Thromboembolic events, hot flashes <$100/mo
Anabolic agents			
Teriparatide	V, NV	20 μg subcutaneously daily	Mild GI symptoms, hypercalcemia, renal events >$1000/mo
Romosozumab	V, NV	210 subcutaneously monthly	Potential for serious CV events Injection site reactions $1000–$2000/mo

oral forms should be taken in the morning with at least 8 ounces of water, in an upright position, with no other ingestions for at least 40 minutes. Even with these measures, there is a risk of esophagitis and upper GI symptoms. These agents are not recommend in patients with esophageal disorders or a creatinine clearance blow 35 mL/min 25-OH vitamin D, and calcium deficiency should be corrected prior to initiation of these agents.[15,18,19,24]

The intravenous (IV) bisphosphonates (zoledronic acid and abandronate) can be utilized for patients who cannot tolerate oral bisphosphonates (ie, inability to sit up for 40 minutes). IV bisphosphonates are sometimes associated with hypocalcemia and influenza-like symptoms.[15,18,19,24]

For patients taking bisphosphonates, most guidelines suggest reassessment of risk, including bone mineral densitometry, after 5 years of oral bisphosphonate therapy or 3 years of IV bisphosphonate therapy. Patients at continued high risk at 3 or 5 years because of low hip T score, a high fracture risk score, or history of fracture on therapy, should be considered for continued bisphosphonate therapy. The maximum duration of therapy is 10 years for oral bisphosphonates and 6 years for IV bisphosphonates. It should be noted that most data are based on osteoporosis in women, and data on optimal management in men are more limited.[15,18,19,24]

The risk of atypical subtrochanteric fracture increases with duration of therapy. In 1 study, the rate of atypical fracture was 1.78 per 100,000 in women taking the drug for less than 2 years (number needed to harm >50,000), increasing to 100 per 100,000 in women taking the drug for 8 years or more (number needed to harm 1000).[25] Both bisphosphonates and denosumab are associated with the rare complication of osteonecrosis of the jaw, which is most commonly seen in patients with severe dental disease.[15,18,19,24]

Denosumab

Denosunab is as a human monoclonal antibody that acts on the key bone resorption mediator RANKL, thus inhibiting osteoclast formation and survival. It has been shown to increase BMD and reduce the incidence of fracture in postmenopausal women. The risk of vertebral fracture appears to increase following discontinuation, making it less attractive as a first-line agent. Denosumab should be considered when there is a contraindication to bisphosphonate therapy (eg, reduced creatinine clearance). Like

bisphosphonates, denosumab is associated with the rare complication of osteonecrosis of the jaw. It also is associated with an increased risk of infection, mild upper GI symptoms, and rash. Because of the increased risk of fractures following discontinuation of therapy, continuing therapy or administration of another agent following discontinuation should be considered.[15,18,19,24,26]

Selective estrogen receptor modulators

Raloxifene inhibits bone resorption and reduced the risk of vertebral fracture, but there is no evidence that it reduces the risk of hip fracture, and for that reason, it is considered a second-line agent. It has potential benefits in reducing the risk of breast cancer, but that it offset by an increased risk of thromboembolic events and hot flashes. It should be considered when the risk of breast cancer is high and there are contraindications to other agents. It is unclear how long SERMs can be safely administered; many clinicians discontinue therapy at 8 years because of lack of safety data beyond that time frame.[15,18,19,24]

Tamoxifen is used for the prevention and treatment of breast cancer but should not be used as a primary agent for osteoporosis. However, women receiving tamoxifen probably receive benefits in BMD.[15,18,19,24]

Sex hormones

Sex hormone replacement may help prevent bone loss in men and women who have other indications for their use (eg, hypogonadism in men, hot flashes in women), but should not be used for established osteoporosis due to lack of efficacy.[15,18,19,24]

Parathyroid hormone/parathyroid hormone-related protein analogs

Teriparatide and abaloparatide are anabolic agents that stimulate bone formation and activate bone remodeling. They are not considered first-line agents for most patients because of cost. They should be considered in women or men with severe osteoporosis (T score of < or = −3.5 or T score < or = −2.5 with a fragility fracture), in patients who are unable to tolerate other therapies, or in patients who fail other therapies. Adverse effects include mild upper GI symptoms, hypercalcemia, and depression. They should not be used longer than 24 months because of a potential risk of osteosarcoma (observed in rats). Patients at high risk for fracture following discontinuation should be treated with an antiresorptive agent.[15,18,19,24]

Romosozumab

Romosozumab is a monoclonal antisclerostin antibody that has been shown to increase BMD and reduce vertebral and nonvertebral fractures. In has been associated with an increased risk of serious cardiovascular events.[27] It should be considered only for patients who fail other agents and are at low risk for adverse cardiovascular outcomes. Therapy is limited to 12 monthly doses. Patients at high risk for fracture following discontinuation should be treated with an antiresorptive agent.[27,28]

Other agents

Bazedoxifine is a SERM that is used in Europe and Japan for women with osteoporosis. It is also used in combination with estrogen for the prevention of osteoporosis. It is not used in the United States for treatment of osteoporosis.[29] Calcitonin is no longer used to treat osteoporosis. However, it may have analgesic properties that can be helpful in the setting of acute osteoporotic vertebral fractures.[30]

Special populations and considerations

There is evidence that bisphosphonates and teriparatide are effective for older patients as well as younger patients.[24] In general, the evidence is insufficient to draw

strong conclusions about the efficacy of pharmacologic treatment of osteoporosis in men.[24] There is some evidence that alendronate, risedronate, and teriparatide are effective in patients taking glucocorticoids.[31]

CLINICAL CARE POINTS

FRAX helps predict a patient's 10 year risk of hip or other major osteoporotic fracture, and can help guide treatment decisions. Fall prevention strategies can reduce the risk of fracture in patients with osteoporosis.

IV bisphosphonate use should be reassessed after 3 years of use; only patients with significant risk of future fracture should continue. Six years is the maximum duration of therapy for IV bisphosphonates.

Oral bisphosphonate use should be reassessed after 5 years of use; only patients with significant risk of future fracture should continue. Ten years is the maximum duration of therapy for oral bisphosphonates.

The risk of vertebral fracture appears to increase following discontinuation of denosumab. It should either be continued indefinitely or followed by administration of another agent.

The risk of atypical fractures of the femur increases with duration of use of bisphosphonates and denosumab. The complication is rare but potentially serious.

SUMMARY

Osteoporosis and its associated complications are common causes of morbidity and mortality in older adults. All healthy adults should be counselled about measures to prevent osteoporosis, including adequate calcium and vitamin D intake, participating in weight-bearing exercise, and avoiding tobacco and excess alcohol consumption.

Women should be screened for osteoporosis beginning at age 65. Screening for osteoporosis in men should be considered when risk factors are present. Appropriate screening intervals are controversial.

Women and men with osteoporosis should be offered pharmacologic therapy. Choice of therapy should be based on safety, cost, convenience, and other patient related factors. Duration of therapy depends on agent chosen and the patient's risk for future fractures.

DISCLOSURE

Neither author has anything to disclose.

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