Osteoporosis screening and risk management

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Abstract: Osteoporosis is common among older adults and results in costly osteoporotic fractures. Screening for this metabolic bone disorder is warranted in most older adults and clinicians must be diligent in identifying persons at risk. The evaluation should include an assessment of risk factors for falls, a bone density test, and consideration of possible secondary causes of osteoporosis. Several medications are available to improve bone density and decrease fractures. Adequate calcium and vitamin D intake (and treatment of vitamin D deficiency) are paramount in the management of osteoporosis.

Keywords: Osteoporosis, Fractures, Vitamin D

Introduction

Osteoporosis is a metabolic bone disorder that affects more than 200 million people worldwide. (Lin and Lane 2004) The disease is characterized by low bone mass, which makes bones fragile and susceptible to fractures. Osteoporotic fractures are more common in the elderly and result in excess morbidity and mortality in this population. Despite numerous effective treatments for osteoporosis, many older adults are not screened for osteoporosis so consequently they go untreated. To prevent the physical and financial burdens of osteoporotic fractures in the elderly, clinicians must implement a comprehensive plan of screening and management of risk factors for osteoporosis.

Background

Osteoporosis is a systemic bone disorder typified by low bone mineral density (BMD). Although reduced bone mass is a hallmark of the disease, microarchitectural deterioration of bone and increased bone fragility are also present. While the prevalence of osteoporosis is more common among some populations (white women, persons with low body mass), osteoporosis is seen in all racial and ethnic groups, all weight categories, and in both men and women. For residents in skilled nursing facilities, the prevalence exceeds 50% regardless of race or gender (Wilkins and Birge 2005).

Osteoporosis and its resulting fractures significantly increase with age. The primary age-related change in bone mass occurs when there is an imbalance in bone formation and bone resorption. Instead of a comparable degree of bone formation and resorption, there is decreased bone formation (osteoblastic activity) and increased bone resorption (osteoclastic activity). This shift in bone remodeling usually begins in the third decade of life and continues with aging. (Fernández et al 2006) The increased osteoclastic activity is significantly exacerbated by estrogen loss, especially during menopause in women.

This age-related bone loss may be additionally affected by both intrinsic and extrinsic factors. A list of both modifiable and nonmodifiable risk factors for reduced bone mass is listed in table 1. It is important to note that while these risk factors increase the risk of developing reduced bone mass, osteoporosis commonly occurs in older persons without additional risk factors. Many clinicians assume that screening need only occur in persons with several of the risk factors listed; however, all older

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adults should be screened and persons with multiple risk factors should be screened earlier.

Two common misconceptions regarding risk for osteoporosis is that only white or Asian women become osteoporotic and that men do not develop osteoporosis unless there are secondary causes. Several studies have found that women of African descent or African Americans also develop osteoporosis. (Bohannon 1999; Kleerkoper et al 1994; Wilkins and Goldfeder 2004) In fact, African American women, especially those with advanced age and lower body mass index (BMI), have similar rates of osteoporosis as white women. (Wilkins and Goldfeder 2004) Additionally, African American women have higher rates of mortality after hip fracture than other groups. (Kellie and Brody 1990)

While research has considerably increased over the last decade regarding osteoporsis in men, the prevalence and impact of osteoporsis in men remains unclear to many clinicians. It is estimated that 20% of men over age 50 will develop an osteoporotic fracture during their lives (Melton et al 1998; Kanis et al 2000) and men are more likely to suffer an osteoporotic fracture than be diagnosed with prostate cancer. (Melton 1995) It appears that due to a higher peak bone mass and no substantial loss in estrogen (as with menopause), men are likely to develop osteoporosis approximately 10 years after women. Certainly men with multiple risk factors for osteoporosis may develop the disease sooner.

Why osteoporosis screening is important

The obvious goal of screening for and treating osteoporosis is to prevent osteoporotic fractures and the functional decline that often accompanies these fractures. While reduced bone density is a major risk factor for fractures, the risk of falling in older adults contributes substantially to osteoporotic fractures, especially nonvertebral fractures. Vertebral fractures are the most common osteoporotic fractures and account for 70% of all fractures. One in 5 women with an asymptomatic or symptomatic vertebral fracture will experience another vertebral fracture within one year (Lindsay et al 2001). Presence of a vertebral fracture also increases risk of nonvertebral fractures.

While both vertebral and nonvertebral fractures are associated with functional decline and increased morbidity, hip fractures have the highest rates of functional decline and mortality. Only 25% of hip fracture patients return to their previous level of function (Birge et al 1994). The highest incidence of hip fractures occurs in nursing home residents, where 50% of the residents fall each year (Chandler et al 2000).

Accordingly, identifying risk factors for falls is as important as ascertaining BMD in preventing nonvertebral fractures. Common risk factors for falls are postural instability, cognitive impairment, and gait imbalance. Table 2 lists other risk factors for falls. Recent studies have also found an association between vitamin D deficiency and falls or postural instability. Additional evidence supports a role of vitamin D in neuromuscular function. It is important to identify vitamin D deficiency in older adults since it may affect both bone density and risk for falls.

Table 1 Risk factors for osteoporosis

Nonmodifiable	Modifiable
Advanced age	Smoking
Female gender	Inadequate calcium intake
White/Asian race	Inadequate vitamin D
Low peak bone mass	Low body weight (BMI <21 kg/m^2)
Family history of osteoporosis	Estrogen deficiency
Personal history of fracture	Hypogonadism
Low Body Mass Index	Chronic glucocorticoid therapy (see table 3 for other medications)

Screening for osteoporosis

All older adults at risk for osteoporosis should be evaluated for osteoporosis and for risk factors for osteoporotic fractures. Persons at risk are those over age 65 and those under age 65 with three or more risk factors (See Table 1). At risk persons should have a history and physical examination, BMD test, and laboratory testing. The medical history should focus on risk factors for low bone density and risks for falls. Questions regarding family history of osteoporosis or hip fracture, personal history of fracture, current or previous smoking, excess alcohol use, menopausal status and medication use should be asked.

The physical examination should include height and weight for body mass index (BMI) and determining any loss of height. A BMI of less than 21kg/m^2 and a loss of more than 5 cm (or 2 inches) are both risk factors for osteoporosis. Presence of a gait disorder, lower extremity weakness, and postural instability all increase risk for falls and fractures. Additionally, evidence of thoracic kyphosis may suggest vertebral fractures.

Bone mineral density testing

The National Osteoporosis Foundation recommends that all men and women over age 65 have a BMD test. Younger

Table 2 Risk factors for falls and nonvertebral fractures

Gait disorders
Lower extremity muscle weakness
Cognitive impairment/dementia
Neurodegenerative disorders of the central nervous system
Hypotension
Vitamin D deficiency
Impaired vision
Impaired hearing
Medications affecting postural stability

postmenopausal women with 1 additional risk factor should also have a BMD test. Persons with hyperthyroidism, hyperparathyroidism and those on chronic glucocorticoid therapy should also be screened for reduced bone density. Other secondary causes of osteoporosis that may warrant screening are listed in Table 3.

Osteoporosis screening should ideally be performed using dual energy X-ray absorptiometry (DXA) to measure BMD of the hip and spine. Currently, central DXA machines are widely available and should be used for baseline screening. Although some peripheral bone densitometers have been found to correlate with central DXA and to predict risk of fracture (Bauer et al 1997), a recent meta-analysis finds that calcaneal quantitative ultrasound does not reliably exclude or confirm osteoporosis (Nayak et al 2006). If patients are unable to obtain a central DEXA of the hip and spine (the person cannot lie comfortably for the exam, exceeds the weight limit), a forearm BMD can be performed using 1/3 of the radius in the nondominant arm. Additionally if the patient does not readily have access to the machine or has radiopaque implants in the measurement area, clinicians may consider using a peripheral machine. Although central BMD measurement is preferable, peripheral measurement may be useful in screening low risk populations. Whenever possible, persons with abnormal peripheral results should subsequently have a central DEXA or quantitative CT scan.

Table 3 Common causes of secondary osteoporosis

Endocrine	**Chronic drug therapy**
Hypogonadism	Glucocorticoids
Hyperthyroidism	Thyroxine
Anorexia nervosa	Anticonvulsants
Hyperparathyroidism	GnRH agonists
	Aromatase inhibitors
Nutritional	**Other**
Malabsorption syndromes	Hypercalciuria
Vitamin D deficiency/resistance	Alcoholism
Calcium deficiency	

GnRH: gonadotropin releasing hormone

When interpreting the BMD results, clinicians should refer to the total hip, femoral neck, and lumbar spine. Local factors affecting bone density such as weight bearing, muscle usage and co-existing osteoarthritis may result in differences in BMD categories between bones. The lowest score should be used to determine whether the patient is normal, has osteopenia or osteoporosis. In persons with normal BMD, repeat testing should occur in 3–5 years and in those with osteopenia, tests should be repeated in 2 years.

Biochemical measures of bone turnover

Biochemical measures (BCM) of bone turnover reflect rates of bone resorption or bone formation and can be found in blood or urine. BCMs may measure products of osteoblasts (bone formation) such as osteocalcin or bone-specific alkaline phosphatase, or they may measure collagen breakdown products that reflect bone resorption, such as pyridinolines or C- or N-terminal telopeptides. Although BCMs are commonly used in clinical trials, their clinical usefulness is limited due to individual patient variability

If the clinician chooses to use a BCM, those that predict bone resorption are most useful (see Table 4) BCMs can be used to predict fracture risk and monitor treatment but should not be used to diagnose osteoporosis. A decrease in resorption markers usually reflects a reduction in bone remodeling activity. To use BCMs for monitoring, obtain a baseline value then recheck every 3 to 6 months until stable. Populations that may benefit from BCM monitoring include diseases with rapid and severe bone loss such as persons using chronic glucocorticoid therapy, with hyperparathyroidism or hypogonadism.

Laboratory testing

Routine laboratory tests for the evaluation of osteoporosis should include a serum calcium, 25-hydroxy vitamin D, a complete blood count, and 24-hour urinary calcium excretion. Elevated calcium suggests hyperparathyroidism and decreased calcium suggests malabsorption or vitamin D deficiency/resistance. Anemia may indicate multiple myeloma. Additional laboratory tests such as parathyroid hormone, thyroid-stimulating hormone, and serum protein electrophoresis may be indicated after the initial evaluation.

Managing risk for osteoporotic fractures

The primary goal of treating osteoporosis is prevention of osteoporotic fractures. Below are recommendations for

Table 4 Biochemical markers of bone turnover

Markers of bone resorption	Markers of bone formation
Pyridinoline	Osteocalcin
Deoxypyridinoline	Bone alkaline phosphatase
Type I collagen telopeptides	Propeptide of type I procollagen
N-terminal crosslinking telopeptide (NTX-I)	N-terminal propeptide of type I procollagen
C-terminal crosslinking telopeptide (CTX-I)	C-terminal propeptide of type I procollagen
Tartrate-resistant acid phosphatase (TRAP)	

treating osteoporosis. Pharmacologic treatment should be instituted in those with BMD T-scores worse than –2.5 (or worse than –2.0 and multiple risk factors) or those with a history of vertebral or hip fracture. Recommendations on nutrients should be implemented in all older adults regardless of BMD.

Nutrition

Treating osteoporosis and osteopenia should begin with appropriate supplementation of calcium and vitamin D. Calcium has been shown to increase BMD when administered with vitamin D and it is co-administered with most therapeutic agents for osteoporosis.(Dawson-Hughes et al 1997) The National Institutes of Health Consensus Panel recommends daily dietary intake of calcium is 1,500 mg/day for men and women aged 65 and older. Preferably, calcium intake should be in the form of dairy products to improve absorption. Calcium carbonate and calcium citrate may be used as dietary supplements. Additionally, calcium should be taken in divided doses to improve absorption.

A meta-analysis of randomized clinical trials in older women finds that a vitamin D dose of 700–800 units/day is associated with decreased risk of hip fractures. (Bischoff-Ferrari et al 2005). Studies have also that vitamin D decreases fall risk, and improves muscle strength and balance. (Pfeifer et al 2000; Prabhala et al 2000; Bischoff et al 2003) It is recommended that older adults with normal vitamin D status consume 800 units/day of vitamin D. There are very few dietary sources of vitamin D (fatty fish such as tuna, salmon, mackerel and sardines or cod liver oil) that provide 100 units or more per serving. Vitamin D fortified milk only contains 100 units of vitamin D per 8 ounce serving. Although sunlight is a major source of vitamin D for most people, several changes occur in older adults that contribute to vitamin D deficiency including reduced exposure to sunlight. Additional recommendations for the management of vitamin D deficiency are addressed below.

Phosphorus intake is essential to normal bone development and mineralization. Although most adults consume more than the recommended 700 mg/day of phosphorus, 10–15% of older adults have inadequate phosphorus intake. (Bischoff et al 2003) Vegetarians are at increased risk for phosphorus deficiency. Caution must be exercised in persons with low phosphorus intake who also use calcium carbonate or citrate supplements as these may bind phosphorus and create a negative phosphorus balance. Alternatively, excessive phosphorus intake may disrupt skeletal homeostasis.

Bisphosphonates

Potent antiresorptive agents, bisphosphonates inhibit osteoclast activity and reduce bone turnover. This class of drugs increases bone density and prevents both vertebral and nonvertebral fractures (see Table 5). Of note, relatively small increases in BMD may reduce fracture risk by 20 to 50%. (Prabhala et al 2000) Unfortunately, most clinical trials have excluded patients over age 80, so the benefit in this population is unclear. In one study of women over age 80, risedronate had no effect on hip fractures, but there was an 80% reduction in new vertebral fractures at one year (Boonen et al 2004).

Bisphosphonates are associated with esophagitis and esophageal/gastric ulcers so the instructions for ingestion must be followed carefully to avoid side effects. Osteonecrosis following dental procedures has also been reported in persons using bisphosphonates, mostly those using large IV doses for hypercalcemia. Although studies in excess of 5 years have shown no unexpected adverse effects, theoretical concerns regarding oversuppression of bone turnover exist. Given this concern, the relatively long half-life of the drugs, and evidence that bone turnover may remain suppressed after discontinuation of the drug, some clinicians consider giving patients a 'holiday' from the drugs after 5 years. At this time, this is not a recommendation of the manufacturers or the Food and Drug Administration and no guidelines for monitoring patients off the drugs have been established.

Selective estrogen receptor modulators (SERMs)

The SERM raloxifene has been shown to increase BMD in both the spine and hip and to decrease vertebral fracture risk by up to 60%. (Ettinger et al 1999) Raloxifene has not been shown to decrease hip fractures or other non-vertebral fracture risk. Raloxifene has also been found to decrease incidence of invasive breast cancer by more than 70%. (Cummings et al 1999) Side effects of SERMs include thromboembolism and vasomotor symptoms.

Table 5 Select interventions for the prevention of osteoporotic fractures

Agent	Dose/day	Cost	Relative efficacy in vertebral	Fracture prevention hip
Hormone Therapy	O.625 mg CEE* 1–2 mg estradiol	$$	+++	+++
Raloxifene 60 mg		$$	+	–
Calcitonin 200 units		$$$	+	–
Alendronate 70mg/wk		$$$	+++	+++
Risedronate 35mg/wk		$$$	+++	+++
Teriparatide (PTH)		$$$$	+++	ND

Notes: *CEE: conjugated equine estrogens; ND: no data.
(–) = no effect; (+) = mildly positive effect; (+++) = strongly positive effect.

Hormone replacement therapy (HRT)

Estrogen therapy has been shown in several studies to increase BMD from 2% to 7% at all sites and to prevent both vertebral and hip fractures (PEPI 1996; Lindsay et al 2005). Unfortunately, HRT has been associated with an increased risk of myocardial infarction, stroke, thromboembolism and breast cancer. Although low dose oral estrogen or transdermal estrogen may minimize or even reduce cardiovascular and stroke risk, there is insufficient evidence that these agents have a beneficial effect in decreasing the risk of nonvertebral fractures. Accordingly, HRT should be reserved for women with significant symptoms of menopause and should be limited to the shortest possible duration.

Parathyroid hormone (PTH)

Teriparatide (recombinant human PTH) is an anabolic agent that stimulates osteoblastic bone formation. Teriparatide increases bone density from 3% to 9% and decreases vertebral fractures by up to 65%. (Neer et al 2001) This agent also decreases nonvertebral fractures by 50% but has not been shown to specifically decrease hip fractures. Teriparatide is administered subcutaneously for up to 2 years.

Calcitonin

Calcitonin inhibits bone resorption and may increase BMD in the spine by up to 3%. It has been shown to decrease vertebral fractures to a lesser degree the other osteoporosis medications and has no benefit in preventing hip fractures (Chestnut et al 2000). Consequently, calcitonin is generally reserved for persons who cannot tolerate other medications. Calcitonin has also been found to reduce bone pain from vertebral compression fractures.

Treating vitamin D deficiency

Vitamin D deficiency is common in the elderly and actual vitamin D levels vary substantially between individuals. Determination of vitamin D status is important in all older adults. Serum 25-hydroxyvitamin D measurement is recommended since the half-life is longer and there are fewer fluctuations that seen in 1,25- dihydroxyvitamin D, the biologically active form of vitamin D. Due to possible vitamin D resistance, it is helpful to also measure serum PTH levels.

The goal 25-hydroxyvitamin D level is greater than 30 ng/ml with a PTH of less than 42 pg/ml. (Wilkins and Birge 2005) For persons with vitamin D levels less than 30 ng/ml and/or PTH greater than 42 pg/ml, therapy with ergocalciferol, 50,000 units every two weeks, should be started. PTH and vitamin D levels should be rechecked in 8 weeks. The dosing interval should be decreased to weekly if the levels are not yet optimal. Once the levels are within goal range, vitamin D and PTH should be followed quarterly and adjusted as needed. If the patient requires more than 250,000 units monthly of ergocalciferol, calcitriol orally or injected should be considered. Referral to an endocrinologist or bone specialist may be indicated.

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