

Osteoporosis in the Hospitalized Patient

Wendy S. Klein, MD
Kelsey Swanson, MD

Osteoporosis is a systemic disorder characterized by decreased bone mass and microarchitectural deterioration leading to bone fragility and an increased susceptibility to fractures. Twenty-five million Americans are currently affected, 80% of them women.¹ While it is a preventable and treatable condition, osteoporosis is insidious and diagnosis is often delayed until after a fracture occurs. However, with reliable techniques for assessing bone mineral density, it is possible to diagnose and treat osteoporosis while it is still asymptomatic. Unfortunately, bone health is frequently overlooked in the hospital. Given the comorbidities that are seen in hospitalized patients, it is especially important to recognize the increased risk of bone loss and to intervene.

Who is at risk?

Because osteoporosis is generally asymptomatic until irreparable damage is done, it is essential to recognize osteoporotic risk. In addition to well-described risk factors that include positive family history, short-thin stature, smoking, high alcohol consumption, high caffeine intake, and sedentary lifestyle, it is important to recognize the additional risk conferred by medications and comorbid diseases in the hospitalized and geriatric patient.²

Common medications, including glucocorticoids, anticonvulsants, heparin, GnRH analogues, thyroid hormone, chemotherapeutic agents, and aluminum-containing antacids, can cause osteoporosis.² Bone loss is now a clearly defined side effect of adjuvant chemotherapy in breast cancer survivors.³ This, coupled with the fact that estrogen-replacement therapy (ERT) is generally contraindicated in breast cancer, mandates increased vigilance for these patients. Glucocorticoids, widely used for the treatment of asthma, chronic lung disease, rheumatoid arthritis, inflammatory bowel disease, and organ transplantation, have clearly been shown to increase bone resorption and decrease bone formation.⁴ Bone loss is most rapid during the first six months of treatment, and continues for its duration.

It is important to remember that secondary osteoporosis can result from a number of disorders including hormonal imbalances (e.g. Cushing's syndrome), cancer (especially multiple myeloma), gastrointestinal disorders (particularly malabsorptive bowel diseases), chronic renal failure, inflammatory

arthritis, and hyperthyroidism.^{5,6} In addition, any factor that results in decreased estrogen, especially before natural menopause, increases the risk of bone loss. This includes women who undergo premenopausal oophorectomy or amenorrhea, which can result from intense athletic training, chemotherapy treatment, or poor nutrition due to an eating disorder. In men, low testosterone due to hypogonadism has been associated with the development of osteoporosis.⁷ Timely identification of osteoporotic risk enables prevention and treatment to be initiated prior to or during the disease's early phase.

Screening and Diagnosis

Osteoporosis is associated with several physical features, including kyphosis, height loss, and fractures. Bone mineral density (BMD) testing can be used to establish or confirm a diagnosis of osteoporosis, assess future fracture risk, and monitor changes in bone density due to treatment or disease progression.¹ Any patient with apparent risk factors or with a condition that might reduce bone mass or accelerate bone loss should be tested.

If secondary causes of osteoporosis are suspected, one or more of the following tests may be performed: complete blood cell count, calcium, phosphate, liver enzymes, alkaline phosphatase, creatinine, electrolytes, and urinalysis. Additional tests may also be useful if a certain cause is suspected: TSH, 24-hour urinary calcium or free cortisol, sedimentation rate, PTH, 25-hydroxyvitamin D, dexamethasone suppression, and other tests for hyperadrenocorticism, acid-base studies, serum or urine protein electrophoresis, and bone marrow or bone biopsy.¹

Prevention and treatment of osteoporosis and osteoporosis-related fractures

In addition to the standard lifestyle modifications for prevention and treatment of osteoporosis, including weight-bearing exercise and elimination of tobacco use and excessive alcohol use, it is important to insure that all patients have an adequate intake of calcium and vitamin D. Calcium supplementation should be the standard of care for all women and for men who are at an increased risk of osteoporosis. All adults should receive at least 1200 mg/day of elemental calcium, while postmenopausal women should take in 1500 mg/day.⁸ In addition to a calcium supplement, we recommend a multivitamin with minerals which will not only provide vitamin D, but also minimum daily requirements of such minerals as zinc and selenium.

Prevention of falls is also a special concern for men and women who are at high risk of fracture. Suggested measures include anchoring rugs or using nonskid mats, removing loose wires and clutter, and installing handrails and proper lighting (including nightlights).¹² In hospitalized patients, the high prevalence of polypharmacy and multiple drug interactions can contribute to the risk of falling and every effort should be made to decrease the number of medications, especially in the geriatric populations. Sedatives, in particular, can contribute to a patient's risk of falling. Fall precautions are also extremely important for post-operative patients, patients with impaired mobility of any kind, and patients with post-hospital debilitation.

Pharmacologic Treatment

Pharmacologic therapy should be initiated to reduce the risk of fracture in women who have a BMD T-score of less than -2 in the absence of risk factors and in those who have a T-score of less than -1.5 if risk factors are present.¹ If a patient presents with physical signs such as kyphosis, pharmacological therapy can be implemented without BMD testing. For those who present with a fracture and who have multiple risk factors it is reasonable to initiate treatment without BMD testing.

Maintaining adequate estrogen levels remains a useful option in preserving bone density and decreasing fracture rates in women after menopause. Postmenopausal women at risk for osteoporosis may be counseled to consider ERT unless they have contraindications, such as increased risk for, or history of cardiovascular disease, thromboembolism, or personal history or significant risk of breast cancer. Treatment with ERT should be considered on an individual risk:benefit basis, and when used, we recommend utilizing low doses of 0.3-0.45 mg per day, which have been shown to stabilize bone. The greatest benefit is seen when ERT is begun soon after menopause, although it has been found to be effective in reducing fractures even when started in women as old as 75 years of age.¹⁰

For patients who have contraindications to ERT, bisphosphonates, such as alendronate or risedronate, can be offered for the prevention and treatment of osteoporosis. It should be noted that in the patient who presents with a hip or other osteoporotic fracture, bisphosphonates would be the first choice unless otherwise contraindicated. By inhibiting bone resorption, these agents increase BMD and decrease the risk of fractures.¹¹ Bisphosphonates must be taken on awakening with

a full glass of water, with the patient remaining upright and fasting for 30 minutes. This inconvenience is minimal when using a once weekly dosing schedule. Because of adverse esophageal and gastrointestinal side effects, they are contraindicated in patients with a history of esophageal pathology or peptic ulcer disease. Renal insufficiency is a relative contraindication.

Selective estrogen receptor modulators (SERMs), such as raloxifene, have been shown to prevent bone loss, and preliminary data suggest that they reduce the risk of vertebral fracture by 40-50% in women with osteoporosis.¹ While raloxifene has been shown to increase BMD in the spine, total hip, and total body, the increase seems to be less than that seen with estrogen or alendronate therapy.¹¹ Recent studies confirm that raloxifene appears to significantly decrease the risk of breast cancer, and therefore this would be the agent of choice for women at risk.^{13,14} As with ERT, a history of thromboembolism is a contraindication.

Calcitonin, a hormone that inhibits bone resorption, is FDA approved for the treatment of osteoporosis. It does not build bone, but in women who are at least 5 years beyond menopause, it slows bone loss and increases spinal bone density.¹² One of its unique characteristics is that it produces an analgesic effect with respect to bone pain and is therefore often prescribed for patients who have had an acute osteoporotic fracture. The increase in BMD from calcitonin is significantly less than that achieved by other agents but can be used when other agents are contraindicated. Calcitonin is delivered in a single daily intranasal spray and therefore is also useful in patients unable to take oral medications.

Osteoporosis in Men

While osteoporosis is more common in women than men, one in eight men over the age of 50 years experiences an osteoporosis-related fracture in his lifetime, and almost 30% of all hip fractures occur in men.⁷ The risk of osteoporosis should therefore be considered in male patients as well. The approach to diagnosis in men is to first search for a secondary cause. The most common causes are hypogonadism, alcoholism and glucocorticoid or anticonvulsant use. If testosterone is low, it should be replaced using a premeasured gel, transdermal patch, or intramuscular injection, along with a bisphosphonate.¹⁵ For men with idiopathic osteoporosis, bisphosphonates are the treatment of choice.¹⁶

Glucocorticoid Induced Osteoporosis

The American College of Rheumatology (ACR) recommends obtaining baseline BMD in patients beginning glucocorticoid therapy that will last greater than six months, with repeated measurements annually to gauge therapeutic response.¹⁷ Bisphosphonate therapy is now the standard of care in preventing glucocorticoid induced osteoporosis in patients taking 5 mg or more of daily prednisone.⁴ As with all bone preserving therapies, calcium with vitamin D is essential.

Summary

In conclusion, when consulting on inpatients, there are several points that should be considered:

- Additional risk for bone loss is conferred by comorbid diseases and concurrent medications, most commonly prednisone, warfarin, and chemotherapeutic agents.
- Physical findings such as height loss and kyphosis are pathognomonic of osteoporosis and should not be overlooked.
- The need for bone preserving therapy should be considered in all fracture patients.
- If osteoporotic risk is apparent, bone preserving therapy can be initiated prior to obtaining BMD results.
- Calcium and a multivitamin should be the standard of care for all women, for men with osteoporotic risk, and for all patients taking glucocorticoids.
- Fall precautions should be emphasized for elderly and frail patients, as well as post-operative patients, patients with impaired mobility, or patients taking sedating medications.

References

1. Eastell, R. Drug therapy: treatment of postmenopausal osteoporosis . NEJM. 1998; 338:736-746.
2. Dawson-Hughes, B. Bone loss accompanying medical therapies. NEJM. 2001; 345: 989-991.
3. Shapiro, CL Recht A. Drug therapy: side effects of adjuvant treatment of breast cancer. NEJM. 2001; 344: 1997-2008.

4. Saag, KG. Alendronate for the prevention and treatment of glucocorticoid induced osteoporosis. NEJM. 1998; 339:292-299.
5. Pfeilschifter, J Diel, I. Osteoporosis due to cancer treatment: pathogenesis and management. J Clin Oncol. 2000; 18: 1570-1593
6. Scott, EM et al. Guidelines for osteoporosis in coeliac disease and inflammatory bowel disease. Gut. 2000; 46: 1-8
7. Amin S, Felson, DT. Osteoporosis in men. Rheum Dis Clin of N Amer. 2001; 27: 19-43.
8. Dawson-Hughes, B et al. Effect of calcium and vitamin D supplementation on bone density in men and women 65 years of age or older. NEJM. 1997; 337: 670-676
9. Manson, JE Martin, KA. Postmenopausal hormone therapy. NEJM. 2001; 345: 34-40.
10. Villareal, DT. Bone mineral density response to estrogen replacement in frail elderly women: A randomized controlled trial. JAMA.2000; 286: 815-820.
11. McClung, M et al. Effect of risedronate on the risk of hip fracture in elderly women. NEJM. 2001; 345: 333-340
12. South-Paul, JE. Osteoporosis: Part II. Nonpharmacologic and pharmacologic treatment. Amer Fam Phys. 2001; 63(6): 1121-1128.
13. Cummings, SR et al. Serum Estradiol Level and Risk of Breast Cancer During Treatment With Raloxifene. JAMA. 2002; 287 (2): 216-220.
14. Lippman, ME et al. Indicators of Lifetime Estrogen Exposure: Breast Cancer Incidence and Interaction with Raloxifene Therapy in MORE Study Participants. J Clin Oncol. 2001; 65:125-134.
15. Snyder, PJ et al. Effects of Testosterone Replacement in Hypogonadal Men. J Clin Endocrinol Metab. 2000; 85: 2670-2677.
16. Orwoll, E et al. Alendronate for the Treatment of Osteoporosis in Men. NEJM. 2000; 343: 604-610.
17. New ACR recommendations for preventing and treating GIO. Osteoporosis Today. 2001;1: 1-2.