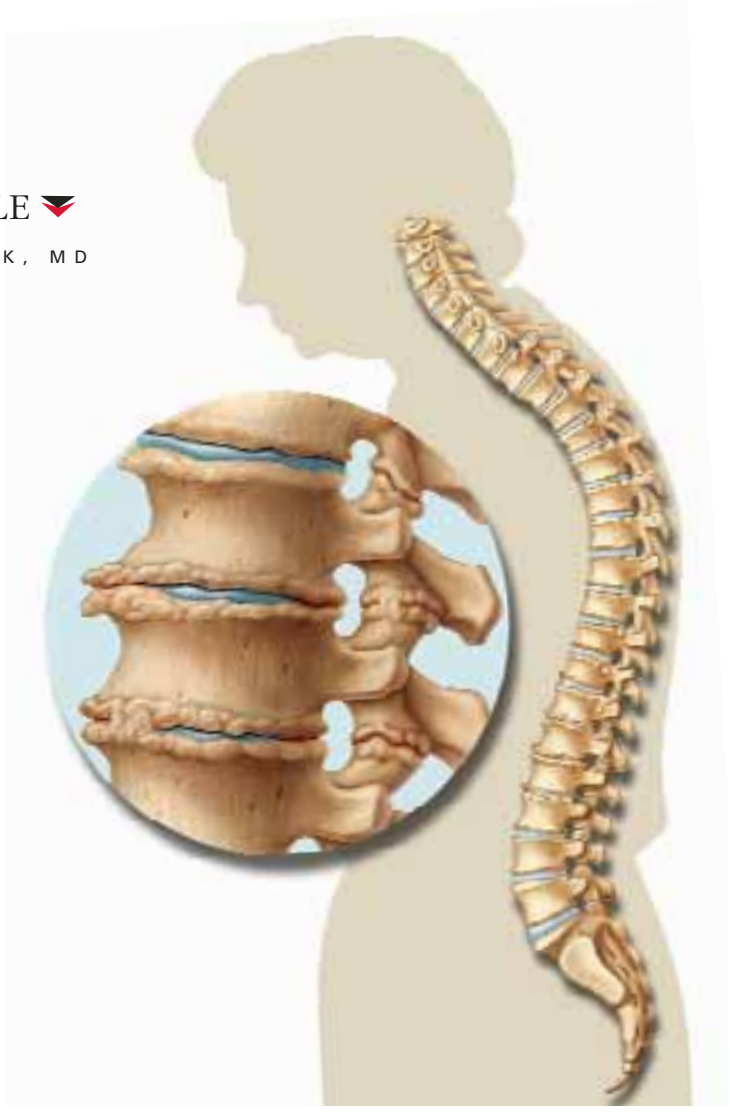
OBG MANAGEMENT

COVER ARTICLE

JUDI L. CHERVENAK, MD



Bony overgrowth typical of osteoarthritic changes in the spine may falsely elevate BMD test results in women with osteoporosis.

Who is at risk of fracture?

Avoid 6 pitfalls of osteoporosis screening

Easily misunderstood symptoms, overlooked history and lifestyle clues, mistaken choice of densitometry site and method—these and other snags can trip up efforts to screen patients adequately and start intervention early.

Osteoporosis has claimed the spotlight. The sheer volume of information published in recent years is astounding. From clinical guidelines to mainstream media, the message is clear: Osteoporosis can be prevented and effectively treated if intervention is early enough. The key? Proper screening of women who may be at risk.

That's where the difficulty begins. Amid a profusion of data, the simple how-to—and when-to—of screening can get lost. But osteoporosis is a potent threat. Over her lifetime, a woman's risk of hip fracture is greater than her risk of breast, endometrial, and ovarian cancer

combined. Since many women are discontinuing hormone replacement therapy in the aftermath of the Women's Health Initiative, the risk seems likely to increase.

This article describes a sensible screening strategy focusing on 6 common pitfalls. Many observations come directly from the clinical setting—specifically, a practice in reproductive endocrinology with special interest in the health-care needs of maturing women.

Scope of the problem

As the National Osteoporosis Foundation (NOF) observes, osteoporosis is a "silent disease until it is complicated by fragility fractures."[1] It affects people of all ages and races, but is most prevalent among postmenopausal white and Asian women. However, even African-American and Hispanic women face a heightened risk.[2-4]

One of every 2 white women will experience an osteoporotic fracture.[1] In fact, after age 65, the incidence of hip fracture in white women is greater than the incidence of stroke, diabetes, or breast cancer.[5]

If a hip fracture occurs, the mortality rate within the first year is 10% to 20%.[1,6] One third of hip-fracture patients break the opposite hip, and only 40% regain their previous level of mobility.[1]

For survivors and their loved ones, the diminished quality of life and loss of independence can be devastating. Not surprisingly, many patients also experience psychological symptoms such as depression.

Vertebral fractures are another dire consequence of osteoporosis, causing back pain, loss of height, kyphosis, and even death.

The economic burden of osteoporosis is no less daunting. In 1995, osteoporotic fractures were the "presumed cause" of 180,000 nursing home admissions, more than 430,000 hospital admissions, and roughly 2.5 million doctor visits.[1] Each year these fractures cost about $17 billion in health care—or $40,000 per hip fracture.[1]

▪ *Dr. Chervenak is assistant professor of obstetrics, gynecology, and reproductive endocrinology and infertility at Albert Einstein College of Medicine, Montefiore Medical Center, Bronx, NY.*

Measuring bone density: The basics

Dual-energy x-ray absorptiometry (DXA) is the gold standard for bone-density measurement. It is recommended by the American Association of Clinical Endocrinologists (AACE), the American College of Obstetricians and Gynecologists (ACOG), and the North American Menopause Society (NAMS). Quantitative computed tomography is also recommended by the AACE.

Quantitative ultrasound, which is gaining in popularity, can yield information on bone structure and elasticity in peripheral locations such as the heel, patella, and tibia. It lacks the ionizing radiation of DXA.

It is important for the clinician to be familiar with all these modalities, though the ultimate selection will vary from patient to patient. **Contraindications** to densitometry include pregnancy. While the risk during gestation is negligible, it still exceeds potential benefits.

Limitations. A patient who has undergone recent gastrointestinal studies and nuclear medicine tests should wait at least 72 hours before having a central DXA scan.

Morbid obesity may limit the options, since the weight limit of most central DXA scanners is 250 to 350 lb. Check with the manufacturer for machine limitations and obtain a forearm measurement if necessary.

CONTINUED

KEY POINTS

- Dual-energy x-ray absorptiometry is the gold standard for bone density measurement.
- Don't rely on bone densitometry alone to estimate fracture risk; combine it with thorough assessment of history and risk factors. Nonetheless, bone densitometry is vital, and can establish a baseline that is useful for monitoring therapy.
- When interpreting densitometry results, base the diagnosis on the lowest score obtained.
- Over her lifetime, a woman's risk of hip fracture is greater than her risk of breast, endometrial, and ovarian cancer combined.

TABLE 1

Defining osteoporosis: World Health Organization thresholds

IF THE T SCORE IS...	THE CONDITION IS...	AND BONE MINERAL DENSITY IS...
-1 or above	**Normal**	Within 1 SD of a normal young adult
Between -1 and -2.5	**Osteopenia** (low bone mass)	1 to 2.5 SD lower than that of a normal young adult
-2.5 or below	**Osteoporosis**	2.5 SD or more lower than that of a normal young adult

SD = standard deviation

A family history of osteoporosis, particularly in the patient's mother or another first-degree relative, is a good predictor of the disease.

Orthopedic instrumentation may interfere with measurement at some sites.[7]

T and Z scores. Osteoporosis is defined by comparing the patient's bone density to 2 different populations: her own age group and young adults.

- When bone density is compared to that of her own age group, the result is conveyed as a "Z" score, which represents the number of standard deviations away from the mean.
- When it is compared to the peak bone mass of a "normal" young adult, the result is given as a "T" score—again, the number of standard deviations away from the mean. The World Health Organization (WHO) defines osteoporosis as a T score at or below –2.5 (TABLE 1).

In general, the relationship between bone mineral density (BMD) and fracture risk is continuous, graded, and inverse.[1]

Diagnosis of osteoporosis should be based on the lowest BMD measurement (hip or spine). For example, if the spinal BMD is a T score of –2.7 and the hip is –1.9, the patient would have a diagnosis of osteoporosis because of the low spinal score.

Laboratory studies. Once osteoporosis is diagnosed, secondary causes of the disease should be ruled out. Laboratory evaluation is helpful, especially if the Z score is at or below –2. Routine tests should include:

- Complete blood count and erythrocyte sedimentation rate, to rule out multiple myeloma, a more common malignancy in the elderly
- Serum calcium, which is elevated in hyperparathyroidism but low in malabsorption syndrome and vitamin D deficiency
- Albumin
- Urinary calcium, which is low in vitamin D deficiency and malabsorption syndrome, but elevated in hyperthyroidism, hyperparathyroidism, multiple myeloma, and renal disease
- Free thyroxine, which is high in hyperthyroidism
- Thyroid-stimulating hormone, which is low in hyperthyroidism but high in hypothyroidism[8]

If BMD at the hip or forearm is significantly lower than at the spine, hyperparathyroidism should be ruled out, since cortical bone loss is greater than trabecular bone loss in this disease.

PITFALL #1

An inadequate history

Peak bone mass. By the time a woman reaches her postmenopausal years, bone density has been influenced by specific factors. One is

the peak bone mass she achieved as a young adult. Skeletal growth is nearly complete by age 18, and different skeletal sites reach their peak density at different times.

For example, the spine reaches maturity at 21 to 27 years, and the hip at 19 to 24 years.[6] If skeletal growth and nutrition are adequate in the formative years, optimal peak bone mass in adulthood is likely; if not, it is unlikely. These patients have lost more bone by menopause than their healthy counterparts.[9]

Peak bone mass status is not readily apparent. The clinician needs to specifically ask about the woman's adolescence and early adulthood, as well as lifestyle, past and current nutrition, and genetic factors, to determine her risk for osteoporosis (TABLE 2). For example, a family history of osteoporosis, particularly in the patient's mother or another first-degree relative, is a good predictor of osteoporosis.

TABLE 2

Risk factors for osteoporosis

Genetic	• Female gender • First-degree relative with osteoporosis	• Caucasian/Asian race • Slender frame; body mass index <20
Modifiable	• Low calcium intake • Vitamin D deficiency • Sedentary lifestyle • Smoking • Excessive alcohol consumption	• High caffeine intake • Premenopausal estrogen deficiency • Amenorrhea (due to exercise, eating disorder, etc)
Drugs	• Anticonvulsants • Cytotoxic agents • Gonadotropin-releasing hormone agonists • Immunosuppressive drugs • Lithium	• Intramuscular medroxyprogesterone acetate • Premenopausal tamoxifen • Thyroxine • Warfarin or heparin
Diseases	• AIDS/HIV • Chronic liver or renal disease • Chronic obstructive pulmonary disease • Cushing's syndrome • Depression • Eating disorders • Hemophilia • Hyperparathyroidism	• Inflammatory bowel disease • Insulin-dependent diabetes mellitus • Lymphoma and leukemia • Multiple myeloma • Multiple sclerosis • Pernicious anemia • Rheumatoid arthritis • Thyrotoxicosis

Other predisposing genetic factors include Caucasian and Asian race and a slender frame (body mass index below 20). African-American women have been shown to have higher BMD than white women.[2,3]

Lifestyle factors contributing to osteoporosis include tobacco use, high alcohol intake, and a diet deficient in calcium and vitamin D.

PITFALL #2

Overlooking symptoms

If a woman complains of acute or chronic back pain, the clinician should consider the possibility of osteoporotic vertebral fractures. With these fractures, pain generally originates in the middle back and is characterized by acute onset.[10]

Excessive exercise that leads to amenorrhea can cause bone loss that is not fully recoverable.

Vertebrae T12 and L1 are the most common fracture sites, with T6 through T9 following closely.[10] Multiple compression fractures may cause kyphosis–one of the obvious signs of osteoporosis.

But the disease is not always so blatant. Wrist fracture and/or tooth loss are other, earlier signs.

CONTINUED

Even when a 50-year-old woman and a 75-year-old woman have the same bone mineral density, the older woman is far more likely to experience a fracture.

Another clue to the presence of osteoporosis is loss of height, which is also caused by vertebral fractures. For this reason, the patient's height should be measured at each visit, and she should be asked about her maximum remembered height. A loss of 1.5 inches or more is cause for screening.

PITFALL #3
Skipping the topic of exercise

Weight-bearing and high-impact exercises such as jumping and running appear to benefit the skeleton, especially the peripheral skeleton. The lumbar spine is less responsive. Muscle-strengthening also can lead to beneficial bone building.

However, too much of anything can be bad. Excessive exercise that leads to amenorrhea can cause bone loss that is not fully recoverable, thus increasing the risk for stress fractures and fractures of the hip and spine. Since the prevalence of amenorrhea in female athletes ranges from 10% to 45%, this is a significant nonmenopause-related risk factor for osteoporosis.[11]

The clinician needs to inquire specifically about exercise levels and menstrual patterns.

PITFALL #4
Failing to ask about medications or diseases

Another common cause of osteoporosis is long-term use of certain systemic agents.

Glucocorticoids directly affect bone by limiting formation and increasing resorption. They also impair the body's ability to absorb calcium from the intestine and increase renal excretion of the mineral. At high doses—ie, 7.5 mg per day or more of prednisone or the equivalent—bone loss can reach 10% within 1 year.[12]

Other drugs to watch for include anticonvulsants, especially phenytoin and phenobarbital,[10] intramuscular medroxyprogesterone acetate, tamoxifen (premenopausal),[1] and thyroxine, especially when daily doses exceed 200 mg,[12] as well as the other agents listed in **TABLE 2.**

Diseases. Among conditions associated with osteoporosis are AIDS/HIV, depression (and other conditions that limit mobility), eating disorders, and thyrotoxicosis **(TABLE 2)**. A thorough evaluation for osteoporosis should include consideration of these entities.

PITFALL #5
Measuring the wrong site

Is the hip, spine, or another site best for measuring bone density? The issue is particularly relevant because of rapid proliferation of portable, low-cost, peripheral bone-measuring devices in some practices—even in shopping malls. This device makes evaluation of a single peripheral skeletal site quite simple. However, peripheral BMD is a better indicator of cortical than trabecular bone density, and may inadequately evaluate spinal bone status.

The gold standard for BMD measurement is the central DXA tabletop machine, which makes it possible to measure multiple skeletal sites, if necessary. In fact, the WHO based its criteria on this standard.

If this technology is not available, the hip is the preferred site, especially in women over 60. The reason? Degenerative osteoarthritic spinal calcifications in older women can give falsely elevated BMD values. In contrast, in early menopause, spinal measurements may be useful, since bone is more rapidly depleted from the spine than from the proximal femur at this stage.[13]

Hip measurement is the best predictor of hip fractures, and usually predicts fractures at other skeletal sites as well.[1]

CONTINUED

TABLE 3

Screening guidelines of 4 organizations

ORGANIZATION	WHO SHOULD BE TESTED	RATIONALE	FOLLOW-UP/COMMENTS
National Osteoporosis Foundation (2003)	All women 65 years and older regardless of risk factors	To obtain a baseline measurement	Follow-up bone mineral density (BMD) measurements—to monitor the response to therapy—generally should be performed after 1 to 2 years. Note that BMD measurement has some precision error (up to 4% in the vertebrae and 6% in the hip)
	Younger postmenopausal women with 1 or more risk factors (other than being white, postmenopausal, and female)	This population is more likely to develop osteoporosis	
	Postmenopausal women who present with fractures	To confirm the diagnosis and determine disease severity	
American College of Obstetricians and Gynecologists (2002)	All women 65 years	To establish baseline BMD	In the absence of new risk factors, follow-up screening should take place every 2 or more years. The usefulness of repeat screening is greatest in older women, those with lower baseline BMD, and women with multiple risk factors
	Postmenopausal women younger than 65 years who have 1 or more risk factors for osteoporosis	These women face a heightened risk	
	Postmenopausal women who present with fractures	To confirm the diagnosis and determine severity	
North American Menopause Society (2002)	All women 65 years and older	High risk for osteoporosis	In untreated postmenopausal women, follow-up testing should take place at 3- to 5-year intervals. In treated women, this interval may be shortened to 2 years
	Postmenopausal women less than 65 with 1 or more risk factors: • Weight less than 127 lb • History of postmenopausal fracture in a site other than the spine • First-degree relative with a hip or spinal fracture	Women under 65 with risk factors should be screened only if result will influence the decision to treat	
	Premenopausal women with: • a history of low-trauma fracture or • a known cause of bone loss		
American Association of Clinical Endocrinologists (2001)	All women 40 years and younger who have had a fracture	These women may already have osteoporosis	If the baseline measurement is within normal limits, follow-up measurement should be performed in 3 to 5 years. If the patient is in a prevention program, testing should take place every 1 to 2 years until BMD is stable. If she is being treated for osteoporosis, BMD measurement should be yearly until stable and then every 2 years
	All women 65 years and older	To obtain a baseline measurement	
	Peri- and postmenopausal women with risk factors for fractures who are considering intervention	To determine whether therapy is indicated	
	Women with x-ray findings suggesting osteoporosis	X-rays cannot detect osteoporosis unless bone loss is 30% or more	
	Women initiating or already taking long-term glucocorticoid therapy	These drugs greatly increase risk of bone loss	
	All adult women with symptomatic hyperparathyroidism, nutritional deficiencies, or diseases associated with bone loss	These conditions greatly increase risk	

CONTINUED

As for the experts' opinions, the NOF recommends measuring the hip, AACE suggests the spine and proximal femur, and NAMS recommends the total hip, femoral neck, or spine.[1,14-16]

In my practice, when DXA is used, I prefer to measure the spine and femoral neck at a minimum. If there is a spinal deformity or another confounder, I obtain a forearm measurement.

PITFALL #6
Relying on bone density measurement alone

Although T and Z scores offer insight about a woman's bone density, they are not definitive measures of the fracture risk. For example, even when a 50-year-old woman and a 75-year-old woman have the same BMD, the older woman is far more likely to experience an osteoporotic fracture.[17] The greater propensity for falls among the elderly may partially explain this difference, but does not account for all of it. Obviously, there are other markers of risk besides BMD.

The take-home message is that, when estimating fracture risk, don't rely on bone densitometry alone. Rather, combine it with a thorough assessment of the patient's history and risk factors.

Nevertheless, bone-densitometry measurements are vital. They can establish a baseline of bone density that is helpful for monitoring progress with therapy.

If a patient with a low-trauma fracture is found to have normal bone density, some other cause of the bone deterioration must be sought.

Clinical recommendations

TABLE 2 lists risk factors for postmenopausal osteoporosis. If a woman under 65 years presents with any of these factors, screening should be considered.[10]

TABLE 3 lists the screening guidelines of ACOG, NAMS, and other organizations.

Appropriate screening is an important tool that must be customized to the patient. In my practice, I discuss the risks and benefits of each option with the patient and we decide together whether screening should be performed.

As a gynecologist, I am most familiar with the ACOG and NAMS screening guidelines. However, I consider it important to be familiar with all the major recommendations, since other physicians who also care for our patients may be using these other guidelines. ▪

REFERENCES

1. *Physician's Guide to Prevention and Treatment of Osteoporosis*. Washington, DC: National Osteoporosis Foundation; 2003. Available at: www.nof.org/professionals/clinical/clinical.htm Accessed October 8, 2003.
2. Melton LJ III, Chrischilles EA, Cooper C, et al. How many women have osteoporosis? *J Bone Miner Res*. 1992;7:1005-1010.
3. Melton LJ III. Epidemiology of fractures in North America. In: Christiansen C, Overgaard K, eds. *Osteoporosis*. Copenhagen, Denmark: Osteopress APS; 1990(1):36-41.
4. Looker AC, Wahner HW, Dunn WL, et al. Updated data on proximal femur bone mineral levels of US adults. *Osteoporosis Int*. 1998;8:468-489.
5. Melton LJ III. Epidemiology of hip fractures: implications of the exponential increase with age. *Bone*. 1996;18(3 Suppl):121S-125S.
6. Nguyen TV, Maynard LM, Towne B, et al. Sex differences in bone mass acquisition during growth: the Fels Longitudinal Study. *J Clin Densitom*. 2001;4:147-157.
7. ISCD clinical track syllabus, version 5.2, Sept 18, 2002:30-31 (JL Chervenak, MD).
8. Wasnich RD, Ross PD, Vogel JM, et al. *Osteoporosis: Critique and Practicum*. Honolulu, HI: Banyan Press; 1989:179-213.
9. Miller PD, Canalis E, Gass MLS. Osteoporosis: a new era in recognition and treatment. Annenberg Center for Health Sciences at Eisenhower; 2003. Available at: www.medscape.com/viewprogram/2664_pnt Accessed October 8, 2003.
10. Management of postmenopausal osteoporosis: position statement of the NAMS. *Menopause*. 2002;9:84-101.
11. A decision tree for the use of ERT/HRT in postmenopausal women: consensus opinion of the NAMS. *Menopause*. 2000;7:76-86.
12. Osteoporosis Task Force. AACE 2001 medical guidelines for clinical practice for the prevention and management of postmenopausal osteoporosis. *Endocr Pract*. 2001;7:293-312.
13. American College of Obstetricians and Gynecologists. *Committee Opinion #270: Bone Density Screening for Osteoporosis*. Washington, DC: *ACOG*; March 2002.
14. NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy. Osteoporosis prevention, diagnosis, and therapy. *JAMA*. 2001;285:785-795.
15. *Menopause Core Curriculum Study Guide*. 2nd ed. Mayfield Heights, Ohio: North American Menopause Society; 2002. Available at: www.menopause.org/edumaterials/studyguide/studyguide.html Accessed October 8, 2003.
16. National Institute of Arthritis and Musculoskeletal and Skin Diseases. *Fact Sheet: Exercise and Bone Health*. Washington, DC: NIH;2001. Available at: http://health.nih.gov/result.asp?disease_id-1161 Accessed October 9, 2003.
17. American College of Obstetricians and Gynecologists. *ACOG Educational Bulletin #246: Osteoporosis*. Washington, DC: ACOG; 1998.

Dr. Chervenak reports that she serves on the speaker's bureau for Berlex, Pfizer, and Wyeth, on the advisory boards of Berlex and Pfizer, and has received grant support from Albert Einstein College of Medicine, American College of Obstetricians and Gynecologists, Berlex, Pfizer, and Solvay.