New Guidance Aids Osteoporosis Screening

BY SHERRY BOSCHERT

FROM THE ANNALS OF INTERNAL MEDICINE

New federal recommendations on screening for osteoporosis provide more detail on when to screen women younger than age 65 years and – for the first time – point to a lack of data for screening decisions in men.

The U.S. Preventive Services Task Force updated its 2002 recommendations on osteoporosis screening to call for routine screening in all women aged 65 years or older and in any younger women whose fracture risk is equal to or greater than that of a 65-year-old white woman who has no additional risk factors (equivalent to a 9.3% or greater risk of fracture within 10 years). Previously, women younger than 65 would be screened if they were at least 60 years old with risk factors for fracture.

For the first time, the USPSTF evaluated the evidence for osteoporosis screening in men and found insufficient evidence to form any recommendation, Dr. Ned Colange, chair of the USPSTF, said in an interview. There's not enough evidence to recommend screening or treatment in men with no prior osteoporotic fractures, and "there's certainly not enough evidence to say, 'Don't' do it."

"While there's not a call to action, that's an important call for research," added Dr. Colange, president and CEO of the Colorado Trust Foundation, Denver.

In women, the recommendations do not say to stop osteoporosis screening at any specific age because the risk of fractures continues to increase with advancing age, and the minimal potential harms of treatment remain small. Clinicians who are considering treating older patients should consider data showing that the benefits of osteoporosis treatment emerge 18-24 months after starting treatment.

To predict an individual's risk for osteoporotic fracture, the USPSTF used the online FRAX tool, developed by the World Health Organization and the National Osteoporosis Foundation.

"The nice thing about the FRAX calculator is, the patient herself can determine that risk. It's available online. It uses measures that the woman should know," Dr. Colange said.

The FRAX tool estimates 10-year fracture risk based on easily obtained information such as age, body mass index, parental fracture history, and tobacco or alcohol use. It asks about results of dual-energy x-ray absorptiometry scans but does not require this information to calculate fracture risk.

Younger women can reach the new threshold for screening because of various risk factors. For example, a white woman would qualify for screening if she is 50 years old, smokes, drinks alcohol daily, has a BMI less than 21, and has a parental history of fracture. A 55-year-old white woman would need only a parental fracture history to warrant osteoporosis screening. A 60-year-old white woman who smokes and drinks alcohol daily would fit the 10-year-risk profile for screening (Ann. Intern. Med. 2011 Jan. 18 [Epub ahead of print]).

White women are more likely than are nonwhite women to develop osteoporosis and fractures. Although there are fewer data on nonwhite women, the USPSTF recommended screening all women at age 65 years because the consequences of failing to identify and treat low bone-mineral density are considerable and the potential risks of treatment are small.

There aren't enough data to recommend when to rescreen women without osteoporosis on their first screen, the USPSTF stated, but an interval of at least 2 years would be needed to assess a change in bone density, and longer still for better prediction of fracture risk.

The recommendations are based on a 2010 review of studies published since 2002 by a team at the University of Oregon Health and Science University's Evidence-Based Practice Center in Portland.

In a new effort at transparency, the USPSTF first published a draft of the new recommendations online last summer and invited public comment. They received more than 50 comments from individuals, professional organizations, advocates, and drug companies, which led the USPSTF to clarify its approach to fracture risk assessment in the final version, Dr. Colange said.

He said he has no pertinent conflicts of interest. ■

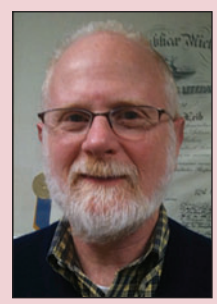
VIEW ON THE NEWS

Online Access Will Help Screening Calculations

For clinicians, the biggest change in the new screening recommendations may be the need to calculate the 10-year fracture risk in women aged younger than 65, two experts suggested in interviews.

"They will need to know what tools are out there to be able to figure out whether a younger person is at equal to or greater risk than a 65-year-old woman with no addition risk factors," Dr. Carolyn J. Crandall said.

The online FRAX calculator that was used by the USPSTF is a "really good tool" for this purpose, said Dr. Crandall. "Clinicians will have to access that tool in their clinics, which means they will either need Internet access at some point, or else they can download versions that are available for iPhone, or print versions that are available."



Dr. Edward S. Leib also commended inclusion of the FRAX tool in the guidelines, but cautioned that it has some weaknesses that were discussed at a November 2010 "position development conference" conducted jointly by the International Osteoporosis Foundation and the International Society for Clinical Densitometry.

Some important risk factors that could affect the 10-year fracture risk would not necessarily be reflected in the FRAX calculation, he said. In addition, the FRAX tool is based on an international model, and although it included U.S. databases, the calculations may not reflect risks in regional populations.

"For example, in a retrospective review of our population of 15,000 postmenopausal women having bone density studies over the past 10 years, we did not find a correlation between history of fracturing and parental history of hip fractures," he said.

Both Dr. Crandall and Dr. Leib also commended the USPSTF for acknowledging the need for more research in men, but Dr. Leib had hoped for more guidance. "It is known that the fracture risk in men who are age 75 is about equivalent to women who are age 65. I would have hoped that the USPSTF would have recommended screening at that age" despite the lack of primary prevention trials, he said.

DR. CRANDALL is professor of medicine at the University of California, Los Angeles. She said she has no pertinent conflicts of interest. DR. LEIB is professor of medicine at the University of Vermont, Burlington. He said he has no pertinent conflicts of interest.

Denosumab Gains New Indication, for Bone Metastases

BY ALICIA AULT

FROM THE FDA

The Food and Drug Administration has approved the monoclonal antibody denosumab (Xgeva), which is indicated for fracture prevention in postmenopausal women at high risk, for the prevention of skeletal-related events in patients with bone metastases from solid tumors.

Denosumab maker Amgen made the announcement. The drug was given a 6-month priority review, indicating that it was considered a major advance in treatment.

"Xgeva has a different mechanism of action than currently approved drugs aimed at reducing bone complications from cancer," Dr. Richard Pazdur, director of the Office of Oncology Drug Products in the FDA's Center for Drug Evaluation and Research, said in a written statement on the approval for the new indication.

A fully human monoclonal antibody with a unique mechanism of action, denosumab specifically targets the receptor activator of the nuclear factor kappa-B (RANK) ligand, the essential mediator of osteoclast fusion. The drug inhibits osteoclast formation, function, and survival, resulting in reduced bone resorption. The RANK ligand pathway was discovered by Amgen scientists in the mid-1990s, according to the company.

Amgen reported that bone metastases occur in 1.5 million cancer patients worldwide. They are most commonly seen in prostate, lung, and breast cancer. Denosumab was not approved for bone metastases related to multiple myeloma.

"A diagnosis of bone metastases is a major event for patients living with cancer, and the consequences can be devastating," Amgen chairman and CEO Kevin Sharer wrote in a statement. "We are pleased to offer this new advance to patients and their health care providers."

The approval of denosumab was based on three phase III head-to-head trials comprising 5,700 patients that compared the drug with zoledronic acid (Zometa).

The drug was superior to zoledronic acid in preventing skeletal-related events (SRE) in breast and prostate cancer. Some of those data were presented in June at the annual meeting of the American Society of Clinical Oncology. Denosumab was noninferior in preventing SREs in multiple myeloma and other solid tumors.

Adverse effects include hypocalcemia, fatigue, hypophosphatemia, and nausea. Osteonecrosis of the jaw can also occur.

Xgeva is delivered every 4 weeks as a 120-mg subcutaneous injection.

Because of the drug's expense, Amgen is launching a new patient assistance program. The Xgeva First Step Coupon Program will provide assistance to eligible patients who need help meeting a deductible, copayment, or coinsurance. The first injection would be covered and subsequent injections would cost a maximum of $25. ■