Guidelines to Take Broader View of Fracture Risk

BY BETSY BATES
Los Angeles Bureau

LA JOLLA, CALIF. — Management of osteoporosis is about to undergo some radical changes, including a new international focus on assessing fracture risk in clinical practice and an emphasis on higher doses of vitamin D, said Dr. Stuart L. Silverman at Perspectives in Women's Health sponsored by FAMILY PRACTICE NEWS, OB.GYN. NEWS, and INTERNAL MEDICINE NEWS.

"We're changing the whole way in which we approach osteoporosis in 2008," said Dr. Silverman, who serves with the International Working Group on Fracture Risk Assessment for the World Health Organization.

New guidelines are imminent that will encourage calculation of each patient's fracture risk based not only on bone mineral density and T score, but also on age, body mass index, family history, and other factors, he explained.

This composite fracture score, expected to be incorporated into software linked with dual-energy x-ray absorptiometry (DXA) equipment by late 2008, will provide a much more comprehensive and easy-to-understand risk profile for physicians and their patients, he said.

"Bone density technicians worldwide are going to start asking questions," said Dr. Silverman, an attending physician in the division of rheumatology at Cedars-Sinai Medical Center in Los Angeles.

"You will get a printout that says your patient has, [for example], a 10-year risk of hip fracture of 3%," he said.

The calculated 10-year risk for clinical fracture of the shoulder, forearm, or vertebra will also be included in a separate score.

Factors in the 10-year predictions of fracture risk include:

► **Age,** which can change the 10-year risk for a woman with a T score of –2.5 at the femoral neck from 2% at age 50 to 12.5% at age 80.

► **History of prior fragility fracture,** which increases fracture risk fivefold.

► **Low body weight/BMI.**

► **History of a hip fracture in the patient's mother or father.**

► **Lifetime history of ever using corticosteroids** at a dose of 5 mg/day or greater for 3 months or longer.

► **Current smoking.**

► **Consumption of more than two alcoholic drinks per day.**

► **Secondary osteoporosis** caused by a disease process or a drug such as an aromatase inhibitor.

In part, the new international guidelines were driven by pragmatism, because not every country has wide availability of DXA machines, and even when they are accessible, "bone mass is only a snapshot in time," said Dr. Silverman, who is also from the University of California, Los Angeles.

Factoring in other criteria that are found to influence fracture rates may prove to be more accurate and clinically useful to all physicians, not just those in China, where there are 300 DXA machines and more than 1 billion people. By comparison, there are 20,000 DXA machines and 300 million people in the United States.

"For a long time, the message you've been getting … is that your responsibility as a physician is reducing the risk of osteoporosis. We're not in that mode any more," he said.

"Your goal is not to reduce risk of osteoporosis, but to reduce the risk of fracture," he emphasized.

In the general population, only half of the people who fracture also have osteoporosis.

Strategies should focus not only on that 50%, but also on the other 50% of people who have only osteopenia or low bone mass and may be unaware of their risk.

One way in which risk can be reduced is through vitamin D supplementation recommendations, which are also likely to change soon, according to Dr. Silverman.

"Recently, we have all come to appreciate that we really need much more vitamin D," he said.

"We're pushing for 800 to 1,000 IU day, and I will tell you that a lot of us in the field … are actually taking more than that."

Findings from new studies show that vitamin D is useful not only for bones, but also for balance and possibly for reducing overall cancer risk, he noted.

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New Biologic Might Help Treatment of Patients With Severe, Refractory Gout

BY DIANA MAHONEY
New England Bureau

BOSTON — A new, long-acting interleukin-1 inhibitor being tested for multiple inflammatory conditions substantially decreased disease activity and pain associated with chronic active gout in a placebo-controlled pilot study.

If the findings are validated in larger investigations, the drug, rilonacept, may offer much-needed relief to patients with severe gouty arthritis who are refractory to other therapies, Dr. Robert Terkeltaub said in a late-breaking poster presentation at the annual meeting of the American College of Rheumatology.

Studies have shown that gout-associated uric acid crystals activate the NALP3 (cryopyrin) inflammasome, resulting in the production of active interleukin-1 (IL-1). Rilonacept, a fusion protein that is given by subcutaneous injection, attaches to and neutralizes IL-1 before the proinflammatory cytokine attaches to cell surface receptors and generates inflammation-triggering signals. Unlike some of the IL-1 blocking agents currently on the market, rilonacept is described as an IL-1–specific cytokine trap: Once the IL-1 attaches to rilonacept, it cannot bind to the cell surface receptors and is eliminated from the body with the rilonacept.

Based on data from preclinical studies and a clinical case series suggesting that blockade of the NALP3 inflammasome IL-1 pathway may be an effective treatment strategy for gout, as well as the promising results of a phase III trial of the drug in patients with cryopyrin-associated periodic syndrome (CAPS) arising from NALP3 mutations, Dr. Terkeltaub, professor of medicine at the University of California, San Diego, and colleagues, sought to assess the utility of the drug in chronic active gout in a multicenter, nonrandomized phase III trial.

The single-blind, placebo-controlled study enrolled 10 patients with severe chronic gout, mean age 62 years, with a mean disease duration of 13 years. Inclusion criteria were a diagnosis of chronic gouty arthritis for at least 6 months, at least one active joint for a minimum of 4 weeks, and a self-reported pain visual analog scale (VAS) of 3 or higher. The study protocol included a run-in period of 2 weekly subcutaneous injections of placebo, followed by 6 weekly injections of rilonacept. Gout activity was assessed using the Subject Pain VAS, Subject and Physician Global VAS, joint count, and serum levels of high-sensitivity C-reactive protein (hs-CRP).

At baseline, the mean and median Subject Pain VAS scores were 5.1 and 5.0, respectively. The mean and median changes in Subject Pain VAS from baseline to week 2 with placebo treatment were 0.25 and –0.25, respectively, and from week 2 to week 8 with rilonacept treatment were –3.2 and –2.25, respectively, Dr. Terkeltaub reported. During the active treatment period, 7 of the 10 subjects showed at least 50% improvement in Subject Pain VAS, and 6 of the 10 showed at least 75% improvement. By treatment week 8, serum CRP levels decreased by 59%, he said. At week 14, which was 6 weeks after the last dose of rilonacept, a trend toward baseline hs-CRP levels was observed.

Rilonacept treatment was not associated with deaths or severe adverse events. It generally was well tolerated with the most common adverse events being mild to moderate injection site reactions, Dr. Terkeltaub said.

The drug might be particularly useful in the treatment of "increasingly complex, refractory cases of gout," said Dr. Terkeltaub. Advanced age, comorbidities such as chronic kidney disease, and concomitant medications complicate management decisions, he noted, as does the lack of new Food and Drug Administration–approved treatment options for "difficult gout." The drug's ability to interfere with the IL-1 inflammatory process suggest it could be useful as an adjunct to uric acid–lowering drugs in gout, which sometimes lead to disease flares, he said.

Dr. Terkeltaub disclosed that he has had financial or other relationships with multiple companies, including TAP Pharmaceutical Products Inc., Savient Pharmaceuticals, ISIS Pharmaceuticals Inc., BioCryst Pharmaceuticals Inc., Novartis AG, and Regeneron Pharmaceuticals Inc., maker of rilonacept. ■

Height Loss Over 3 Years Predicts Osteoporosis in Patients Over Age 50 Years

VANCOUVER, B.C. — Measuring a patient's height during routine primary care visits may be one of the simplest and least expensive ways to predict osteoporosis risk and to guide screening, according to a study at Virginia Commonwealth University, Richmond.

Height loss of 1.5 inches (about 4 cm) or more over 3 years was associated with almost a doubling of osteoporosis risk in patients aged 50 years or older in the study of 1,039 primary care patients, reported Dr. Emmeline Gasink at the annual meeting of the North American Primary Care Research Group.

Mean height loss in the study population was 0.596 inches, said Dr. Gasink, a resident in the family medicine program at Riverside Healthcare System in Carrollton, Va.

Among the 16% of patients who had a height loss of at least 1.5 inches, 3% had a diagnosis of osteoporosis (odds ratio, 1.8) of developing the disease.

Some patients (13%) had significant height loss but were not diagnosed with osteoporosis. Another 8% did not have significant height loss but had osteoporosis, perhaps representing osteoporosis in a nonvertebral site, said Dr. Gasink in an interview at the meeting.

Nonetheless, a height loss of 1.5 inches or greater over 3 years provided a positive predictive value of 21% for osteoporosis, she said.

The study population was 71% female, so the risk may be slightly less for males. Also, people with low bone density tend to lose height more rapidly than do those with greater bone density.

Still, the overall conclusion of the study, together with findings from five longitudinal trials reviewed by Dr. Gasink, suggest a "strong relationship" between height loss and a new vertebral fracture, lending strength to her findings.

"Height measurement should definitely be a part of a yearly physical for patients 50 and older, as recommended by the U.S. Preventive Health Task Force," he said after the meeting. "As a family physician who follows these people over a period of years, [I suggest that] it would be an easy piece of data to help determine early risk factors for osteoporosis."

—Betsy Bates