BMD, FRAX Underestimate Risk in Diabetes

BY MARY ANN MOON

FROM JAMA

VITALS

Major Finding: In older adults with diabetes, any given BMD T score or FRAX score carried a higher fracture risk than did the same score in those without diabetes. The risk of hip fracture in a woman with diabetes was equivalent to that of a nondiabetic woman with a T score of about 0.5 units lower.

Data Source: Analysis of data from three prospective observational studies involving more than 16,000 older subjects in whom fractures were tracked for about 10 years.

Disclosures: This study was funded by an investigator-initiated grant from Amgen to Dr. Schwartz. She and her associates also reported receiving support from Novartis, Merck, Pfizer, Nycomed, and Roche.

Two measures of fracture risk – bone mineral density T score and FRAX score – are clinically useful in patients with type 2 diabetes, even though they tend to underestimate the increased fracture risk in this patient population, according to the results of a large study.

But to be more accurate for older adults with diabetes, these treatment and diagnostic algorithms should undergo "refinements," said Ann V. Schwartz, Ph.D., of the department of epidemiology and biostatistics, University of California, San Francisco, and her associates (JAMA 2011;305:2184-92).

Type 2 diabetes is known to be associated with a higher bone mineral density (BMD) but, paradoxically, also with a higher risk of fracture. There has been concern that established methods for predicting fractures "may not perform adequately in patients with type 2 diabetes," the researchers said.

In what they described as the first study to prospectively examine the relationship between BMD and fractures in older adults with type 2 diabetes, Dr. Schwartz and her colleagues analyzed data from three large, prospective, observational studies that all used radiology reports and radiographs to confirm fracture diagnoses. The three studies also ascertained subjects' diabetes status.

The Study of Osteoporotic Fractures (SOF) involved 7,926 white women at four U.S. clinical centers who underwent femoral neck-hip BMD measurement and were followed for the occurrence of fractures from 1988 through 2008. The Osteoporotic Fractures in Men Study (MrOS) involved 5,994 men at six U.S. clinical centers who underwent hip BMD measurement and were followed from 2000 through 2009. And the Health, Aging, and Body Composition (Health ABC) study involved 1,523 women and 1,442 men in their 70s, approximately half of whom were white and half black, who underwent hip BMD measurement and were followed from 1997 through 2007.

The FRAX (Fracture Risk Algorithm) scores were calculated for subjects in the SOF and MrOS studies by the World Health Organization (WHO) Collaborating Center for Metabolic Bone Disease, but not for subjects in the Health ABC study.

Dr. Schwartz and her associates found that both low BMD T score and high FRAX score were predictive of hip and nonspinal fracture in patients with diabetes. "However, for a given T score and age, those adults with diabetes had a higher risk of fracture than those without diabetes," they said.

For example, the risk of hip fracture in a woman with diabetes was equivalent to that of a nondiabetic woman with a T score of about 0.5 units lower.

The subjects with diabetes showed higher rates of fracture at any given FRAX score than did subjects who did not have diabetes, they noted.

"Interpretation of T score or FRAX score in an older patient with diabetes must take into account the higher fracture risk associated with diabetes. For example, ... a T score in a woman with diabetes is associated with hip fracture risk equivalent to a woman without diabetes with a T score of approximately 0.5 units lower," the investigators said.

"The FRAX score has been incorporated into U.S. guidelines for prevention and treatment of osteoporosis. The FRAX algorithm does not currently include type 2 diabetes as a risk factor for fracture, and our results indicate that use of the FRAX score in patients with diabetes will likely underestimate risk.

"An adjustment of this algorithm for type 2 diabetes seems justified, given the prevalence of diabetes among older adults," Dr. Schwartz and her associates said.

The reason diabetes raises fracture risk even as it appears to protect against loss of BMD is not understood. "Bone strength may be compromised through changes that are not captured with dual-energy x-ray absorptiometry, such as higher levels of advanced glycation end products in bone collagen. More frequent falls in older adults with diabetes could also increase fracture risk for a given BMD," they said.

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Evidence Doesn't Support High-Dose Vitamin D Intake

BY SHARON WORCESTER

EXPERT ANALYSIS FROM THE CONGRESS OF CLINICAL RHEUMATOLOGY

DESTIN, FLA. – More is not necessarily better when it comes to vitamin D.

"The optimal intake and blood levels are probably much more moderate than many have led us to believe," Dr. JoAnn E. Manson said at the meeting.

As a member of the 14-person Institute of Medicine Committee charged with developing a recently published report on dietary reference intakes of vitamin D and calcium, Dr. Manson assisted in a "rigorous comprehensive review" of more than 1,000 studies, and while many researchers and clinicians have argued that people need much higher levels than the 400-800 IU/day intake (depending on age) recommended by the IOM to promote optimal health, the available evidence simply has not borne that out, said Dr. Manson, professor of epidemiology at Harvard University and chief of the division of preventive medicine at Brigham and Women's Hospital, Boston.

Although some IOM report naysayers advocate for levels up to 6,000 IU/day – and the lay press is replete with stories touting vitamin D as a panacea, it is actually very difficult to find any solid data showing increased benefit with higher doses, she said.

In fact, the committee's findings indicate that adequate intake for infants through age 12 months is 400 IU/day, and that the Recommended Dietary Allowance for individuals aged 1-70 years should be at least 600 IU/day, and those over age 70 years it should be 800 IU/day. The upper intake levels are 1,000 and 1,500 IU/day for those ages 0-6 months and 6-12 months, respectively, 2,500 IU/day for those ages 1-3 years, 3,000 IU/day for those ages 4-8 years, and 4,000 IU/day for those over age 8 years, according to the IOM report (J. Clin. Endocrinol. Metab. 2011;96:53-8).

These minimum levels represent the intake needed to meet the vitamin D requirements of 97.5% of the population, and correspond to a serum 25-hydroxyvitamin D (25-OHD) level of 20 ng/mL, which the data indicate is the optimal level. At levels above the upper intake level, which correspond to a serum 25-OHD level of about 50 ng/mL, adverse effects have been reported, Dr. Manson said.

In WHI, adjusted hip fracture rates were highest in those with serum 25-OHD levels of 19.04 ng/mL and those greater than 28.3 ng/mL, and lowest in those between these levels.

Emerging evidence suggests excess intake may be associated with increased all-cause mortality, cancer, cardiovascular disease, falls, and fractures, she noted.

National Health and Nutrition Examination Survey (NHANES) data from 2008, for example, showed that age-adjusted mortality was highest among those with serum 25-OHD levels below 19 ng/mL in African Americans and below 27.5 ng/mL in the entire cohort, and that mortality decreased with increasing levels – but only to a certain point. At levels in the 50 ng/mL range for African Americans, and above 85 ng/mL in the entire cohort, mortality increased steadily.

Data on the effects of vitamin D on skeletal health, which provided the strongest basis for the IOM committee's report as they were most plentiful and convincing in terms of showing cause and effect (although evidence regarding numerous other diseases such as cancer, diabetes, and more were also considered), also suggest that too much vitamin D can lead to adverse effects. Women's Health Initiative findings, for example, show that adjusted hip fracture rates are highest among those with serum 25-OHD levels of 19.04 ng/mL and those greater than 28.3 ng/mL, and lowest among those between these levels (Ann. Intern. Med. 2008;149:242-50), Dr. Manson said.

In older men in the Osteoporotic Fractures in Men (MrOS) study, the adjusted risk of hip fractures was shown to be highest in those with serum 25-OHD levels less than 19 ng/mL (odds ratio 2.36, compared with those with levels greater than 28 ng/mL), with risk declining steadily in those with levels up to 28 ng/mL (J. Bone Miner. Res. 2010;25:545-53).

Other findings indicate the skeletal benefits of vitamin D are dependent on adequate calcium intake, which the committee determined is 200 and 260 mg/day for those aged 0-6 and 6-12 months, respectively; 700 mg/day for those aged 1-3 years; 1,000 mg/day for those aged 4-8 years, 19-70 years, and for women aged 19-50 years who are pregnant or lactating; 1,200 mg/day for those aged 51 years and older; and 1,300 mg/day for those aged 9-18 years, and for women aged 14-18 years who are pregnant or lactating.

An Agency for Healthcare Research and Quality report in 2009, for example, showed that three randomized controlled trials indicated no significant effect of vitamin D alone on fracture risk, but that one randomized controlled trial showed a benefit in those who received 800 IU of vitamin D_3 plus 1,200 mg/day of calcium for 2 years (odds ratio of fractures 0.80), Dr. Manson said.

Dr. Manson has received funding from the National Institutes of Health to conduct a large-scale randomized trial of vitamin D and omega-3 fatty acids. ■