Watch Bone Density in Breast Cancer Survivors

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MONTREAL — Aromatase inhibitors can wreak havoc on bone mineral density and increase the risk of fracture in patients being treated for breast cancer, Dr. Eugene McCloskey said at the annual meeting of the International Bone and Mineral Society.

Breast cancer has long been known to be linked with poor bone health, said Dr. McCloskey of the metabolic bone center at the University of Sheffield (England). In fact, results of the Women Health Initiative Observation Study revealed that postmenopausal women with a history of breast cancer have a higher risk for clinical fractures than do women with no such cancer history, even after adjusting for factors related to hormone levels, risk of fall, fracture history, medication use, comorbidity, and lifestyle (Arch. Intern. Med. 2005;165:552-8).

Although some of this might be explained by the fact that women with a history of breast cancer avoid hormone replacement therapy (which helps bone but may increase the risk of cancer relapse), it appears that the link between poor bone health and breast cancer is mediated mainly by the treatment used.

In premenopausal women, chemotherapy for breast cancer has been associated with reductions in bone mineral density when it induces ovarian failure, resulting in early menopause. Women who have already undergone menopause naturally do not generally experience ill effects of chemotherapy on bone.

Cancer treatments that induce ovarian failure have the worst effects on bone, Dr. McCloskey said, but these are followed closely by aromatase inhibitors (AIs), which have been shown to worsen the risk for both joint pain and fractures. Because of their superior efficacy and safety, these agents are becoming the standard treatment for early breast cancer, replacing tamoxifen, a drug that may have a beneficial effect on bone.

One solution to the effect of AIs on bone health that has been put forward is to combine these agents with tamoxifen. Unfortunately, adding tamoxifen to an AI has been shown to wipe out the additional cancer-fighting effect of the AI.

It appears that all currently available AIs have at least some negative effect on bone health. Both letrozole and anastrozole have been shown to increase the risk of fracture by about the same amount. There was some hope that the newest AI, exemestane, would have bone-sparing properties because of its androgeniclike metabolite. So far, however, evidence supporting that hope is, at best, weak. In fact, a 2007 update of a clinical trial with exemestane has shown a significantly increased risk of fracture among women taking exemestane, compared with those taking tamoxifen (Lancet Oncol. 2007;8:89-91).

Given that the benefits of AIs far outweigh their negative effect on bone health in women with breast cancer, ways to treat AI-related bone loss must be sought.

Given that the benefits of AIs far outweigh the disadvantages in many women with breast cancer, clinicians must look for ways to treat AI-related bone loss. Dr. McCloskey reviewed the literature on potential treatments and said that bisphosphonates remain the best bet when used at the same doses as those used to treat osteoporosis. Exercise, although associated with an improved quality of life, does not affect bone mineral density in women who are also taking bisphosphonates. Calcium and vitamin D supplementation is also important. Estrogen replacement could also be beneficial, but this therapy is controversial because of its possible association with an increased risk of cancer recurrence.

The question remains, which breast cancer patients require treatment to prevent fracture? Based on guidelines put forth by the American College of Clinical Oncology, women considered at high risk for fracture should receive treatment. Currently, the greatest known risk factors for fracture are age, geographical region, and treatment used. It remains unclear, however, exactly who is "high risk," and additional guidelines in this area are needed, Dr. McCloskey said. ■