Targeted Bone Scans Advised in Premenopause

Of 301 women referred for DXA because of possible increased risk, 41% had abnormal scans.

BY DIANA MAHONEY
New England Bureau

HARROGATE, ENGLAND — Targeted use of bone densitometry in premenopausal women can identify a significant number of patients who would benefit from bone protection, a study has shown.

Of 301 premenopausal women referred to London's Queen Elizabeth Hospital during a 4-year period for dual energy x-ray absorptiometry (DXA) because of possible increased risk of osteoporosis, 41% had abnormal scans, reported said Elizabeth Koshy, M.D., in a presentation at the annual conference of the National Osteoporosis Society.

Premature menopause accounted for 43 (14%) of the patients referred for DXA. Of these, 37% had abnormal scans.

Steroid use accounted for 19% of the referrals, of which 47% of the scans were abnormal. Of the approximately 14% of referrals based on family history, 27% resulted in abnormal scan. Osteopenia or previous fracture was the primary or coexisting indication for 37 or 12% of the patients, and among these, 54% were abnormal. Amenorrhea was the impetus for 11 (3.7%) of the scans, and 64% of these were abnormal, reported Dr. Koshy of Imperial College London.

The medical conditions associated with the highest proportion of abnormal scans were anorexia nervosa (57%) and inflammatory bowel disease (52%), Dr. Koshy noted.

A logistic regression analysis identified low calcium/vitamin D intake, a body mass index of less than 20 kg/m^2, and amenorrhea as significant risk factors associated with a lower bone mineral density. Such findings, Dr. Koshy said, suggest that "focused use of bone densitometry in women younger than 50 with any of these risk factors can help to identify patients with future fracture risk who may merit osteoporosis prevention."

In most premenopausal women, it may be that the best treatment option remains supplementation with calcium and Vitamin D, Dr. Koshy stated. However, "selective DXA does seem to identify a significant number who could benefit from additional intervention."

While much attention in recent years has been focused on the importance of routine bone density testing for postmenopausal women, the findings of this study add weight to the argument that younger women who have significant risk factors should be tested as well, "ideally at peak bone mass [between ages 21 and 35]," said Dr. Koshy. ■

Breast Cancer Prevention Seen With Extended Use of Raloxifene

BY BRUCE JANCIN
Denver Bureau

SAN ANTONIO — Raloxifene continued to markedly reduce breast cancer incidence in postmenopausal osteoporotic women over the course of 8 years in an extension of the landmark Multiple Outcomes of Raloxifene Evaluation trial, according to Silvana Martino, D.O., of the John Wayne Cancer Institute, Santa Monica, Calif.

An attempt to learn in the extended MORE study whether a single baseline serum estradiol measurement might identify subgroups of osteoporotic women who are particularly likely or unlikely to benefit from long-term raloxifene in terms of breast cancer risk reduction proved largely unsuccessful. The magnitude of reduction in invasive breast cancer with raloxifene turned out to be independent of estradiol level, although the absolute benefit was greater in women with a level of at least 5 pmol/L, Dr. Martino said at a breast cancer symposium sponsored by the Cancer Therapy and Research Center.

The incidence of invasive breast cancer was reduced 59% in the raloxifene group, compared with the placebo group.

DR. MARTINO

MORE was a 4-year randomized double-blind trial in roughly 7,700 women that led to marketing approval of raloxifene (Evista), which is a selective estrogen-receptor modifier (SERM) for prevention and treatment of postmenopausal osteoporosis. Among the predefined secondary end points in MORE was the incidence of invasive breast cancer, which was 72% less with raloxifene, compared with placebo.

Because breast cancer incidence was merely a secondary end point in MORE, however, an extension trial—the Continuing Outcomes Relevant to Evista (CORE) study—was undertaken to evaluate the safety and efficacy of an additional 4 years of raloxifene use, this time with invasive breast cancer prevention as the primary outcome measure. A total of 3,510 postmenopausal osteoporotic women randomized to raloxifene in MORE were assigned to an additional 4 years of the SERM at 60 mg per day. In addition, 1,703 women from the MORE placebo arm continued on placebo.

MORE and CORE were sponsored by Eli Lilly & Co. Dr. Martino serves as a consultant to the company.

During the 4 years of the extended trial, the incidence of invasive breast cancer was reduced 59% in the raloxifene group, compared with the placebo group. Estrogen receptor–positive invasive breast cancer was reduced 66% with raloxifene as well. Thus, the magnitude of risk reduction during the second 4 years of raloxifene therapy was similar to that noted during the initial 4 years.

This is significant because raloxifene for osteoporosis is essentially lifelong therapy. Moreover, the maximal recommended duration for the use of tamoxifen to reduce the incidence of breast cancer in high-risk women is 5 years.

During the 8 years of the combined MORE and CORE studies, the incidence of invasive breast cancer was reduced 66% with raloxifene, compared with placebo, while the rate of estrogen receptor–positive invasive breast cancer was 76% less in the raloxifene arm than the placebo arm.

There was no difference between the two study arms in the incidence of estrogen receptor–negative invasive breast cancer or noninvasive breast cancer in CORE, nor in the full 8-year combined experience, Dr. Martino continued.

In CORE, the incidence of thromboembolism in raloxifene-treated women was 2.9 events per 1,000 woman-years, two times greater than with placebo. The rates in MORE were similar to those in CORE. No new safety concerns emerged with the use of raloxifene during years 4-8 of treatment, she said.

The baseline serum estradiol data suggested the existence of a threshold effect, with women having an estradiol of at least 5 pmol/L—half of all study participants—deriving greater benefit in terms of reduction in invasive breast cancer.

Audience members noted that CORE didn't address the issue of whether raloxifene is beneficial for prevention of breast cancer in at-risk women who don't have osteoporosis. ■

Calcium, Vitamin D Intake Dismal in Breast Cancer Patients

BY BRUCE JANCIN
Denver Bureau

SAN ANTONIO — Inadequate calcium and vitamin D intake—and outright deficiencies—are even more common among breast cancer patients than in the general population, according to studies presented at the annual breast cancer symposium sponsored by the Cancer Therapy and Research Center.

This is particularly unwelcome because women with a history of breast cancer are at elevated risk for skeletal problems due to treatments that induce early menopause. The breast cancer population is also seeing rapidly rising adjuvant use of aromatase inhibitors, a class of drugs that can accelerate bone mineral loss.

Rachel S. Zinaman, a dietitian at Memorial Sloan-Kettering Cancer Center, New York City, noted that 2003 American Society of Clinical Oncology guidelines call for physicians to make screening for and treatment of osteoporosis in breast cancer patients a greater priority. She said it's time for physicians to step up and implement programs to increase breast cancer patients' awareness of the importance of calcium and vitamin D to bone health.

The increased vulnerability of breast cancer patients to calcium and vitamin D deficiencies was underscored by her retrospective chart review of 100 consecutive patients with early-stage breast cancer. The most disturbing finding was that only 10% of the women consumed the recommended daily minimum of 1,000 mg of calcium and 400 U of vitamin D. Indeed, 63% of the women had no significant dietary calcium intake at all, according to Ms. Zinaman.

That's even worse than in the United States at large. A National Institutes of Health consensus conference has concluded that 50%-60% of the older general population meets the established recommended daily intakes of calcium and vitamin D.

In a separate presentation, Marie E. Taylor, M.D., reported finding vitamin D deficiency in fully two-thirds of 233 patients with a current or past diagnosis of breast cancer who presented with a complaint of moderate to severe generalized musculoskeletal discomfort and stiffness with or without localized musculoskeletal symptoms.

The prevalence of vitamin D deficiency as defined by a serum 25-OH vitamin D level below 30 ng/mL varied by race. It was 57% among 162 white patients—but 91% among African Americans, said Dr. Taylor of Washington University, St. Louis.

A total of 65% of the women were hyperparathyroid as defined by a parathyroid hormone level in excess of 72 pg/mL.

Dr. Taylor speculated that the use of aromatase inhibitors may enhance vitamin D requirements and exacerbate a background vitamin D deficiency, resulting in the clinical symptoms of osteomalacia. She and her coinvestigators have prescribed vitamin D for the deficient women in her study cohort and are now following them to see if this leads to symptomatic improvement and better tolerance of adjuvant therapy.

The vitamin D replacement regimen they are using consists of 50,000 U of 25-OH vitamin D once weekly for 8-12 weeks, then cutting back to once every 2 weeks as maintenance therapy. This is coupled with the standard dietary recommendations for calcium and vitamin D intake via food sources and over-the-counter supplements. ■