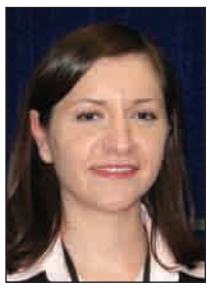
Early Oophorectomy Linked to Osteoporosis and Arthritis

BY BRUCE JANCIN

FROM THE SAN ANTONIO BREAST CANCER SYMPOSIUM

SAN ANTONIO – Bilateral oophorectomy in women younger than age 45 is associated with a subsequent doubled prevalence of osteoporosis and a similarly elevated rate of arthritis, compared with women with intact ovaries.

The findings from a new analysis of the Third National Health and Nutrition Examination Survey (NHANES III) had a further twist: The likelihood of having low bone mineral density and/or arthritis was even greater in the subgroup of women not on hormone replacement therapy following their surgically-induced abrupt menopause, Anne Marie McCarthy said at the symposium.



'Women who've had their ovaries removed at a young age can now be informed about their risk for bone loss.'

DR. McCARTHY

"The implication of our findings is that women who've had their ovaries removed at a young age can now be informed about their risk for bone loss over the long term. However, additional studies are needed to determine the frequency of monitoring for osteoporosis and the appropriateness of various preventive strategies in women who've had their ovaries removed," said Ms. McCarthy, a doctoral candidate in epidemiology at Johns Hopkins University, Baltimore.

The bone mineral density analysis included 3,660 women who underwent femoral neck bone density measurement by dual energy x-ray as part of their participation in NHANES III, which was conducted in a U.S. nationally representative sample in 1988-1994.

The age-standardized mean femoral neck bone density was significantly lower in women with oophorectomy before age 45 than in those with intact ovaries: 0.711 compared with 0.743 g/m^2 ($P = .017$). In a multivariate logistic regression analysis, women with early oophorectomy had an adjusted 1.78-fold increased likelihood of osteoporosis, compared with women with intact ovaries. Upon exclusion of hormone therapy users, the odds climbed so that oophorectomy before age 45 was associated with a 2.92-fold increased likelihood of osteoporosis, she said.

The Johns Hopkins researchers are doing a study in which they're measuring bone mineral density before and after prophylactic oophorectomy in women who carry high-risk BRCA mutations.

The arthritis analysis included 4,039 women. Those who had undergone oophorectomy were significantly more likely to report having been informed by a physician that they have arthritis, by a margin of 45.4% to 32.1% (*P* less than .001). In the subset of women with oophorectomy before age 45, the prevalence of arthritis was higher at 47.7%. In a multivariate analysis, women with oophorectomy before age 45 had a 1.78-fold increased odds of arthritis compared with those with intact ovaries. If they didn't use hormone therapy, however, those odds rose to 1.99-fold.

The researchers did not study the NHANES III subjects' medical records, so they were unable to say which forms of arthritis were more prevalent in the early oophorectomy group. Ms. McCarthy said the oophorectomy-arthritis association needs confirmation by other studies. There are animal data supporting such a link, she noted.

"We think estrogen is important for the health of cartilage, so losing estrogen can lead to inflammation and damage of cartilage, perhaps," Ms. McCarthy said.

Prophylactic bilateral oophorectomy is a widely accepted procedure to reduce the risks of breast and ovarian cancer in BRCA mutation carriers. But this indication accounts for only a small fraction of oophorectomies performed in this country. About 600,000 women per year undergo hysterectomy for indications such as fibroids, abnormal bleeding, endometriosis, and uterine prolapse, according to the Centers for Disease Control and Prevention, and about half of them have both ovaries removed at that time to prevent ovarian cancer.

NHANES III was conducted by the CDC. Ms. McCarthy said she had no relevant financial disclosures. ■

New Anticonvulsants Did Not Impair Bone Density in VA Study

BY BRUCE JANCIN

FROM THE ANNUAL MEETING OF THE AMERICAN SOCIETY FOR BONE AND MINERAL RESEARCH

SAN DIEGO – Newer anticonvulsants do not appear to be associated with the reduced bone mineral density seen with traditional anticonvulsants, based on results from a retrospective Veterans Affairs study.

Observational studies have linked traditional anticonvulsants, such as phenytoin, carbamazepine, and valproic acid, to reduced bone mineral density (Neurology 2004;62:2051-7). There are few data on this score regarding the newer anticonvulsants, including gabapentin, levetiracetam, lamotrigine, and topiramate, drugs increasingly prescribed not only for seizure disorders but for mood disorders and neuropathic pain as well.

Dr. Richard Lee and coworkers at Duke University Medical Center, Durham, N.C., performed a retrospective study of 1,799 patients who underwent bone mineral density measurement at the Durham VA Medical Center from 2005 through June 2010. The study population comprised 679 patients on newer anticonvulsants and 382 on traditional antiepileptic drugs.

Bone mineral density in patients on traditional anticonvulsants was progressively lower at the lumbar spine, total hip, and femoral neck with each additional 90-day period on medication during the previous 10 years, based on a multivariate logistic regression analysis.

In contrast, bone density increased at the lumbar spine and total hip with exposure to the newer nonenzyme-inducing anticonvulsants. There was a nonsignificant trend for increasing bone density at the femoral neck with greater exposure to these agents. For every 90 days on one of the newer nonenzyme-inducing anticonvulsants (lamotrigine, gabapentin, levetiracetam, pregabalin), dual-energy x-ray absorptiometry T scores increased significantly by 0.13 at the lumbar spine and by 0.087 at the total hip.

Topiramate, unlike the other newer anticonvulsants, is enzyme inducing, yet it also showed favorable bone-boosting trends that did not reach statistical significance.

The analysis was adjusted for age, race, body mass index, alcohol and tobacco use, prior fractures, and medical comorbidities. Dr. Lee said he had no disclosures. ■

Analysis Challenges Link Between Vitamin D Deficiency and Cancer

FROM THE SAN ANTONIO BREAST CANCER SYMPOSIUM

SAN ANTONIO – A new meta-analysis of 16 studies challenges the notion that breast cancer risk is inversely related to serum vitamin D level.

In 10 studies, vitamin D was measured before diagnosis of breast cancer; in the other 6 studies, blood samples were gathered for vitamin D measurement only after the diagnosis.

When data from all 16 studies were pooled, lower vitamin D levels were linked with a significant 1.5-fold increased rate of breast cancer (*P* less than .001). Thus, low vitamin D might be causally related to breast cancer, and, by extension, vitamin D supplementation might be an effective option for breast cancer prevention. But a major difficulty with this line of thinking arose when the two groups of studies were analyzed separately, Dr. Eitan Amir said at the meeting.

Only 1 of the 10 studies in which vitamin D was measured before diagnosis of breast cancer showed a significant relationship between low levels of vitamin D and subsequent increased likelihood of the malignancy. But all six studies in which serum vitamin D was measured after the diagnosis showed a significant inverse relationship. In the pooled analysis of these six studies, lower serum vitamin D was associated with a highly significant, 2.63-fold increased likelihood of breast cancer (*P* less than .001), said Dr. Amir of the University of Toronto.

Breast cancer cells have been shown to express vitamin D catalytic enzymes that may interfere with accurate measurement of serum levels of the vitamin, added Dr. Amir, who said he had no disclosures.

–Bruce Jancin

Low Vitamin D Levels Tied to Psychotic Symptoms in Teens

FROM THE ANNUAL MEETING OF THE AMERICAN ACADEMY OF CHILD AND ADOLESCENT PSYCHIATRY

TORONTO – Low vitamin D levels were linked with more psychotic features in mentally ill adolescents, in a small study.

Studies have linked vitamin D deficiency with seasonal affective disorder, schizophrenia, and depression, Dr. Barbara L. Gracious of Ohio State University, Columbus, said at the meeting. She and her colleagues studied 104 consecutive teens seen for acute or partial hospital stays for psychiatric symptoms over an 18-month period. Patients' average age was 15, 27% were male, and 73% were white. Overall, 72% had low vitamin D levels (25-OHD levels less than 30 ng/mL), and 34% were vitamin D deficient (25-OHD levels less than 20 ng/mL). By comparison, 9% of a cohort of teens from the NHANES (National Health and Nutrition Survey) were vitamin D deficient, the researchers noted.

Psychotic features were seen in 40% of the teens with low vitamin D levels and 16% of those with normal levels, a statistically significant difference. Black ethnicity was linked with vitamin D deficiency, but vitamin D–deficient black teens were not significantly more likely than were vitamin D–deficient white teens to exhibit psychotic features.

No studies indicate that vitamin D deficiency is a causative factor in psychosis.

Dr. Gracious is a consultant for Johnson & Johnson. None of her coauthors reported conflicts. The study was supported by the National Institutes of Health, Ohio State University, and the University of Rochester (N.Y.).

–Heidi Splete