Development of an estrogen-related dietary pattern and lifestyle score to examine breast cancer risk in postmenopausal women

By

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Introduction: Studies examining the association between individual dietary components and breast cancer have been inconclusive. The use of dietary patterns is a holistic approach which may yield stronger associations. We aimed to develop a dietary pattern based on an estrogen metabolite (EM) profile hypothesized to increase breast cancer risk (high unconjugated estradiol and low ratio of 2- to 16-hydroxylated EMs (2/16 ratio)). This estrogen-related dietary pattern (ERDP) was examined for associations with postmenopausal breast cancer in two study populations and was incorporated into an estrogen-related lifestyle score (ERLS) with other modifiable risk factors for breast cancer. Methods: EM and dietary data from 653 postmenopausal women from the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial (PLCO) were used to develop the ERDP. Reduced rank regression modeling was applied to identify food groups which explained the largest variation in the two EMs. The resulting dietary pattern was then applied separately in 28,304 and 37,752 women from PLCO and the Sister Study (SS), respectively, to examine associations with breast cancer using Cox proportional hazards models. The ERDP was incorporated into the ERLS with alcohol consumption, body mass index, and physical activity. Increasing scores of the ERLS represent a lower combined exposure to estrogen with a total range of scores from 0 to 6. Results: ERDP scores contained foods with pro-estrogenic weights (non-whole/refined grains, tomatoes, cruciferous vegetables, cheese, fish/shellfish high in ω-3 fatty acids, franks/luncheon meats) and foods with anti-estrogenic weights (nuts and seeds, other vegetables, fish/shellfish low in ω-3 fatty acids, yogurt,
coffee). In PLCO, a 1-unit increase in the ERDP score was associated with a 9%, 13%, and 13% increase in total (HR: 1.09, 95%CI: 1.01-1.18), invasive (HR: 1.13; 95%CI: 1.04-1.24) and estrogen receptor-positive (HR: 1.13, 95%CI: 1.02-1.24) breast cancer, respectively. No association was observed in SS. Participants in the highest ERLS category had a 34% (HR: 0.66; 95%CI: 0.56-0.78) reduction in risk of total breast cancer compared to the lowest category.

**Conclusions:** A dietary pattern correlated with a high-risk estrogen profile was positively associated with postmenopausal breast cancer within the cohort in which it was derived. Potential differences in other risk factors or dietary assessment tools may explain differences in associations seen between PLCO and SS. Adopting a lifestyle that has a lower combined exposure to estrogen is likely effective in reducing the risk of postmenopausal breast cancer.