Circulating estrogen metabolites and risk of breast cancer in postmenopausal women.


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BACKGROUND: It has been hypothesized that predominance of the 2-hydroxylation estrogen metabolism pathway over the 16α-hydroxylation pathway may be inversely associated with breast cancer risk.

METHODS: We examined the associations of invasive breast cancer risk with circulating 2-hydroxyestrone (2-OHE1), 16α-hydroxyestrone (16α-OHE1), and the 2-OHE1:16α-OHE1 ratio in a case-control study of postmenopausal women nested within two prospective cohorts: the New York University Women's Health Study (NYUWHS) and the Northern Sweden Mammary Screening Cohort (NSMSC), with adjustment for circulating levels of estrone, and additional analyses by tumor estrogen receptor (ER) status. Levels of 2-OHE1 and 16α-OHE1 were measured using ESTRAMET 2/16 assay in stored serum or plasma samples from 499 incident breast cancer cases and 499 controls, who were matched on cohort, age, and date of blood donation.

RESULTS: Overall, no significant associations were observed between breast cancer risk and circulating levels of 2-OHE1, 16α-OHE1, or their ratio in either cohort and in combined analyses. For 2-OHE1, there was evidence of heterogeneity by ER status in models adjusting for estrone (P ≤ 0.03). We observed a protective association of 2-OHE1 with ER+ breast cancer [multivariate-adjusted OR for a doubling of 2-OHE1, 0.67 (95% confidence interval [CI], 0.48-0.94; P = 0.02)].

CONCLUSIONS: In this study, higher levels of 2-OHE1 were associated with reduced risk of ER+ breast cancer in postmenopausal women after adjustment for circulating estrone.

IMPACT: These results suggest that taking into account the levels of parent estrogens and ER status is important in studies of estrogen metabolites and breast cancer.

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