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3294 / 14 - Urinary estrogen metabolites and long-term all-cause and cause-specific mortality following breast cancer diagnosis: A population-based study

April 2, 2019, 8:00 AM - 12:00 PM | Section 27

Presenter/Authors

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Disclosures

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Abstract

Background: Estrogen metabolites play a role in breast cancer development. Previous studies have particularly focused on the two competing metabolism pathways which yield metabolites 2-hydroxyestrone (2-OHE_1) and 16-hydroxyestrone (16-OHE_1). 2-OHE_1 has been shown to have antiestrogenic effects, but 16-OHE_1 has strong estrogenic and even genotoxic activity. No study has investigated their biologically plausible role in predicting prognosis/mortality among women diagnosed with breast cancer.

Methods: In the Long Island Breast Study Project**,** spot urine samples were obtained from 687 women diagnosed with first primary breast cancer (shortly after diagnosis) in 1996-1997. Urinary concentrations of estrogen metabolites 2-OHE_1 and 16-OHE_1 were measured using enzyme linked immuno-assay. Vital status was determined by the National Death Index through December 31, 2014; 244 deaths (84 breast cancer-specific and 80 cardiovascular diseases-specific) were identified. We used multivariable-adjusted Cox proportional hazards regression model to estimate hazard ratios (HRs) and 95% confidence intervals (95% CIs) for all-cause, breast cancer and cardiovascular diseases mortality as related to the two individual metabolites and their ratio (2-OHE_1/16-OHE_1). Multiplicative interactions with menopausal hormone therapy, body mass index, menopausal status, and breast cancer treatments were evaluated with likelihood ratio tests.

Results: During a median follow-up of 18 years**,** urinary concentration of the 2-OHE_1/16-OHE_1 ratio (> median of 1.8 vs. ≤ median of 1.8) was associated with reduced risk of all-cause mortality (HR=0.74, 95% CI=0.56-0.98) among women with breast cancer. This inverse association with the 2-OHE_1/16-OHE_1 ratio was also observed for breast cancer mortality (HR=0.73, 95% CI=0.45-1.17) and cardiovascular diseases mortality (HR=0.76, 95% CI=0.47-1.23), although the 95%CIs included the null. The 2-OHE_1/16-OHE_1 ratio-mortality associations did not significantly differ by menopausal hormone therapy, body mass index, and menopausal status at the time of urine collection ($P_{interation}$ >0.05). Consistent patterns of association were not observed between the individual metabolites and mortality outcomes.

Conclusion: To our knowledge, our study represents the first population-based epidemiologic evidence suggesting that the urinary concentration of the

2-OHE_1/16-OHE_1 ratio measured shortly after breast cancer diagnosis may be associated with improved overall mortality for breast cancer survivors. Future investigation is necessary to confirm our findings and to further understand the underlying biological mechanisms for estrogen metabolism–mortality relationships following breast cancer diagnosis.