Measuring hormones could help improve breast cancer risk prediction

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Including the levels of several hormones in currently used breast cancer risk prediction models improves prediction, and this could help better identify women who would benefit from chemoprevention, according to results presented here at the 12th Annual AACR International Conference on Frontiers in Cancer Prevention Research, held Oct. 27-30.

"Postmenopausal women with high levels of the hormones estrogens, androgens, and prolactin, have a higher risk of breast cancer than women with low levels," said Shelley S. Tworoger, Ph.D., associate professor in the Channing Division of Network Medicine at Brigham and Women's Hospital and Harvard Medical School in Boston, Mass. "At this point in time, however, no hormones are included in breast cancer risk prediction models. Our study suggests that adding estrone sulfate, testosterone, and prolactin levels may provide the biggest improvement in risk prediction for breast cancer."

To predict a woman's risk for breast cancer, the National Cancer Institute designed a statistical method called the Gail model, which takes into account factors that can be determined using a questionnaire or at a doctor's office, including number of pregnancies and age at menarche. Similar risk estimates can be made using another model, called the Rosner-Colditz model. These models, however, currently do not consider the levels of hormones in a woman's blood to predict the risk.

"The improvement in prediction when adding circulating hormone levels

was better than the improvement observed by other studies that included mammographic density and genetic factors," said Tworoger. "With additional studies verifying our results, we hope that current breast cancer risk prediction models could be modified to incorporate measurement of sex hormones, as well as mammographic density and genetic factors, when assessing a woman's breast cancer risk."

Tworoger and colleagues identified 473 postmenopausal women with invasive breast cancers and 770 matching controls, none of whom were using postmenopausal hormones at the time of blood draw, and analyzed levels of estradiol, estrone, estrone sulfate, testosterone, prolactin, and sex hormone binding globulin (SHBG) in blood samples taken one to 20 years before diagnosis.

The researchers initially used statistical modeling to identify the subset of hormones that were most associated with risk and then added these hormones to the Gail and Rosner-Colditz models to assess how much risk prediction improved. To do this, they measured the "area under the curve" (AUC). An AUC of 1 means that one can predict perfectly which women will get breast cancer over the next five years and which women will not; if the AUC is 0.5, that means that the model does no better than a flip of a coin, according to Tworoger.

The researchers found that including individual hormones improved the AUC of Gail score by 0.02 to 0.076 units and the AUC of Rosner-Colditz score by 0.002 to 0.039 units.

When they divided the data into a training set and a test set, simultaneous inclusion of estrone sulfate, testosterone, and prolactin levels improved prediction of invasive breast cancer using the Gail model by 0.086 units in the training set. Inclusion of estrone sulfate, testosterone, prolactin, and SHBG improved the prediction of estrogen receptor-positive breast cancer by 0.125 units and 0.083 units in the two

prediction models, respectively, in the test set.

"Because of the large number of postmenopausal women on whom we had many hormones measured, we were able to identify the best subset of hormones that could be examined in future studies to confirm our findings," said Tworoger. "We are getting closer to helping women better understand their risk for breast cancer so that they can make informed decisions about their health care."

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