

New predictive tool can help determine treatment of breast cancer patients

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A new predictive measurement, called a PEPI score, could bring good news to many women diagnosed with early stage breast cancer — a low PEPI (preoperative endocrine prognostic index) score could show that they have little risk of relapse and can safely avoid chemotherapy after surgery.

For others, a high PEPI score could warn that the risk of relapse after breast surgery is large and indicates that careful follow-up and aggressive therapy may be needed, say researchers at Washington University School of Medicine in St. Louis and collaborating institutions in Europe.

A team led by Matthew Ellis, M.D., Ph.D., a breast-cancer specialist with the Siteman Cancer Center at Washington University and Barnes-Jewish Hospital, developed and validated the PEPI score. Ellis asserts that predictive tools such as this are vital to breast cancer treatment and research.

"At present about 83 percent of patients are cured of breast cancer," he says. "The key is to identify that 83 percent so we can treat them with effective available therapies and focus our research efforts on the 17 percent who are resistant to current treatments."

The PEPI score was derived from tumor characteristics present after women with stage 2 and 3 breast cancer underwent four months of anti-estrogen therapy before having breast surgery. Presurgical anti-estrogen therapy with drugs such as tamoxifen and letrozole can shrink tumors

that depend on estrogen for their growth and potentially allow breast-conserving surgery. The majority of breast cancer patients have these estrogen receptor-positive tumors.

"This is a groundbreaking approach to predicting outcomes for patients with hormone receptor-positive breast cancer," says Ellis, the Anheuser-Busch Endowed Professor in Medical Oncology at the School of Medicine. "In essence, we are looking at how tumors respond to anti-estrogen therapy in the short term to predict how well patients will do in the long term."

The study was published in the Sept. 23, 2008 online issue of the *Journal of the National Cancer Institute*.

The PEPI score takes into account four factors present after presurgical anti-estrogen therapy to estimate risk of relapse and survival rates:

- the size of the breast tumor,
- whether cancer is present in nearby lymph nodes,
- how fast tumor cells are multiplying, and
- whether tumors lose their estrogen receptors.

The researchers found that women with a PEPI score of 0 had almost no risk of cancer recurrence during the five-year follow-up. They could safely avoid taking chemotherapeutic agents after surgery.

"Chemotherapy after breast surgery is used to reduce relapse risk," Ellis says. "Since the rate of relapse in this group is so low, there is little chance that chemotherapy would be helpful to them."

Women with PEPI scores of 4 or above are at very high risk of having their cancer return and should be given all appropriate post-surgical treatments, according to the report. Those with PEPI scores of 1 to 3 fall

in an intermediate group, and more studies are needed to determine the best courses of treatment for them, Ellis says.

PEPI scores are derived by assigning a certain number of points to each of the four PEPI factors. Patients with a PEPI score of 0 had a tumor that shrank to stage 0 or 1 or 2A after anti-estrogen therapy, and no cancer was present in lymph nodes. Their tumors also had low levels of a marker of cell growth and remained estrogen-receptor positive after anti-estrogen therapy.

Women with PEPI scores of 4 or more tended to have larger tumors after anti-estrogen therapy and were also likely to have cancer in lymph nodes, high rates of tumor cell growth and tumors that lost their estrogen receptors. These women had about a 50 percent chance of relapse.

An intermediate group with PEPI scores of 1 to 3 had either large tumors but few of the other dangerous markers or small tumors with more of the dangerous markers.

Further study will be needed to determine the relapse risk for this group as well as to validate the PEPI model for predicting breast cancer death. Preliminary data showed that, as expected, women with low PEPI scores survived longer on average than those with high PEPI scores.

"We're entering a completely different diagnostic situation now, where we can profile stage 2 and 3 tumors after anti-estrogen therapy and use the results to guide the next treatment steps," Ellis says. "Further research will determine whether a similar approach can predict outcomes in women with earlier stage breast cancers."

Source: Washington University School of Medicine

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