Breast Cancer Recurrence After Hormonal Treatment Linked To Initial Status

Women diagnosed with early estrogen-receptor positive (ER+) breast cancer are typically treated with surgery to remove the tumor and any affected lymph nodes. Then, chemotherapy and estrogen-blocking drugs such as tamoxifen or aromatase inhibitors are prescribed. These drugs are usually used for five years, after which they are likely to be halted. But sometimes the tumors recur — sometimes as much as 20 years later — and the question arises as to whether or not they should have remained on the drug treatments and if so, for how long. However, there can be adverse side effects from longer treatment with tamoxifen or aromatase inhibitors such as pulmonary embolus or uterine cancer for the former and bone fracture for the latter. Thus, simply advising all women to continue them past the five year threshold would be problematic — but which patients (if any) should be advised to continue drug treatment isn't clear.

To gain insight into this question, Dr. Hongchao Pan from the University of Oxford in England and colleagues performed a meta-analysis of women enrolled in 88 studies of breast cancer. These women all had ER+ disease and were scheduled to receive endocrine therapy (tamoxifen and/or an aromatase inhibitor) for 5 years and then stop. A total of nearly 63,000 women from these studies were included in the analysis. At the 5-year mark, they were all event-free and were then followed for the next 15 years.

Characteristics of the cancers investigated included size (T1-less than 2 cm, or T2-2 -5 cm), and the number of lymph nodes that had been determined to have cancer cell metastases (N0-N9). Thus a small tumor with no lymph nodes involved would be T1N0.

The investigators found that the original TN descriptor was predictive of the risk of distant recurrence of the cancer, and both tumor size and nodal involvement were important. For
example, women whose tumors fell into the T1 category had an increased risk of 13 percent if no nodes had been involved, 20 percent with 1 to 3 involved nodes, while those with four to 9 nodes with metastases had an increased 34 percent risk of recurrences.

If the women had T2-sized tumors, the corresponding increased risks were 19 and, 26, and 41 percent respectively. In addition, they found that the risk of death from breast cancer was similarly linked to the women's initial TN status.

The authors stated:

Our main aim was to determine whether we could identify subgroups of women who stop endocrine therapy after 5 years in whom long-term risks are so small that any additional benefits from extended therapy would be unlikely to outweigh the additional side effects. However, even among women with T1N0 disease, the cumulative risk of distant recurrence was 13 % during years 5 to 20.

However, there were some caveats about the studies that contributed to the meta-analysis. In particular, not all participants had completed the full 5 years of drug therapy — which could have biased the results towards increased risk of recurrence. Still, the investigators concluded that the TN status is strongly predictive of future recurrence. Clearly, women with larger tumors and more involved lymph nodes and their physicians should consider these result when planning long term followup and treatment strategies.

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