Is Mammography-Detected Breast Ca Less Deadly?

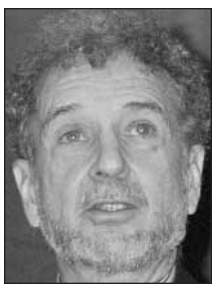
BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

Women whose breast cancers were detected by screening mammography were 53% less likely to die of breast cancer over a 10- to 15-year period than those whose cancers were detected symptomatically, Donald Berry, Ph.D., and his colleagues have reported.

The study of more than 150,000 women doesn't mean that screening mammography is beneficial, however, Dr. Berry told this newspaper. The real reason behind the survival shift, he said, is that mammography picks up tumors that grow more slowly and are less biologically lethal than those discovered symptomatically.

Dr. Berry, chairman of the department of biostatistics and applied mathematics at the University of Texas, Houston, and his coinvestigators examined survival outcomes in three large North American breast cancer screening trials containing about 152,000 women: the breast cancer screening trial of the Health Insurance Plan of Greater New York (HIP) and two Canadian National Breast Screening Studies (CNBSS-1 and CNBSS-2).

The HIP screening was carried out in the 1960s, while both CNBSS trials were conducted in the 1980s. Follow-up ranged from 15 to 20 years (J. Natl. Cancer Inst. 2005;97:1195-203). The researchers looked at the occurrence of screen-detected cancers, cancers detected in control groups (no screening mammography), and interval/incident cancers (cancers detected either less than 1 year or more than 1 year after the last negative screen).



The relative risk of breast cancer death was 53% greater for women with interval or incident cancers.

DR. BERRY

There was a clear shift toward earlier stage cancers in the screening groups. In the HIP trial, 76% of screen-detected cancers were stage I, compared with 51% of interval/incident cancers and 49% of cancers in the control group. Control subjects and women who failed to attend their screenings had the highest percentage of stage III/IV cancers—14% and 22%, respectively.

In the CNBSS-1, 55% of screen-tested cancers, 40% of interval/incident cancers, and 47% of cancers in the control group were stage I. In the CNBSS-2, 62% of the screen-detected cancers, 44% of the interval/incident cancers, and 47% of the cancers in the control group were stage I. In both trials, the highest percentage of stage III/IV cancers occurred in the interval/incident group (about 20%). Tumor sizes were smaller in the screening groups in all three studies; there was a significantly higher proportion of negative lymph nodes among women with screen-detected cancers in all three studies.

These characteristics reflect lead-time bias, Dr. Berry said, and he adjusted the analysis to compensate for this. However, even after adjustment for tumor characteristics, women whose cancers were detected by screening had the longest survival time. The relative risk of breast cancer death was 53% greater for women with interval/incident cancers and 36% greater for those in the control group with cancer than for women with screen-detected cancers.

The survival advantage seems to arise from the mammogram's tendency to detect less-aggressive tumors, he said. "Cancers found via screening include a higher proportion of slowly growing tumors, some of which might never be found by other means." Paradoxically, this "overdiagnosis bias" means that the study cannot discern whether screening mammography is beneficial.

"In addition to detecting the lethal tumors, screening also detects some [tumors] of the nonlethal variety," Dr. Berry said. Some of the women with screen-detected nonlethal tumors may have unnecessary surgery or other treatment; still, the researchers said, "A woman whose nonmetastatic tumor was detected on a mammogram has reason to be happier than a woman who had a tumor with the same characteristics detected symptomatically."

The investigators noted several limitations of the study. Since all women were screened in the 1960s or 1980s, the trials not only used less-sophisticated mammographic techniques, but they also did not reflect tumor grading with modern biomarkers. ■

DCIS Patients Tend to Overestimate Their Risk

BY DIANA MAHONEY
New England Bureau

BOSTON — Many women with newly diagnosed ductal carcinoma in situ harbor grossly inaccurate perceptions of the breast cancer risks they face, which in turn can influence their decision making and health behaviors as well as psychosocial outcomes, reported Ann H. Partridge, M.D.

The most common type of noninvasive breast cancer, ductal carcinoma in situ (DCIS) is a relatively low-risk disease. With early detection, the 5-year survival rate is nearly 100%, "thus it has a very small impact on a woman's overall survival," Dr. Partridge said in a presentation at a breast cancer meeting sponsored by Harvard Medical School.

In contrast, a longitudinal study has shown the perception of risk among women diagnosed with the condition to be "substantial," she said.

In a cohort of 499 women newly diagnosed with DCIS participating in a study of psychosocial concerns, risk perceptions, and health behaviors, 55% believed that it was at least moderately likely the disease would recur within 5 years. Additionally, 68% of the women reported a moderate or greater likelihood of lifetime recurrence; 38% thought they were at risk for invasive disease in the next 5 years; 53% perceived a greater lifetime risk of invasive disease; and 28% indicated a moderate or greater likelihood of their breast cancer spreading to other parts of their body, reported Dr. Partridge of the Dana-Farber Cancer Institute in Boston.

A multivariate model showed that anxiety at baseline, as measured by the Hospitalized Anxiety and Depression Scale and the Revised Impact of Event Scale, was associated with the belief that DCIS would spread. These perceptions were independent of age, race, education, marital status, employment, financial status, comorbidity, anxiety, oncology consultation, treatment, and satisfaction with treatment.

Preliminary follow-up data indicated that patients' risk perceptions persisted over time, with nearly one-quarter of those surveyed at 18 months believing there was a moderate or greater chance that DCIS would spread to other parts of their body. "Some patients' perception of risk increased over time and others' decreased without a consistent trend," Dr. Partridge said.

Multivariate analysis of the 18-month data showed that nonwhite race, less than full-time employment status, lack of satisfaction with treatment, and having taken tamoxifen were associated with heightened risk perceptions.

Given the possibility that the pervasive risk misperceptions could have a negative impact on psychosocial functioning and health-related decision making, "clinicians caring for women with ductal carcinoma in situ should be aware of these inaccurate perceptions" and should encourage women to communicate their fears and provide education and support for dispelling altered risk beliefs, Dr. Partridge said. ■

Switch to Anastrozole After Tamoxifen Beneficial in Hormone-Sensitive Cancer

BY DOUG BRUNK
San Diego Bureau

Postmenopausal women with hormone-sensitive early breast cancer who were switched to anastrozole after 2 years of tamoxifen treatment were 40% less likely to experience disease recurrence, compared with those who remained on tamoxifen, according to a combined analysis of two large European studies.

Tamoxifen resistance might be overcome by a treatment change, or aromatase inhibitors might be a better option.

DR. JAKESZ

"There are two possible explanations for this finding: tamoxifen resistance might be overcome by a change in treatment; or aromatase inhibitors might simply be a better treatment option, since they reduce peripheral estrogen concentrations to extremely low levels, whereas tamoxifen is a partial agonist," wrote the investigators, who were led by Raimund Jakesz, M.D., of Vienna Medical University, Austria.

He and his associates studied the combined results of the Austrian Breast and Colorectal Cancer Study Group trial and the German Adjuvant Breast Cancer Group trial, which were both randomized, prospective, open-label trials with similar inclusion criteria. Eligible patients were postmenopausal women with locally radically treated invasive or minimally invasive breast cancer without previous chemotherapy, hormone therapy, or radiotherapy. The cancers were hormone sensitive (Lancet 2005;366:455-62).

Of the 3,224 women in both trials who had completed at least 2 years of adjuvant oral tamoxifen 20-30 mg daily, 1,618 went on to receive 1 mg of the aromatase inhibitor anastrozole daily while 1,606 continued to receive 20-30 mg of tamoxifen daily for the remainder of their adjuvant therapy. The primary end point was event-free survival, defined as time to relapse at any site or incidence of contralateral breast cancer.

After a median follow-up of 28 months, there were 67 events in women who were switched to anastrozole, compared with 110 in those who remained on tamoxifen. This translates into a 40% decrease in the risk of an event for those who were switched to anastrozole, compared with those who remained on tamoxifen. "We noted significantly more fractures and significantly fewer thromboses in patients treated with anastrozole than in those who received only tamoxifen," Dr. Jakesz and his associates wrote. "However, we also noted a nonsignificant tendency toward fewer emboli and endometrial cancers in women on anastrozole."

They also pointed out that the results of their investigation "apply only to those women who have successfully completed 2-3 years' adjuvant therapy for early breast cancer. They are not applicable to newly diagnosed patients, and should not be used to support a treatment strategy of starting with tamoxifen with the intention of changing to an aromatase inhibitor after 2 or more years. Overall, however, the results of these studies show the efficacy advantages attached to treatment with an aromatase inhibitor." ■