

Breast Density Predicts Recurrence After DCIS

BY BRUCE JANCIN
Denver Bureau

SAN ANTONIO — Women who are treated for ductal carcinoma in situ are threefold more likely to develop invasive breast cancer in the other breast if their breasts are mammographically dense, Dr. E. Shelley Hwang said at a breast cancer symposium sponsored by the Cancer Therapy and Research Center.

The clinical implication of this new observation is that women undergoing treatment for ductal carcinoma in situ (DCIS) are particularly likely to benefit from preventive strategies aimed at contralateral breast risk reduction—such as adjuvant systemic hormone therapy with tamoxifen—if they have high breast density, according to Dr. Hwang of the University of California, San Francisco.

DCIS affects roughly 60,000 women per year in the United States. It is treated aggressively because it is considered a precursor to invasive breast cancer. Today, roughly one-third of women with DCIS receive lumpectomy without radiation, 38% get lumpectomy with radiotherapy,

and 28% undergo mastectomy. Of women with DCIS, 10%-15% progress to invasive cancer in 10 years. However, the overall prognosis for women treated for DCIS is excellent, with a long-term breast cancer-specific mortality of 1%.

The search is on for easily monitored risk factors for cases of DCIS that are likely to progress to invasive disease. Breast density, which can be categorized simply and reproducibly via the widely used four-level American College of Radiology Breast Imaging Reporting and Data System (BIRADS) of mammographic classification, seemed like a promising candidate.

Twin studies indicate breast density has a heritable component that explains 60% of individual variation; exposure to endogenous and exogenous hormones also plays an important role.

To examine the relationship between breast density and invasive recurrence risk

following local therapy for DCIS, Dr. Hwang studied 3,274 women diagnosed with DCIS as a result of screening mammography conducted at a National Cancer Institute Breast Cancer Screening Consortium site. They were followed for a mean of 42 months following lumpectomy plus adjuvant radiotherapy or lumpectomy alone. During that time, there were 133 invasive recurrences.

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DR. HWANG

BIRADS score of 1 or 2 and women who had BIRADS scores of 3 or 4. Thus, ipsilateral invasive recurrence was independent of breast density.

In contrast, three-quarters of all contralateral invasive cancers occurred in women who had BIRADS scores of 3 or 4. In a Cox proportional hazard analysis adjusted for age and the use of radiother-

apy, women with high breast density were 3.1 times more likely to develop contralateral invasive cancer than were those with BIRADS scores of 1 or 2. This increased risk remained stable over time, contradicting the notion that a masking phenomenon was at work.

The increased risk of contralateral invasive recurrence in DCIS patients with high breast density was present regardless of whether the women received adjuvant radiation. Patients with BIRADS scores of 3 or 4 who received radiotherapy were 3.6 times more likely to experience contralateral invasive cancer than were those with BIRADS scores of 1 or 2.

Similarly, women who did not receive radiotherapy were 2.7-fold more likely to develop contralateral invasive cancer if they had high breast density compared with low breast density.

However, the risk of ipsilateral invasive cancer was essentially the same regardless of whether a patient did or did not receive radiation, and regardless of how dense her breasts were.

Dr. Hwang's study was supported by the National Institutes of Health. ■



Breast Cancer Recurrence May Be Tied to Biopsy Type, Narrow Surgical Margin

BY MITCHEL L. ZOLER
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PALM BEACH, FLA. — Narrow surgical margins and use of core-needle biopsy appeared to correlate with recurrent breast cancer in a series of 223 women with ductal carcinoma in situ who were treated with skin-sparing mastectomy.

The series included seven patients with local recurrences (3%). The seven local recurrences were not found until they were palpable masses detected by the patients themselves, and six of the seven local recurrences were invasive cancers, Dr. Grant W. Carlson said at the annual meeting of the Southern Surgical Association. When the primary tumor was noninvasive, a ductal carcinoma in situ (DCIS), having six of seven local recurrences develop into invasive cancers is "unsettling," said Dr. Carlson. "This is a potentially curable disease," he added.

He and his colleagues reviewed the outcomes of all women with DCIS who were treated at Emory University in Atlanta with skin-sparing mastectomy and immediate reconstruction between 1991 and 2003. The average follow-up was 82 months, said Dr. Carlson, a professor of surgery at the university. None of the patients received adjuvant radiation therapy.

During the first phase of the series, suspected tumors were confirmed with a wire-localization biopsy. The most recent 59 patients were diagnosed with stereotactic core-needle biopsy.

A total of 11 patients (5%) had recurrences. Seven of the recurrences were local, two were regional, and two were at distant sites.

The rate of total recurrences and of local recurrences was similar to rates previously reported for women with DCIS who underwent conventional mastectomy.

Dr. Carlson and his colleagues explored a possible link

between local recurrence and several potential risk factors. The only significant association they found was between biopsy type and local recurrence. Among women with local recurrences, 71% had undergone a core-needle biopsy, compared with a 25% rate of core-needle biopsies in women without recurrences, Dr. Carlson said.

The investigators did not find a statistically significant link between recurrence and other potential risk factors, including age of 50 or less, tumor size of 40 mm or more, tumor grade, or presence of necrosis in the tumor, although each of these markers was associated with a nonsignificant increase in the incidence of local recurrence.

A greater, nonsignificant link was seen between a narrow surgical margin and recurrence. Surgical margins

of 1 mm or less occurred in 29% of women who had local recurrences, compared with 9% of women who did not have recurrences.

As a result of this experience, Dr. Carlson now recommends that women treated with skin-sparing mastectomy for DCIS undergo some form of routine follow-up imaging. Mammography is useful when the images are read by an experienced mammographer who is not misled by the artifacts of a reconstructed breast. An alternative is MRI, which makes it easier to find recurrent tumors early in women with reconstructive implants.

Other measures that Dr. Carlson has instituted are to seriously consider using radiation adjuvant therapy in women whose tumor excisions had narrow surgical margins of less than 1 mm, and to excise the track from the core-needle biopsy to remove any tumor cells that may have leaked into the track.

This report is important because it includes more patients than all of the previously published reports on DCIS recurrences combined, commented Dr. Kelly M. McMasters, chairman of the department of surgery at the University of Louisville (Kentucky). ■

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Many Breast Ca Patients Have Renal Impairment: Watch for Nephrotoxicity

SAN ANTONIO — Renal insufficiency is extremely common in breast cancer patients—and so is the use of potentially nephrotoxic anticancer drugs, Dr. Vincent Launay-Vacher reported at a breast cancer symposium sponsored by the Cancer Therapy and Research Center.

He presented the results of a large multicenter French observational study that sounded a cautionary note regarding the heightened potential for adverse renal effects in patients undergoing cancer treatment.

The French IRMA study included all patients with solid cancers who presented to 15 participating cancer centers during two designated 15-day periods in 2004. Of the 4,684 cancer patients, 1,898 had breast cancer.

Fifty-two percent of the breast cancer patients had renal impairment as defined by a creatinine clearance of less than 90 mL/minute by the Cockcroft-Gault formula, as did 51% by the Modification of Diet in Renal Disease (MDRD) Study formula.

Ten percent of the breast cancer patients weren't on any anticancer drugs at the time of the study. Ninety percent of the rest were on at least one anticancer drug requiring a dose adjustment in the setting of renal impairment or for which no data are available regarding use in renally impaired patients. Seventy-seven percent of women received at least one potentially nephrotoxic drug, according to Dr. Launay-Vacher of Salpêtrière Hospital, Paris.

Moreover, 44% of recipients of potentially nephrotoxic drugs had a serum hemoglobin level below 12 g/dL, and 21% had a hemoglobin of less than 11 g/dL. This becomes clinically relevant because anemia magnifies the nephrotoxicity risk, the physician added.

The findings in the overall IRMA study population were similar to those in the subgroup with breast cancer. Overall, 60% of cancer patients had a creatinine clearance of less than 90 mL/minute. Eighty percent of cancer patients were receiving one or more nephrotoxic drugs.

—Bruce Jancin