Breast Ca Diagnosis

Ultrasound *from page 1*

lessen trauma and cost, while limiting mammography would reduce cost and unnecessary radiation.

Dr. Lehman described the two studies in a press briefing at the annual meeting of the Radiological Society of North America. Both were retrospective reviews of data from the University of Washington.

In the first analysis, investigators reviewed all breast exams performed on women under age 30 from Feb. 1, 2002, to Aug. 30, 2006, and found 1,091 lesions in 830 patients. Three malignancies were found, and all were identified as suspicious by ultrasound. No malignancy was found in any patient with a negative, benign, or probably benign ultrasound.

The rate of biopsy was high, and the yield was low. For example, of the 140 patients with a Breast Imaging–Reporting and Data System (BI-RADS) 3 lesion (probably benign), 46 (33%) underwent tissue sampling, and none of these lesions was found to be malignant.

Mammography was not indicated in this setting, and close surveillance might be a preferred alternative to tissue sampling, the authors concluded.

The second study, which included women aged 30-39 years, also found ultrasound to have 100% sensitivity. In this study, investigators reviewed 1,327 lesions in 1,032 patients, finding that 98% (1,301/1,327) were benign and 2% (26/1,327) were malignant. Ultrasound and mammography had been used to evaluate 91% (1,207/1,327) of cases, yet all cancers at the site of clinical concern were detected by ultrasound and none by mammography alone.

In a solitary case (1/1,327, 0.08%), mammography resulted in detection of a malignancy in an asymptomatic area.

The authors concluded that ultrasound has 100% sensitivity in evaluating women 30-39 years of age presenting with focal signs or symptoms.

Mammography helped one woman with 'an area of cancer identified in another region of the breast, but in all other women, there was no added value of the mammogram.'

"The added value of mammography in this setting is less apparent," Dr. Lehman said. "It did help one woman who had an area of cancer identified in another region of the breast, but in all other women, there was no added value of the mammogram."

In answer to a question from the audience, Dr. Lehman said that ultrasound is recommended as a diagnostic tool and not as a screening tool.

"We strongly recommend women have screening mammography annually, age 40 and older, and if they are shown to be at high risk, that they add MRI to that. We don't recommend ultrasound as a screening tool," she said, because the specificity of ultrasound is low.

At the scientific session, Dr. Michael Portillo, one of Dr. Lehman's coauthors, was asked whether his institution had changed its practice in the wake of this study.

"At this point we're still following the [American College of Radiology guidelines], but we are currently considering changing our practice," said Dr. Portillo, who worked on the project while a fellow at the University of Washington.

Scientific session moderator Dr. Ellen B. Mendelson of Northwestern University in Chicago commented: "For every patient 30 years old or older who we'd biopsy, we'd do mammography first.

"In a patient younger than that … the first imaging exam you'd do for something palpable, or that is symptomatic, would be ultrasound. Then, depending on what you find … we would go to bilateral mammography first, before biopsy," she said.

Both studies were funded by the University of Washington. Dr. Lehman disclosed work as an instructor with General Electric Co. Dr. Portillo had nothing to disclose. ■

Multigene Assay Spots Patients Who Can Forego Chemo

BY BRUCE JANCIN

SAN ANTONIO — The Oncotype DX 21-gene recurrence score assay can identify a sizeable subgroup of postmenopausal women with node-positive, estrogen receptor–positive breast cancer who are at such low risk of recurrence that they are unlikely to benefit from adding chemotherapy to 5 years of adjuvant tamoxifen, a study showed.

The 21-gene test is already widely ordered to help physicians select breast cancer patients with axillary node–negative disease who need adjuvant chemotherapy, an application endorsed in American Society of Clinical Oncology guidelines since 2007 (J. Clin. Oncol. 2007;25:5287-312).

The new study is the first to show that the test is also prognostic for patients with positive lymph nodes, Dr. Kathy S. Albain noted in presenting the results at the San Antonio Breast Cancer Symposium.

Such patients now routinely receive adjuvant chemotherapy as standard practice. The new study challenges that approach by demonstrating that patients with a low 21-gene recurrence score—irrespective of their number of positive nodes—appear able to safely forego chemotherapy, with its toxicities and other costs, said Dr. Albain, professor of medicine at Loyola University, Maywood, Ill.

Conversely, patients with a high recurrence score on Oncotype DX showed marked clinical benefit from subsequent adjuvant chemotherapy in this new retrospective analysis of prospectively collected data from the phase III Southwest Oncology Group (SWOG)-8814 study.

Dr. Albain reported on 367 participants in SWOG-8814, all of whom were postmenopausal with node-positive, estrogen receptor–positive disease. This analysis included the 148 women randomized to 5 years of adjuvant tamoxifen and the 219 assigned to chemotherapy with cyclophosphamide, doxorubicin, and fluorouracil followed by tamoxifen (CAF-T) whose stored tumor specimens contained sufficient RNA for analysis using Oncotype DX.

Of the 367 women in the study, 40% were at low risk, with a recurrence score of less than 18. In this group, CAF-T offered no advantage over the 60% 10-year disease-free survival rate among the patients who were assigned to tamoxifen alone (hazard ratio 1.02). Nor did CAF-T provide significant benefit over the 49% 10-year disease-free survival with tamoxifen alone in patients who had an intermediate recurrence score of 18-30 (HR 0.72).

In contrast, in the 32% of subjects who had a recurrence score of 31 or more, the 10-year disease-free survival rate was 55% with CAF-T, significantly greater than the 43% rate with tamoxifen alone (HR 0.59).

The same trends were seen in terms of 10-year overall survival: no significant advantage for the addition of adjuvant chemotherapy in patients with a low or intermediate recurrence score, but pronounced benefit in the high-score subgroup (68% in the CAF-T group vs. 51% in the tamoxifen alone group).

Similarly, 10-year breast cancer–specific survival in women with a high recurrence score was 73% in the CAF-T group and 54% with tamoxifen alone, but didn't differ according to the assigned adjuvant regimen in patients with low or intermediate recurrence scores.

Larger prospective randomized studies using state-of-the-art chemotherapy and aromatase inhibitors are needed to definitely establish the prognostic role of Oncotype DX and other multigene assays, according to Dr. Albain.

Dr. Eric P. Winer said the SWOG-8814 analysis, while retrospective and involving a relatively small number of patients, is reassuringly consistent with other study findings.

"I personally think that for the vast majority of patients who have a low recurrence score—even those who have larger tumors and positive lymph nodes—the benefit of chemotherapy is likely to be extremely small," Dr. Winer said at a subsequent satellite continuing medical education symposium supported by AstraZeneca, Genentech, and Genomic Health.

"That being said, faced with a 55-year-old woman who has a 6-cm cancer and nine positive lymph nodes, in late 2009 I still find it difficult not to use chemotherapy," admitted Dr. Winer, chief of the division of women's cancers at the Dana-Farber Cancer Institute and professor of medicine at Harvard University, both in Boston.

Dr. Joyce O'Shaughnessy said she orders the Oncotype DX assay selectively, mainly for confirmation in women she's already disinclined to treat with adjuvant chemotherapy. "I like to handpick the patients. The patient who is over age 60, with an estrogen receptor/progesterone receptor–positive, HER2-negative tumor that is slowly proliferative—that's somebody I'd be comfortable ordering the recurrence score for, and if it were low I'd be comfortable just going with endocrine therapy," explained Dr. O'Shaughnessy of US Oncology, Dallas.

The SWOG-8814 analysis was funded by the National Cancer Institute and Genomic Health, which markets the Oncotype DX test. Dr. Albain disclosed serving on the speakers bureau for Genomic Health, as well as receiving research funding from the company.

Simultaneous with her San Antonio presentation, the study results were published online in Lancet Oncology (doi:10.1016/S1470-2045(09)70314-6).

A separate analysis of SWOG-8814 also was published online in the Lancet (doi:10.1016/S0140-6736(09)61523-3). In this study, Dr. Albain and coworkers concluded that CAF chemotherapy followed by tamoxifen appears to be more effective than CAF with concurrent tamoxifen. ■

MY TAKE

Promising Test Raises Questions

This is a pacesetting genetic test for the future of medical practice. Although it costs nearly $3,000 per test, it has the potential to identify a large group of patients who could safely avoid the morbidity and costs that are associated with adjuvant chemotherapy.

DR. GOLDEN

Clearly, testing patients without acting on the results of the test would not be cost effective. Should payers insist that patients who receive a low score on this test forgo chemotherapy or repay the cost of the test?

Will patients have enough faith in the test to choose the less intensive care path, even with values near cutoff scores?

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