Update: SLN Biopsies In, PET/CT Scans Out

BY PATRICE WENDLING

HOLLYWOOD, FLA. — Recommendations in favor of sentinel lymph node biopsy and against PET/CT scanning are key changes in the latest update to the breast cancer guidelines from the National Comprehensive Cancer Network.

Sentinel lymph node biopsy (SLNB) was an option in the staging of clinically negative axilla breast cancer in previous guidelines, but now becomes the standard recommendation, Dr. Robert W. Carlson reported at the National Comprehensive Cancer Network (NCCN) annual conference on clinical practice guidelines and quality cancer care.

The move is the most important change in the updated guidelines because it impacts 95% of women with newly diagnosed breast cancer, he said in an interview. A recent study reported that by 2005, 65% of women who presented with stage I/II breast cancer had their axilla evaluated by sentinel lymph node biopsy (J. Natl. Cancer Inst. 2008;100:462-74).

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SLNB allows identification of the sentinel lymph node in more than 95% of cases in the hands of an experienced clinician, has a false-negative rate of less than 5% in recent series, and results in an axillary recurrence rate of less than 1% if the sentinel lymph node is negative, said Dr. Carlson, professor of medicine at Stanford (Calif.) University and chair of the NCCN breast cancer panel. The procedure also results in edema rates of about 7%, compared with 10%-20% among women undergoing formal axillary dissection.

Dr. Carlson acknowledged that SLNB surgeons are not available in all parts of the United States, SLNB may not be generalized to other countries because of resource limitations, and the recommendation could conceivably promote the adoption of SLNB by providers who are not skilled in the procedure.

The guidelines specify, however, that patients who are sentinel node candidates without access to an experienced sentinel node team should be referred to an experienced team.

For candidates with access to an experienced team who are node positive at the time of diagnosis, the recommendation is for an axillary lymph node dissection. An alternative is to perform a fine-needle aspiration or core biopsy of the suspicious lymph node and, if it is found to be negative, to proceed to sentinel lymph node mapping and evaluation, he said.

For patients who have access to an experienced team and have node-negative axilla, the recommendation is for sentinel node mapping; only if the sentinel node is positive or could not be identified would the woman then go on to formal axillary dissection, he said.

SLN biopsy is reasonable to perform in women with pure ductal carcinoma in situ who are undergoing mastectomy or other surgeries that can compromise the ability to perform a SLN procedure should invasive cancer be found, according to a footnote in the new guidelines.

PET and PET/CT Scanning

The panel spoke out on the use of PET and PET/CT scanning—an area in which it had been silent in previous guidelines. The decision was prompted by the overuse of PET and PET/CT scans, despite their having relatively low sensitivity and specificity in the evaluation of breast cancer, Dr. Carlson said. Sensitivity was only 20%-60% in early disease in two studies; in a review of nine studies in recurrent/metastatic disease, sensitivity was 81%-93% and specificity 75%-100%.

"It's a situation where a positive result is at least as likely to mislead you as it is to assist you in determining optimal treatment sequences," he said.

As for what's fueling the overuse, Dr. Carlson suggested in an interview that it may be that the technology is new and the scans are simple to order and very expensive, so there are financial rewards for those who perform the test frequently.

"We live in a society where if something has a high price tag, we assume it has value. And so I think that a lot of patients misunderstand that the newest technology is not necessarily the best technology, even if it is extraordinarily expensive," he said.

The panel added a footnote stating that "PET or PET/CT is not indicated in the staging of clinical stage I/II or operable stage III breast cancer."

Based on level IIb evidence, PET/CT is considered an "optional study" in stage III inoperable cancer and may be most helpful where standard staging studies are equivocal or suspicious.

Another new footnote states that PET or PET/CT scanning "should generally be discouraged for the evaluation of metastatic disease, except in those clinical situations where other staging studies are equivocal or suspicious. Even in these situations, biopsy of equivocal or suspicious sites is more likely to provide useful information."

Genetics

Genetic counseling was upgraded from a footnote to a recommended component of the general work-up, if the patient is at high risk for hereditary breast cancer. The major reason for the emphasis is to make sure physicians perform genetic testing, Dr. Carlson said.

"Doing genetic testing is not really part of breast cancer treatment, but it is so central to what we should be doing that it's important to do and consider early," he said. "There are also some subtleties, in terms of how you treat the breast locally, that are affected by whether the BRCA1 and BRCA2 mutations are present … and might shift the balance towards mastectomy, as opposed to breast conservation."

The panel also recommended that the general work-up should include determination of tumor estrogen/progesterone (ER/PR) status and HER2 status. The recommendation is based on two studies utilizing a 21-gene assay (Oncotype DX) in women with hormone receptive–positive, node-negative cancer who receive tamoxifen alone or with chemotherapy.

In the NSABP (National Surgical Adjuvant Breast and Bowel Project) B-14 trial, women with a low recurrence score based on their genetic test had superior survival at 10 years, compared with those with intermediate or high recurrence scores. In the NSABP B-20 trial, only those women with high recurrence scores benefited from tamoxifen plus chemotherapy.

"The recurrence score might be able to stratify women who will benefit from the application of cytotoxic chemotherapy," Dr. Carlson said.

He went on to note, however, that major use of the assay is limited to ER-positive, HER2-negative, node-negative disease because the assay has been validated only in this setting and in women who were treated with tamoxifen and first-generation chemotherapy, and because most HER2-positive disease has a high recurrence score. There were insufficient data to make a recommendation on the 70-gene Mammoprint assay, he said.

Paclitaxel

Doxorubicin/cyclophosphamide followed by paclitaxel every 3 weeks was removed from the list of recommended adjuvant regimens based on data showing that the thrice-weekly regimen was inferior to paclitaxel every 2 weeks or weekly.

HER2-Targeted Therapy

The panel declined to add either trastuzumab or lapatinib in combination with endocrine therapy to its algorithm as preferred agents for the treatment of ER-positive, HER2-positive,

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metastatic disease. They cited a lack of evidence demonstrating an overall survival benefit with the agents, and concerns that early use of HER2-targeted therapies in combination with endocrine therapy may negatively impact survival benefit from trastuzumab therapy downstream.

The subject was revisited after the Food and Drug Administration recently added an indication to the lapatinib (Tykerb) package insert for lapatinib in combination with letrozole (Femara) for patients with advanced, ER-positive, HER2-positive cancer in whom hormone therapy is indicated. Overall NCCN panel recommendations regarding HER2 targeted therapy and endocrine therapy will be announced at a later date, Dr. Carlson said. ■

__Disclosures:__ Dr. Carlson disclosed receiving research support from and being a consultant for AstraZeneca Pharmaceuticals LP, receiving grant support from BiPAR Pharmaceuticals and Genentech Inc., and being a consultant for Pfizer Inc.

VERBATIM

'This study on the decline in hours worked per week by physicians highlights a gathering storm in the field of primary care medicine. This finding comes at a time when hospitals are under increasing pressure to decrease the workload and hours worked by residents—and by extension—practicing physicians.'

Dr. E. Albert Reece, p. 46