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Axillary burden of disease following false-negative preoperative axillary evaluation

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Abstract

BACKGROUND: Preoperative axillary ultrasound (AUS) and fine-needle aspiration (FNA) are sensitive and specific for breast cancer nodal metastases. We hypothesize that false-negative result predicts minimal axillary disease (≤ 2 +nodes).

METHODS: A retrospective review of breast cancer patients receiving AUS identified T1/T2 tumors and positive sentinel node with axillary dissection. Chi-square analysis was performed using Fisher's exact test.

RESULTS: Of 903 AUS cases, 384 had T1/T2 tumors. False-negative rate of AUS ± FNA was 48% and 45%, respectively. Of 384 cases, 73 were sentinel node positive and had axillary dissection; 55 (75.3%) were invasive ductal carcinoma (IDC). Negative predictive value for greater than or equal to 2 nodes was 71% in IDC versus 44% for in non-IDC patients. Sixteen (29.0%) IDC patients had greater than or equal to 3 positive nodes versus 10 (55.5%) non-IDC ($P = .05$) patients.

CONCLUSION: The high negative predictive value for AUS with FNA for IDC suggests that the AUS plus FNA interpretation may be better limited to the ipsilateral nodes of IDC.

With widespread adoption of the sentinel lymph node procedure, efforts are now focusing on preoperative identification of axillary metastasis as this may alter surgical and medical approaches, from neoadjuvant chemotherapy to breast reconstructive options.[1] Currently, both physical evaluation and breast-directed imaging modalities including ultrasound, mammography, and magnetic resonance imaging are being used to evaluate the presence and extent of disease. Because physical examination has poor sensitivity (35% to 41%) and high false-positive rates (53%) with regards to the axilla, recent attention has turned toward focused axillary imaging.[2]

As a result, the use of preoperative axillary ultrasound has increased in breast cancer patients.[3] Axillary ultrasound has a sensitivity of 50% to 70% and a specificity of 87% to 95% for axillary metastasis, far superior to physical examination alone.[4,5] Multiple studies have shown that in combination with fine-needle aspiration, the sensitivity, specificity, positive predictive value, and

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negative predictive value of axillary ultrasound are increased significantly, with specificity and positive predictive value up to 100%.[4,5] The sensitivity of axillary ultrasound has been shown to increase with not only the size of the primary breast lesion, but also the size of the nodal metastasis and the number of lymph nodes involved.[4,6] Axillary ultrasound coupled with fine-needle aspiration has a false-negative rate of 25% with reduced sensitivity for micrometastatic disease (axillary metastasis between .2 and 2 mm) resulting in a higher false-negative rate for that subgroup.[7,8] This supports the idea that axillary ultrasound and a fine-needle aspiration generally identify gross nodal disease. If metastases are identified preoperatively, patients generally forego sentinel lymph node biopsy proceeding directly to axillary lymph node dissection.[8–11]

Recently, the American College of Surgeons Oncology Group (ACoSOG) Z0011 results suggested that select node-positive patients on sentinel node biopsy could forego axillary node dissection. This trial did not specify the use of axillary ultrasound findings, allowing for a wide variation of its use in participating centers.[12] Based on these data, incorporation of axillary ultrasound and percutaneous biopsy (via either fine-needle aspiration or core biopsy) remains an open issue in preoperative planning. A retrospective patient study by Ibrahim-Zada et al[13] supports the use of preoperative axillary ultrasound in the Z0011 population for identification of macrometastatic lesions and eliminating the need for intraoperative sentinel lymph node testing. We hypothesize that in patients without palpable adenopathy, a negative axillary work up of axillary ultrasound (with or without fine-needle aspiration) is predictive of minimal axillary disease ($\leq$2 positive nodes), even if patients are pathologically node positive at definitive surgery.

Methods

A single-institution, institutional review board approved, prospective database of patients receiving axillary ultrasound from 2004 to 2013 was reviewed for female breast cancer patients with clinical T1 or T2 tumors and node negative by physical examination. Node-negative patients on clinical examination were identified based on their documentation in the medical records. Patients who underwent preoperative chemotherapy, had recurrent breast cancer, had incomplete medical records, or had inconclusive fine-needle aspiration (2 cases) were excluded. Clinical breast tumor size was determined by both imaging and clinical examination with priority given to magnetic resonance imaging followed by ultrasound, mammography, and then physical examination.

All images and procedures were either completed or confirmed at a single tertiary comprehensive cancer center by breast fellowship-trained radiologists. Abnormal lymph nodes on axillary ultrasound were defined as having cortical thickening greater than 3 mm, rounded shape, or loss/replacement of the fatty hilum (Fig. 1). If an abnormal node was identified, ultrasound-targeted lymph node biopsy was performed, primarily by fine-needle aspiration. At our institution, the current practice is to obtain ipsilateral axillary ultrasound on all invasive breast cancers greater than 2 cm on clinical examination or radiographic imaging; for smaller lesions, axillary ultrasound is performed based on clinical suspicion.

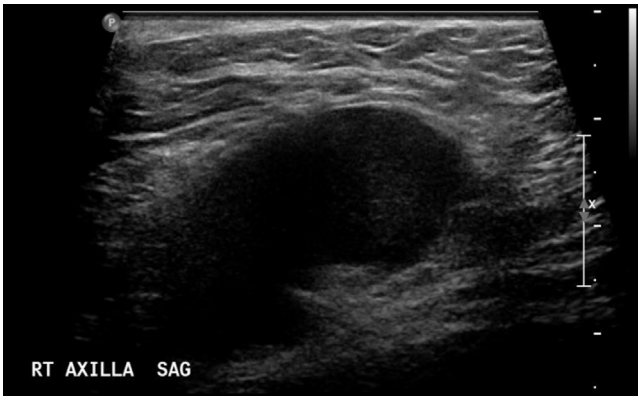

Figure 1 Ultrasound imaging of abnormal lymph node (image courtesy of A. Chau, Department of Breast Imaging; H. Lee, Moffitt Cancer Center and Research Institute).

Patients with a negative evaluation ($\pm$ fine needle aspiration) but a subsequent positive sentinel node biopsy and completion axillary lymph node dissection were selected for further evaluation. Both breast conserving surgery and mastectomy patients were included. Clinical, radiologic, and pathologic data were collected, including axillary ultrasound and fine-needle aspiration results, tumor histology and grade, hormone receptor status, and total number of lymph nodes with metastasis. Minimal axillary disease was defined as less than or equal to 2 positive nodes after sentinel lymph node biopsy plus axillary lymph node dissection. Data were then analyzed by chi-square test using Fisher's exact test. Fig. 2 illustrates the case distribution.

Results

The study population consisted of 384 women who fit the inclusion criteria; 24.5% (94/384) had breast conserving surgery, and 213/384 (55.5%) patients had a negative axillary ultrasound. The sensitivity and specificity for axillary ultrasound and fine-needle aspiration in this population was 55% and 93%, respectively. The negative predictive value was 78%, with a false-negative rate of 48% (Table 1).

From this population, 115 cases had negative preoperative axillary work up and a subsequent positive sentinel lymph node biopsy. Forty-two patients had a positive sentinel lymph node biopsy but declined completion axillary lymph node dissection. The remaining 73 patients went on to completion axillary lymph node dissection; this subset was selected for further analysis. The median age