The Value of Ultrasonographic Detection for Metastatic Axillary Lymph Nodes in Breast Cancer

Jung Hee Shin, M.D., Asiry Hwang, M.D., Hye-Young Choi, M.D., Seung Yon Baek, M.D.

Purpose: We evaluated the significance and accuracy of sonographic detection of metastatic axillary lymph nodes (LNs) in breast cancer.

Materials and Methods: We retrospectively reviewed the sonographic findings and postoperative results of axillary LNs in 47 patients with breast cancer. The sonographic criteria for metastatic LNs were defined as the loss of the echogenic hilum and any uneven cortical thickness of over 3 mm. We analyzed the correlation between the preoperative sonographic findings and the postoperative results of the LNs.

Results: Out of 47 patients, 22 patients showed 43 sonographic metastatic LNs. Among these 22 patients, 18 patients had 183 histopathologically proven metastatic LNs. The pathological examination of the remaining 25 patients revealed metastatic LNs in 6 patients. The overall sensitivity, specificity and accuracy of ultrasonography for detecting metastatic axillary LNs in breast cancer were 75%, 82.6% and 78.7%, respectively. As the number of metastatic LNs detected on sonography increased, the number of histologically proven metastatic LNs increased.

Conclusion: Ultrasonographic evaluation of axillary LNs in breast cancer can provide relatively accurate information about the presence or absence of metastasis. Therefore, it is useful to decide the initial staging and treatment planning of patients with breast cancer.

Index words: Breast neoplasms
Ultrasonography
Lymph Nodes

Axillary lymph node status is important for staging, prognosis and determining the optimal treatment for breast cancer. Axillary lymph node metastasis occurs in 30-40% of all patients with breast cancers [1, 2]. A physical examination alone is neither a sensitive nor reliable way to ascertain lymph node status because the metastatic lymph nodes are often not palpable and reactive lymph nodes may be mistaken for metastasis [3, 4].

There are several imaging techniques that have been used to evaluate lymph nodes, including mammography, computed tomography (CT), MR imaging, lymphangiography and scintigraphy, and all these methods have unsatisfactory sensitivity and specificity. For example, the sensitivity of mammography ranges from 18-41% and the specificity ranges from 80-90% [4-6]. The sensitivity of CT is 50% and its specificity is about 75% [7]. Among the imaging modalities, ultrasound has been the most frequently investigated because of its noninvasive nature and the ease of its use for evaluating the axil-
la. It is used to detect alterations in the size, shape and contours of lymph nodes, as well as detecting changes in the morphology and texture of the nodal cortex: it can thereby identify the presence of the underlying metastasis [6].

The purpose of this study was to evaluate the significance and accuracy for the sonographic detection of metastatic axillary lymph nodes in breast cancer.

**Materials and Methods**

During a 3-year period, forty-seven patients with breast cancer underwent formal axillary lymph node dissection together with or immediately after lumpectomy or mastectomy, and all the patients were histologically proved as having an invasive breast cancer. In these 47 patients (46 females and one male), the preoperative ultrasonographic (US) images and postoperative histologic findings of the axillary lymph nodes were analyzed. We excluded those patients with unavailable preoperative US findings. The patients’ ages ranged from 25 to 75 years (mean age: 46 years).

All the scans were performed by an experienced radiologist with real-time ultrasound using a 10 MHz linear array probe XP 10 (Acuson, Mountain view, CA), or an HDI 5000 (Advanced Technology Laboratories, Bothell, WA). A careful search for adenopathy was performed along the axilla in the longitudinal and transverse planes using the axillary vessels as landmarks. On preoperative US, we evaluated the size of the breast cancer, the presence of echogenic hilum, the uneven degree of cortical thickness and the number of axillary lymph nodes. Sono-graphic criteria of metastatic lymph nodes were defined as the loss of the echogenic fatty hilum and any uneven cortical thickness over 3 mm. We then analyzed the correlation between the preoperative US findings that were suggestive of metastatic lymph nodes and the postoperative results. For the control study (48 lymph nodes in 31 negative cases), the ratio of the shortest axis to the longest axis (S/L), the cortical thickness, and the obliteration of the echogenic hilum of the lymph nodes were compared between the metastatic and benign lymph nodes. For statistical analysis, Spearman’s correlation coefficients were obtained. Correlation was considered significant at the 0.01 level.

**Results**

Out of 47 patients, 22 patients showed 43 lymph nodes that were suggestive of metastasis on US examination. Axillary dissection revealed metastasis in 24 of 47 patients (51.1%). The correlation between the ultrasonography and histopathology is presented in Table 1. Among the 22 sonographically positive patients, 18 patients (18/22, 81.8%) had histopathologically proven breast cancers with 183 metastatic lymph nodes (Fig. 1). The remaining 25 patients revealed no evidence of metastatic lymph nodes on US (Fig. 2), but 6 of these patients (6/25, 24%) were histologically confirmed as having 11 metastatic lymph nodes. Each of these 6 patients had three or less metastatic lymph nodes on histologic examination. One of four false positive patients was confirmed histologically as having tuberculous lymphadenitis. Three false positive patients showed reactive hyperplasia. The overall sensitivity of ultrasonography for the detection of metastatic axillary lymph nodes in breast cancer was 75%, the specificity was 82.6%, the accuracy was 78.7%, the positive predictive value was 81.8% and the negative predictive value was 76%. The greater the number of nodes that were suggestive of metastasis on US, the greater was the number of histo-

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<thead>
<tr>
<th>Table 1. Correlation between Ultrasonography and Histology</th>
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<tbody>
<tr>
<td><strong>Histologic Findings</strong></td>
</tr>
<tr>
<td>No. of patients</td>
</tr>
<tr>
<td>US Positive</td>
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<tr>
<td>Negative</td>
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<tr>
<td>Total</td>
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No.: Number, US: Ultrasonography

<table>
<thead>
<tr>
<th>Table 2. Correlation between Metastatic Lymph Nodes on Ultrasoundography and Histologically Positive Lymph Nodes</th>
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<tbody>
<tr>
<td><strong>No. of metastatic</strong></td>
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<td>-----------------------</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2- 3</td>
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<td>≥ 4</td>
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No.: Number, LNs: lymph nodes, US: Ultrasonography

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<tr>
<th>Table 3. Correlation between Tumor Size and Number of Metastatic Lymph Nodes</th>
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<tbody>
<tr>
<td><strong>Tumor size [cm]</strong></td>
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<tr>
<td>---------------------</td>
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<tr>
<td>≤ 1</td>
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<td>1- 2</td>
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<td>2- 5</td>
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No.: Number, LNs: lymph nodes
logically proven metastatic lymph nodes that were identified \( p < 0.01 \) (Table 2). Moreover, there was a statistically significant correlation between the size of the breast mass and the number of histologically proven metastatic lymph nodes \( p < 0.01 \) (Table 3). When comparing the control and metastatic lymph nodes, the ratio of the shortest axis to the longest axis (S/L), and the cortical thickness were 0.38 and 1.46 mm, respectively, in the benign nodes and 0.74 and 6.11 mm, respectively, in the metastatic nodes. Twenty-seven (81.8\%) of thirty-three lymph nodes that were suggestive of metastasis on US showed the obliteration of the fatty hilum. All three of the criteria we selected for the presence of metastasis showed statistically significant results \( p < 0.01 \).

**Discussion**

The axillary lymph node status is, in the absence of distant metastasis, the single most important factor for predicting breast cancer patient survival. Axillary
lymph node dissection is routinely performed as a part of the surgical treatment for breast cancer, and it is mainly done for staging and planning the adjuvant therapy according to the number of metastatic lymph nodes that are found (1, 2). However, in most patients, axillary dissection has proved to be unnecessary after the histological node examination. Moreover, axillary node dissection has significant complications, such as lymphedema, pain in the arm, nerve injury and a prolonged hospital stay. The newer surgical approaches, such as sentinel node dissection or selective node dissection, have been proposed to reduce the number of unnecessary axillary dissections and these techniques are currently under investigation. An accurate noninvasive preoperative diagnostic method to assess the axillary lymph node status would help reduce the need for axillary operations.

US has been proved to have a higher sensitivity (45–84%) and specificity (72–97%) for the detection of metastatic axillary lymph nodes in breast cancer than a clinical examination or the other imaging techniques (3–6, 8). Similar to the results of earlier studies, the sensitivity, specificity and accuracy of ultrasonography were 75%, 82.6% and 78.7%, respectively, in our current study. According to previous studies, false negative cases had three or less microscopically invaded lymph nodes on histologic examination (9, 10). In our study, the six false negative patients had less than three metastatic lymph nodes. It appears that the common factors associated with the discrepancy between the US findings and the pathological results are the failure to visualize lymph nodes during US examination of the axilla, the small number of metastatic lymph nodes and the presence of micrometastasis. Ultrasonography alone cannot always differentiate reactive or inflammatory conditions from the malignant causes due to the overlap of their sonographic features. The four false positive cases in our study were considered to be benign reactive hyperplasia, and one of these cases was confirmed by histology as tuberculous lymphadenitis. As for the causes of the other false positive nodes, pathological sinusoid hyperplasia and irregular, thickened capsules represented the uneven sonographic cortical thickening. Also, the rich vascular structures within the lymph node can cause the compression or absence of hilum. US-guided fine-needle aspiration (FNA) may increase the specificity or reliability in such cases. In a study by Kirshnamurthy et al, the overall sensitivity, specificity, diagnostic accuracy, positive predictive value and negative predictive value of US-guided FNA were 86.4%, 100%, 79%, 100% and 67%, respectively (10).

There was a positive correlation between the number of nodes that were suggestive of metastasis on US and the number of histologically proven metastatic lymph nodes that were identified (p < 0.01).

According to Lam and associates and also Yang and colleagues, a normal axillary lymph node was defined as having an ovoid hypoechoic C-shaped rim of lymphoid tissue (usually 1 to 2 mm thick) around a central echogenic fatty hilum, and lymph nodes that were suggestive of metastasis were rounded and hypoechoic with or without the associated eccentric cortical hypertrophy and obliteration of the fatty hilum (5, 6). Size was not considered an important factor. In an in vitro US study for axillary node analysis by Feu et al., absence of the hilum was found to be the most specific sonographic feature for the diagnosis of metastasis (12). The increased long-to-short axis ratio was the finding that caused the most false-negative interpretations, indicating that lymph nodes appearing elongated or ovoid can be metastatic. Yet in other study by Tateishi et al, a circular shape (i.e., a ratio between 0.5 and 1.0 for the shortest axis to the longest axis) was the best single feature for distinguishing metastatic from nonmetastatic lymph nodes (13). In our study, we defined metastatic lymph nodes as those nodes having obliteration of the fatty hilum and if they had over 3mm of uneven cortical thickness.

The prevalence of axillary nodal involvement in breast cancer is 40–70%, and the prevalence of axillary nodal involvement has been shown to be related to tumor size. The risk for having a positive node is known to be 30% if the primary tumor is larger than 1 cm, and it’s 15% if the primary tumor is less than 1 cm. In patients with T3 cancer, up to 60% will have axillary nodal metastasis at presentation (14). In a current study, there was a statistically significant correlation between the size of the breast mass and the number of proven metastatic lymph nodes (p < 0.01).

The accuracy of ultrasonographic axillary lymph node detection will probably improve with the support of more advanced sonographic scanners and better-defined nodal differential criteria. Additional studies will be necessary to determine the value of ultrasonographic evaluation for the detection of metastatic axillary lymph nodes due to the limited number of cases in this study.

In conclusion, if the axillary lymph nodes in patients with breast cancer show an increased ratio of the short-
est axis to the longest axis, the obliteration of fatty hilum and over 3 mm of uneven cortical thickness on US, then they should be considered as having metastasis. As the number of metastatic LNs detected on US was higher or the size of breast mass was larger, the number of histologically proven metastatic nodes increased. The relatively high accuracy and the positive and negative predictive values of US for detecting metastatic axillary lymph nodes indicate that it is a useful modality for the initial staging of breast cancer, and this US modality can be immensely valuable for planning the appropriate management of breast cancer patients.

References


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