Ultrasound combined with fine needle aspiration cytology for the assessment of axillary lymph nodes in patients with early stage breast cancer

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Abstract
This study aimed to explore the clinical usefulness of ultrasound-guided fine needle aspiration cytology (USG-FNAC) for the evaluation of axillary lymph nodes in patients with early stage breast cancer (BC) among the Chinese Han female population. Around 124 patients with early stage BC were included in this retrospective study. All patients underwent USG-FNAC (group A). Patients with proven metastasis also underwent axillary lymph node dissection (ALND) (group B). In addition, sentinel lymph node biopsy (SLNB) was performed 2 to 5 hours prior to the surgery. The sensitivity, specificity, accuracy, and positive predictive value (PPV) of axillary ultrasound were 75.0%, 75.0%, 75.0%, and 82.6%, respectively, while for USG-FNAC, they were 80.8%, 100.0%, 88.7%, and 100.0%, respectively. Significant differences were found in specificity, accuracy, and PPV between the 2 procedures (P < .05). The results of this study demonstrated that USG-FNAC was effective for selecting patients with early stage BC using ALND or SLNB among the Chinese Han female population.

Abbreviations: ALND = axillary lymph node dissection, BC = breast cancer, FNAC = fine needle aspiration cytology, PPV = positive predictive value, SLNB = sentinel lymph node biopsy, USG-FNAC = ultrasound guided fine needle aspiration cytology.

Keywords: axillary lymph node, breast cancer, fine needle aspiration cytology, ultrasound

1. Introduction
Breast cancer (BC) is one of the most common cancers among women.\textsuperscript{1-4} Its incidence and mortality contribute to a major public health problem.\textsuperscript{5-8} It has been estimated that 25.1% new cases of BC and 14.7% deaths from this cancer occurred in 2012.\textsuperscript{9} In addition, its incidence is 94.2/100,000 in Europe, with 60% to 80% of these patients being newly diagnosed as BC in 2012.\textsuperscript{10,11} It has also been estimated that about 268,600 women (15.1%) were diagnosed and 69,500 (6.9%) died of BC in 2015.\textsuperscript{12-15} It has been reported that axillary lymph node dissection (ALND) was used to treat patients with BC.\textsuperscript{12-15} However, because of its high morbidity, sentinel lymph node biopsy (SLNB) has been used as the standard nodal staging procedure instead.\textsuperscript{16-18} Previous studies have confirmed that the way of histopathological examination method of the sentinel node was tested for the prediction of the total axillary lymph node that involved patients with BC.\textsuperscript{17} Unfortunately, sentinel node procedures often involve higher costs and longer anesthesia. Additionally, histopathological diagnosis is also challenging for pathologists, and sometimes, no sentinel node may be found.\textsuperscript{18} Fortunately, such detection method can be replaced by ultrasound-guided fine needle aspiration cytology (USG-FNAC) before surgery. Thereby, decreasing the operation cost and anesthesia time is in addition to reduce the workload for pathologists. Such techniques are useful, especially for patients detected with the false-negative from sentinel node procedures, because of their extensive metastatic involvement.\textsuperscript{19}

Currently, the availability of USG-FNAC data in BC patients among the Chinese population is limited. Thus, in this study, we aimed to evaluate the clinical usefulness of USG-FNAC for the assessment of axillary lymph nodes in BC at early stage.

2. Methods
This study was formally approved by the Medical Ethical Committee of The Second Affiliated Hospital of Mudanjiang Medical University, and the informed consent was obtained from all patients. It was conducted at The Second Affiliated Hospital of Mudanjiang Medical University from January 2015 to March 2017. This study recruited 124 patients with the diagnosed with early stage BC. All patients aged from 30 to 75 years. They all did not present clinical unequivocal malignant nodes, and did not receive chemotherapy, radiotherapy, or breast surgery. In addition, this study excluded pregnant or lactating patients. Finally, patients with benign USG-FNAC were assigned to Group A. Patients with SLNB procedure were assigned to Group B.
Ultrasound of axillary was conducted by 2 experienced radiologists in breast examination using a Siemens ATL 5000 (Philips, Best, Netherlands) with linear probe 13 MHz. The assessment of targeted lymph nodes included irregular or <3-mm cortex. USG-FNAC was performed on the suspicious ones. The most suspicious one was selected for puncture if several nodes seemed to be affected.

FNAC was performed by a 23-gauge needle attached to a 10-mL syringe. It was used to sample the targeted node(s). A ThinPrep cytologic test was used by a cytologist to process and examine the sample. Results were classified as negative for malignancy, positive for malignancy, or suspicious (uncertain diagnosis).

Patients underwent SLNB by using 99m technetium-labeled Rituximab (99m Tc-Rituximab) alone or combined with patent blue before the surgery. A hand-held gamma probe was used to record and identify the sentinel nodes. The images were obtained after the injection of 99m Tc-Rituximab.

All nodes in this study were removed from the axilla, and then freed from adipose tissue. If the nodes were larger than 5 mm in diameter, they were bisected longitudinally before being embedded. If the nodes were smaller than 5 mm at their greatest diameter, the whole tissue was embedded. Three different parts from the nodes were acquired, each between 0.4 and 1.0 mm in diameter. They were then stained with hematoxylin and eosin. The nodes were finally prepared for the detection of micrometastases.

The outcomes included sensitivity, specificity, positive predictive value (PPV), and accuracy in this study.

2.1. Statistical analysis

Chi-square tests were used to analyze the categorical data among the difference of USG-FNAC and the histopathological results. The statistical significance level was set at \( P < .05 \).

3. Results

A total of 166 patients were initially screened for eligibility (Fig. 1). Of these, 42 were either excluded as they did not meet the inclusion criteria (n = 38) or they met the exclusion criteria (n = 4). Thus, 124 patients underwent the FNAC. Sixty-five negative patients underwent SLNB, and 59 patients received ALND. Among the 65 negative patients, 14 were positive and received ALND, and the remaining 51 were negative (Fig. 1).

The patient characteristics are summarized in Table 1. All patients were Chinese Han ethnicity. The mean age of the included patients was \( 54.1 \pm 11.3 \) years. The median tumor size was \( 22 \) mm with range of 6 to 38 mm. The histopathology included invasive ductal cancer (n = 108), invasive lobular cancer (n = 12), and others (n = 4). The median grade was 2 with range from 1 to 3, including I (n = 23), II (n = 85), and III (n = 16).

The characteristics of lymph nodes are showed in Table 2. The total number of clinical palpable lymph nodes was 154. The mean node sizes were \( 16.1 \pm 6.8 \) mm. Of these, 97, 24, and three patients presented with 1, 2, and 3 nodes, respectively. The total number of nonpalpable abnormal nodes was 15. The mean sizes were \( 11.6 \pm 4.4 \) mm. The number of sentinel lymph node foci

| Table 1 | Characteristics of included patients. |
|---------|--------------------------------------|
| Characteristics | Value |
| Mean age, years | 54.1 (11.3) |
| Ethnicity (Chinese Han) | 124 (100.0) |
| Occupation | |
| Employed | 79 (63.7) |
| Unemployed | 11 (8.9) |
| Retired | 34 (27.4) |
| Marital status | |
| Married | 88 (71.0) |
| Divorced | 20 (16.1) |
| Widowed | 16 (12.9) |
| Tumor size, mm | |
| Median size | 22 (6–38) |
| 0–10.0 | 12 (9.7) |
| 10.1–15.0 | 30 (24.2) |
| 15.1–20.0 | 75 (60.5) |
| More than 20 | 7 (5.6) |
| Histopathology | |
| Invasive ductal cancer | 108 (87.1) |
| Invasive lobular cancer | 12 (9.7) |
| Others | 4 (3.2) |
| Grade | |
| Median | 2 (1–3) |
| I | 23 (18.5) |
| II | 85 (68.6) |
| III | 16 (12.9) |

Note: Data are present as mean ± standard deviation or number (%).

| Table 2 | Characteristics of lymph node. |
|---------|--------------------------------|
| Characteristics | Value |
| Clinical palpable lymph nodes | |
| Total numbers | 154 |
| Size, mm | 16.1 (6.8) |
| Patients with 1 node | 97 (78.2) |
| Patients with 2 nodes | 24 (19.4) |
| Patients with 3 nodes | 3 (2.4) |
| Nonpalpable abnormal nodes | |
| Total numbers | 15 |
| Size, mm | 11.6 (4.4) |
| Positive with FNAC | 10 (66.7) |
| Negative with FNAC | 5 (33.3) |
| Number of sentinel lymph node foci | |
| 1 | 28 (43.1) |
| 2 | 31 (47.7) |
| 3 | 5 (7.7) |
| 4 | 1 (1.5) |

FNAC = fine needle aspiration cytology.

Note: Data are present as mean ± standard deviation or number (%).
was follows: 28 patients, 1; 31 patients, 2; 5 patients, 3; and 1 patient, 4. The results of USG-FNAC are listed in Table 3. The sensitivity, specificity, accuracy, and PPV of axillary ultrasound were 75.0%, 75.0%, and 82.6%, respectively, while they were 80.8%, 100.0%, 88.7%, and 100.0%, respectively, for UGFNAC. Significant differences were found between 2 procedure regarding the specificity, accuracy, and PPV (P < .05).

### 4. Discussion

Several previous studies explored the usefulness of the USG-FNAC in the evaluation of lymph node status before SLNB in patients with BC.

One study assessed the clinical usefulness of SLNB-combined preoperative axillary ultrasound with FNAC in patients with BC with clinically palpable lymph nodes among the Kuwait population.[20] The authors concluded that preoperative axillary ultrasound with FNAC may be used for the selection of patients with BC for ALND or SLND.[20] Another study evaluated the preoperative detection of axillary metastasis in patients with BC among the Belgian population by combining USG-FNAC with liquid-based cytology to decrease the number of sentinel node procedures.[21] The authors recommended that USG-FNAC with liquid-based cytology should be used for axillary lymph node detection in patients with BC at the preoperative stage.[21] Another study compared the efficacy of physical examination, ultrasound, and USG-FNAC in patients with BC among the Chinese population to evaluate node status before SLNB.[22] The previous study’s results indicated that USG-FNAC was effective and may be used for the triage of axillary stage in patients newly diagnosed with BC.[22]

The results of our study were consistent with that of a previous study.[20] In our study, we evaluated the clinical usefulness of USG-FNAC for the assessment of axillary lymph nodes in patients with early stage BC among the Chinese female population. Our results showed that the sensitivity, specificity, accuracy, and PPV were 75.0%, 75.0%, 75.0%, and 82.6% for ultrasound, respectively, while they were 80.8%, 100.0%, 88.7%, and 100.0% for UGFNAC, respectively. Thus, it was more effective to use USG-FNAC to detect axillary lymph nodes in these patients.

This study has several limitations. First, this study only included the ethnicity of Chinese Han population; it may be not generalized to the other ethnicities in China. Second, we only included patients with early stage BC; thus, further studies in patients with BC at other stages are required. Third, the included number of patients with early stage BC was small, which may have affected the results of this study.

### 5. Conclusions

The results of this study demonstrated that USG-FNAC is effective and may be used for patient selection for the management of ALND or SLNB in patients with early stage BC among the Chinese Han female population.

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