Observational Study

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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 the most common cancers among women.[1,2] Its incidence and mortality contribute to a major public health problem.[3–5] It has been estimated that 25.1% new cases of BC and 14.7% deaths from this cancer occurred in 2012.[6] 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.[7,8] It has also been estimated that about 268.600 women (15.1%) were diagnosed and 69.500 (6.9%) died of BC in 2015.[9–11]

It has been reported that axillary lymph node dissection (ALND) was used to treat patients with BC.[12,13] However, because of its high morbidity, sentinel lymph node biopsy (SLNB) has been used as the standard nodal staging procedure instead.[14–16] Previous studies have confirmed that the way of histopathological examination method of the sentinel node was tested for the predication of the total axillary lymph node that involved patients with BC.[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.[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.[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.

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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}technetiumlabeled 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 ± 11.3) years. The median tumor size was 22 mm with range of 6 to 38 mm. The histopathology

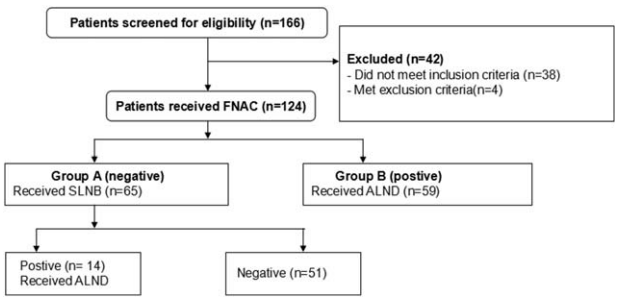

Figure 1. Flowchart of patient diagnosis during this study.

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 (%).

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 ± 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 ± 4.4 mm. The number of sentinel lymph node foci

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 (%).

Table 3

Results of ultrasound and fine needle aspiration cytology.

Items	True-positive	False-positive	True-negative	False-negative	Sensitivity	Specificity	Accuracy	PPV
Axillary ultrasound	57	12	36	19	75.0%	75.0%	75.0%	82.6%
UGFNAC	59	0	51	14	80.8%	100.0%	88.7%	100.0%

PPV = positive predictive value, UGFNAC = ultrasound guided fine needle aspiration cytology.

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%, 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.[20–22] 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.

References

[1] Krekel NMa , Zonderhuis BM, Schreurs HWH, et al. Ultrasound-guided breast-sparing surgery to improve cosmetic outcomes and quality of life. A prospective multicentre randomised controlled clinical trial comparing ultrasound-guided surgery to traditional palpation-guided surgery (COBALT trial). BMC Surg 2011;16:8.

[2] Xu F, Zhang C, Cui J, et al. The prognostic value and potential drug target of phosphatase and tensin homolog in breast cancer patients: a meta-analysis. Medicine (Baltimore) 2017;96:e8000.

[3] Du J, Mo H, Fan L, et al. Robot-assisted internal mammary lymph chain excision for breast cancer: a case report. Medicine (Baltimore) 2017;96: e7894.

[4] Zhang J, Huang Y, Wang C, et al. Efficacy and safety of endocrine monotherapy as first-line treatment for hormone-sensitive advanced breast cancer: a network meta-analysis. Medicine (Baltimore) 2017;96: e7846.

[5] Camacho FT, Tan X, Alcalá HE, et al. Impact of patient race and geographical factors on initiation and adherence to adjuvant endocrine therapy in medicare breast cancer survivors. Medicine (Baltimore) 2017;96:e7147.

[6] Ervik M, Lam F, Ferlay J et al. Cancer Today. International Agency for Research on Cancer, World Health Organization, Lyon 2016. Available at: http://gco.iarc.fr/today. Accessed June 2017.

[7] Senkus E, Kyriakides S, Ohno S, et al. Primary breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2015;26(suppl 5):v8–30.

[8] Eichler C, Hübbel A, Zarghooni V, et al. Intraoperative ultrasound: Improved resection rates in breast-conserving surgery. Anticancer Res 2012;32:1051–6.

[9] Chen WQ, Zheng RS, Baade PD, et al. Cancer statistics in China, 2015. CA Cancer J Clin 2016;66:115–32.

[10] Zhang B, Dong JN, Sun P, et al. Effect of therapeutic care for treating fatigue in patients with breast cancer receiving chemotherapy. Medicine (Baltimore) 2017;96:e7750.

[11] Yao J, Jin Q, Wang XD, et al. Aldehyde dehydrogenase 1 expression is correlated with poor prognosis in breast cancer. Medicine (Baltimore) 2017;96:e7171.

[12] Veronesi U, Paganelli G, Viale G, et al. A randomized comparison of sentinel-node biopsy with routine axillary dissection in breast cancer. N Engl J Med 2003;349:546–53.

[13] Rodier JF, Velten M, Wilt M, et al. Prospective multicentric randomized study comparing periareolar and peritumoral injection of radiotracer and blue dye for the detection of sentinel lymph node in breast sparing procedures: FRANSENODE trial. J Clin Oncol 2007;25:3664–9.

[14] Mansel RE, Fallowfield L, Kissin M, et al. Randomized multicenter trial of sentinel node biopsy versus standard axillary treatment in operable breast cancer: the ALMANAC trial. J Natl Cancer Inst 2006;98:599–609.

[15] Schwartz GF, Veronesi U, Clough KB, et al. Consensus conference committee, consensus conference on breast conservation, Milan, Italy, April 28–May 1. Breast J 2005;12:398–407.

[16] Lyman GH, Somerfield MR, Giuliano AE. Sentinel lymph node biopsy for patients with early-stage breast cancer: 2016 American Society of Clinical Oncology Clinical Practice Guideline Update Summary. J Oncol Pract 2017;13:196–8.

[17] Veronesi U, Paganelli G, Galimberti V, et al. Sentinel-node biopsy to avoid axillary dissection in breast cancer with clinically negative lymph-nodes. Lancet 1997;349:1864–7.

[18] Tanis PJ, van Sandick JW, Nieweg OE, et al. The hidden sentinel node in breast cancer. Eur J Nucl Med Mol Imaging 2002;29:305–11.

[19] Dequanter D, Hertens D, Veys I, et al. Sentinel node involvement in T0–T1 breast cancer. Ann Chir 2001;126:654–8.
[20] Usmani S, Ahmed N, Al Saleh N, et al. The clinical utility of combining pre-operative axillary ultrasonography and fine needle aspiration cytology with radionuclide guided sentinel lymph node biopsy in breast cancer patients with palpable axillary lymph nodes. Eur J Radiol 2015;84:2515–20.
[21] Schiettecatte A, Bourgain C, Breucq C, et al. Initial axillary staging of breast cancer using ultrasound-guided fine needle aspiration: a liquid-based cytology study. Cytopathology 2011;22:30–5.
[22] Feng Y, Huang R, He Y, et al. Efficacy of physical examination, ultrasound, and ultrasound combined with fine-needle aspiration for axilla staging of primary breast cancer. Breast Cancer Res Treat 2015;149:761–5.