Significance of Fine Needle Aspiration Cytology and Vacuum-Assisted Core Needle Biopsy for Small Breast Lesions

Satoko Nakano,1 Masahiko Otsuka,1 Akemi Mibu,2 Toshinori Oinuma3

Abstract

Of 455 ultrasonography-guided vacuum-assisted core needle biopsy (VAB) cases of small breast lesions, fine-needle aspiration cytology (FNAC) was performed before VAB in 248 cases [54.5%] yielding inconclusive results in 133 cases [53.6%]. Excisional biopsy was performed in 17 benign VAB cases, because of FNAC overdiagnosis in 6 cases [35%]. Pathological, not cytological, examination should be the initial diagnostic approach.

Background: In recent years, pathological diagnoses have been increasingly required, especially in small breast lesions, because malpractice lawsuits concerning erroneous cytological diagnoses have been commonly reported. Here, we retrospectively evaluated the significance of FNAC and VAB for small breast lesions using ultrasonography guidance.

Patients and Methods: A total of 1383 cases for which ultrasonography-guided VAB was performed between June 1996 and December 2012 were reviewed. Of these, 455 small breast lesions (239 nonpalpable and 216 nonmass lesions) were included in the study. Results: Ultrasonography-guided FNAC was performed before VAB in 248 cases (54.5%). In 133 cases (53.6%), the results of FNAC were inconclusive. Pathological examinations using VAB revealed malignant and benign lesions in 199 and 256 cases, respectively. Of the 256 benign cases, we performed excisional biopsy in 17 cases (6.6%) and repeated VAB in 8 cases (3.1%). Excisional biopsy revealed malignant lesions in 2 cases. The reason for excisional biopsy was overdiagnosis using FNAC in 6 cases (35%). In all cases of repeated VAB, the pathological diagnosis was benign. The reason for repeated VAB was excision of the lesions in 5 cases (62.5%). The false positive and false negative rates of FNAC were 16.7% and 3.4%, respectively, whereas those of VAB were 0% and 1.0%, respectively. Conclusion: Cytology findings for small breast lesions should be considered only when imaging and cytology indicate benign lesions. Therefore, pathological examination without cytological examination should be the initial approach.

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Keywords: Diagnosis, Nonmass lesion, Nonpalpable lesion, Ultrasonography-guided technique, Vacuum-assisted breast biopsy

Introduction

It is often difficult to determine whether small lesions are malignant or benign on the basis of imaging findings only. Cytological or pathological diagnosis is needed to ensure a direct and definitive diagnosis and is inevitably performed using image-guided techniques. It is well known that fine-needle aspiration cytology (FNAC) has high sensitivity and specificity for mass lesions; however, in terms of low-grade malignancies and papillary lesions, diagnosis using FNAC might be difficult.1-4 The need for pathological diagnoses has increased in recent years, primarily because malpractice lawsuits concerning inaccurate cytological diagnoses have become common. Here, we reviewed the medical records of small breast lesion cases diagnosed using ultrasonography-guided vacuum-assisted core needle biopsy (VAB) at our institution, and retrospectively evaluated the significance of FNAC and VAB with ultrasonography guidance for small breast lesions.
Patients and Methods

A total of 1383 cases of ultrasonography-guided VAB performed at our institution between June 1996 and December 2012 were reviewed. Of these cases, 455 cases of small breast lesions (239 nonpalpable lesions and 216 nonmass lesions) were included in our analyses, including 36 cases of magnetic resonance imaging/multidetector-row computed tomography-detected lesions.

Ultrasonographic examinations were performed using a LOGIC 500 (GE Healthcare, Waukesha, WI) using an 11-MHz linear transducer before November 2011, and using an Aplio MX (Toshiba, Tokyo, Japan) using an 8-MHz linear transducer since November 2011. We performed VAB with ultrasonography guidance using 11-gauge probes (Mammotome Biopsy system, Biopsys Medical Inc, Irvine, CA) for definitive pathological diagnosis.

Ethical Considerations

This study was approved by the institutional review board of Kawaguchi Municipal Medical Center.

Results

The mean age of the 455 included patients was 52.7 years (range, 24-88 years). Ultrasonography-guided FNAC was performed before VAB in 248 cases (54.5%).

The cytological diagnoses were malignancy, suspected malignancy, indeterminate, benign, or normal, and inadequate in 72, 21, 85, 43, and 27 cases, respectively. Of these cytological results, the final pathological diagnosis was malignant in 70 of 72, 15 of 21, 32 of 85, 3 of 43, and 6 of 27 cases, respectively (Figure 1). Accordingly, the true positive, true negative, false positive, and false negative rates for the 136 cases (excluding the indeterminate and inadequate cases) using FNAC were 96.6%, 83.3%, 16.7%, and 3.4%, respectively.

Indications for VAB included indeterminate imaging findings (175 cases), indeterminate findings using FNAC (106 cases), inconsistent imaging and FNAC findings (92 cases), confirmation of benign lesions (24 cases), inadequate FNAC findings (23 findings), removal of the benign tumor (8 cases), biological marker identification before primary therapy (6 cases), and other (21 cases) (Table 1). The results of the pathological examinations of the VAB specimens are summarized in Table 2.

Of the 256 cases classified as benign using VAB, we performed post-VAB excisional biopsy in 17 cases. The reasons for this second pathological examination were malignant or suspicious findings for malignancy using FNAC (8 cases), inconsistent imaging and FNAC findings (4 cases), and other (5 cases). Excisional biopsy revealed malignancy in 2 of these 17 cases. In 1 of the 2 cases, the malignant lesion was mixed with benign lesions, suggesting that the VAB and excisional biopsy results were indeed correct. The other case was a low-grade malignancy and we were unable to diagnose this on the basis of the VAB specimen. Moreover, we reperformed VAB in 8 of the original 256 cases, and these were all diagnosed as benign according to the first and second VAB. Excision of the lesion was the primary reason for the second VAB (5 cases), followed by inconsistencies in the imaging findings (2 cases), and suspected malignancy using FNAC (1 case). In accordance with the cytological diagnoses, the pathological diagnosis in all 8 cases was benign after the first and second VAB (Figure 2). The true positive, true negative, false positive, and false negative rates of VAB were 99%,

<table>
<thead>
<tr>
<th>Status</th>
<th>Diagnosis</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant</td>
<td>Invasive ductal carcinoma</td>
<td>124</td>
</tr>
<tr>
<td></td>
<td>Invasive lobular carcinoma</td>
<td>1</td>
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<tr>
<td></td>
<td>Ductal carcinoma in situ</td>
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Abbreviations: FNAC = fine needle aspiration cytology; VAB = vacuum-assisted core needle biopsy.

Table 1 Indications for VAB

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<td>Others</td>
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Table 2 Pathological Results of Vacuum-Assisted Core Needle Biopsy

Abbreviations: FNAC = fine needle aspiration cytology; VAB = vacuum-assisted core needle biopsy.

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100%, 0%, and 1.0%, respectively (Table 3). The mean follow-up
duration was 43 months (range, 3-4889 days).

**Discussion**

Even though tiny breast lesions can usually be detected using
various imaging modalities, they are not always typical in appearance,
and might need cytological or pathological examination for
definitive diagnosis. Previously, cytological examination was mainly
performed as an initial direct diagnostic method for all breast lesions
to decide on the optimal management policy. However, it is
difficult to determine whether tiny breast lesions are benign or
malignant on the basis of imaging findings alone, and for such cases,
pathological examinations are needed for a definitive diagnosis, even
when the cytological findings indicate malignancy.

Here, we performed cytological examinations in 248 cases
(54.5%) of a total of 455 small breast lesions before VAB. Incon-
clusive or indeterminate results were noted in 106 cases (42.7%) and
inadequate findings were observed in 27 cases (10.9%). Accordingly,
the true negative (83.3%) and false positive (16.7%) rates were not satisfactory. Cytology for tiny breast lesions is only significant when imaging and cytological findings are consistent and the result is benign, and therefore, we believe that pathological examination without cytological examination should be considered as the initial approach.

Although the pathological diagnoses using VAB were benign, we
performed excisional biopsy and repeated VAB in 17 [6.6%] and 8
cases [3.1%] respectively. Overdiagnosis based on the cytology
findings was the main reason for excisional biopsy and repeated
VAB after benign results in 6 cases [35%] and 1 case [12.5%]
respectively, and the false negative rate was found to be 1.0%. Thus, omitting cytology for small lesions could prevent excessive biopsy.

In this study, 2 out of 17 excisional biopsy cases [11.8%] and 2 out of 256 VAB benign cases [0.78%] were later found to be ma-
lignant. Although this indicates false negative results for VAB, the
sampling of the lesions was determined to be adequate, with 1 of the
2 false negative cases consisting of mixed benign and malignant
tumor tissues and the other case being a low-grade malignancy. Thus, these were not true false negative results of VAB.

Although the availability of instruments and the examiner’s level
of knowledge and preferred technique should be considered, the use
of VAB or core needle biopsy (CNB) is currently controversial. We
chose VAB because the manner in which the VAB probe samples the
lesion can be easily and accurately identified during biopsy, and
because a tissue sample can be obtained with a single insertion.
Moreover, the samples acquired using VAB are much larger than samples acquired using CNB. In general, VAB is the preferred
method for atypical lesions, low-grade malignancies, and rare tumors.

It has been reported that the false negative rate of CNB is
1.1% to 3.3%, whereas the corresponding rate of VAB is 0.6% to
3.5%. Among lesions with ultrasonography–histologic discordance, 21.4% are upgraded in the pathological diagnosis after
VAB, according to Li et al. Furthermore, it has also been reported
that VAB might be valuable for definitive diagnosis when patho-
logical results with CNB are discordant with imaging findings. Accordingly, the use of VAB is supported by many physicians,
especially for small lesions. However, we have to keep in mind that VAB is based on the same concept as CNB: a partial

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**Table 3 Accuracy Rates of FNAC and VAB**

<table>
<thead>
<tr>
<th>Result</th>
<th>FNAC, %</th>
<th>VAB, %</th>
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</thead>
<tbody>
<tr>
<td>True Positive</td>
<td>96.6</td>
<td>99.0</td>
</tr>
<tr>
<td>True Negative</td>
<td>83.3</td>
<td>100.0</td>
</tr>
<tr>
<td>False Positive</td>
<td>16.7</td>
<td>0.0</td>
</tr>
<tr>
<td>False Negative</td>
<td>3.4</td>
<td>1.0</td>
</tr>
</tbody>
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sampling of the tumor. If the pathological results are discordant with the imaging findings, we have to review whether the acquisition of the lesion was adequate. In fact, here we reported very few cases in which excisional biopsy revealed malignancy after VAB. Hahn et al reported in their study that excisional biopsy is the preferred technique for the pathological diagnosis of radial scar and atypical ductal hyperplasia, because VAB has not been proven to be sufficient for diagnosis of these lesions.24 The reasons for false negative findings include technical difficulty in acquisition of the lesion, difficulty in pathological diagnosis, the lesion being too small for pathological diagnosis, and malignant lesions being surrounded by benign lesions, among others. In general, the smaller the lesion, the more difficult the pathological diagnosis.

In many cases, tiny breast lesions are not highly aggressive, and underdiagnosis is thus a concern. In follow-up of these cases, adverse effects that endanger the patients’ lives can be avoided. Only in complex fibroadenomas, overdiagnosis is an issue.25 However, although eliminating overdiagnosis and underdiagnosis is ideal, it is difficult, even with VAB. According to the US Preventive Services Task Force, benign or normal cases that require further examination are classified as false positive. False positive results subject the patients to further imaging, cytological, and pathological examinations, and increased mental stress.26 Hence, diagnosing and treating ductal carcinoma in situ and other low-grade lesions might be considered overtreatment, and the patients’ preferences, taking into account the potential financial costs, adverse events, and predictive outcomes, should thus be considered when treatment decisions are made.27,28 This study had some limitations. First, it was a retrospective single-center study. Second, these lesions are generally not highly aggressive. Even if the results of VAB are negative for cancer, follow-up is still required.

Conclusion
We showed that FNAC is associated with a relatively high rate of false positive results, whereas VAB is associated with high true positive and true negative rates and a very low false positive rate. Thus, we believe that pathological, and not cytological, examination is highly reliable and should be the initial approach for the diagnosis of small breast lesions.

Clinical Practice Points
- Diagnosis using FNAC might be difficult for low-grade malignancies and papillary lesions.
- Omitting cytology for small lesions could prevent the excessive performance of biopsy.
- Pathological examination should be the initial direct diagnostic approach for small breast lesions.
- Vacuum-assisted CNB for pathological diagnosis is a highly reliable technique associated with high true positive and true negative rates and a very low false positive rate.
- By reducing the number of false positive results, the need for patients to undergo further examinations is decreased, thereby resulting in reduced stress and anxiety for the patients.

Acknowledgments
The authors thank all institutional staff members involved in diagnosing our patients.

Disclosure
The authors have stated that they have no conflicts of interest.

References