Impact of Preoperative Ultrasonography and Fine Needle Aspiration of Axillary Lymph Nodes on the Surgical Management of Primary Breast Cancer.

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<ABSTRACT>

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Purpose: To evaluate the accuracy of preoperative ultrasonography (US) and US-guided fine needle aspiration (US-FNA) for detecting axillary lymph node (ALN) metastasis.

Material and methods: We retrospectively reviewed 382 breast cancer patients with clinically negative ALN who underwent US and/or US-FNA for ALN. US-FNA of ALN was performed in 121 patients with suspicious findings on US. The diagnostic performance of US and addition of US-FNA for detecting ALN metastasis were calculated on the basis of the final pathologic reports of ALN surgery.

Results: Among a total of 382 patients, 129 had metastatic ALNs while 253 exhibited no signs of axillary metastasis on final pathology. The sensitivity, specificity, PPV, and NPV of axillary US alone were 56.6% (73/129), 81.0% (205/253), 60.3% (73/121) and 78.5%(205/261), respectively. Addition of US-FNA resulted in a sensitivity, specificity, PPV, and NPV of 39.5% (51/129), 95.7% (242/253), 82.3% (51/62) and 75.6% (242/320), respectively. Excluding complete responders to neoadjuvant chemotherapy, the specificity and PPV after adding US-FNA were increased to 99.6% (242/243) and 98.1% (51/52), respectively. The sensitivity, specificity, PPV and NPV of ALN metastasis between the palpable and non-palpable breast cancer groups were similar; however, after adding US-FNA, NPV was increased in the non-palpable breast cancer group

compared to palpable breast cancer (p= 0.0398). By including preoperative axillary US and US-FNA, 16.2% (62/382) of all breast cancer patients were able to avoid unnecessary SLNB.

Conclusions: The combination of axillary US and US-FNA is useful in preoperative work-up of breast cancer patients and provides valuable information for planning proper breast cancer management.

Key words : axillary lymph node, ultrasonography, ultrasonography-guided fine needle aspiration, breast cancer.

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I. INTRODUCTION

In patients with breast cancer, evaluation of axillary lymph nodes (ALNs) is very important, as it is a powerful prognostic indicator and decisive factor for developing a breast cancer treatment plan [1-4].Traditionally, axillary lymph node dissection (ALND) has been used for nodal staging, but currently the use of sentinel lymph node biopsy (SLNB) has increased in frequency as an alternative procedure for patients with early breast cancer [5-8]. Importantly, while SLNB has decreased the morbidity of staging by avoiding unnecessary ALND, it is also an invasive method and an inconvenience for some patients to undergo a two-stage surgical procedure [9]. Therefore, it would be of great clinical benefit if a reliable imaging method or minimally invasive procedure for determining ALN status was available. If so, if there were no evidence of ALN metastasis in preoperative staging, SLNB would be performed. On the other hand, patients with ALN metastasis found in preoperative staging would directly undergo ALND or neoadjuvant chemotherapy.

In terms of pre-operative evaluation for ALN metastasis, physical examination has a low sensitivity, between 34% and 76% [10-12]. Ultrasonography (US) of ALN has superior diagnostic accuracy in many

studies when combined with US-guided fine needle aspiration biopsy (US-FNA) of sonographically suspicious lymph nodes [13-17]. The sensitivity and specificity of US examination in the evaluation of ALN metastasis had been reported to be between 36-92% and 69-100% [12, 14, 18-22] and addition of US-FNA to axillary US may increase specificity by up to 93-100% [6, 16, 19, 22-26]. However, the majority of previous studies on US-FNA have consisted of small patient groups or have been intended for patients with a high incidence of metastatic LNs, and thus a study targeting a larger sample of unspecified individuals is needed.

The aim of our study was to evaluate the accuracy of preoperative US and US-FNA for detecting ALN metastasis and to assess how often SLNB could be avoided in breast cancer patients with clinically negative ALN in a large patient population.

II. MATERIALS AND METHODS

Our institutional review board approved this retrospective study and the requirement for informed consent was waived. Between October 2007 and December 2008, a total of 401 patients who had breast cancer with clinically negative ALN underwent axillary US before receiving surgical treatment. Nineteen patients who did not receive surgical treatment such as SLNB or ALND were excluded from the study for a total of 382 patients. Of the final patient sample, 79 had been previously diagnosed with breast cancer by US guided biopsy, and 303 patients had highly suspicious breast masses at the time of ALN US. Two experienced breast surgeons examined each patient to determine whether the primary breast cancers were palpable.

1. Ultrasound Evaluation

US was performed using a high-frequency linear array transducer (L12-5

MHz) on a Phillips ATL HDI (Philips Medical systems, Bothell, WA, USA), GE LOGIQ 9 (GE Medical Systems, Milwaukee, WI, USA) or Siemens Acuson Antares (Siemens Medical Solutions, Mountain View, CA, USA) by five breast radiologists with 1 to 11 years of experience. ALN was classified as suspicious when one or more suspicious US finding were noted. Suspicious US finding for ALN metastasis included loss of fat hilum, cortical thickening of more than 3 mm, irregular shape, markedly hypoechoic cortex, a round shape, or increased peripheral blood flow [6, 13, 15, 17, 27-30].

2. Fine needle aspiration biopsy of ALN

US-FNA was performed only for cases of suspicious ALN on US, and was performed by the same five radiologists who performed US as described above. For US guidance, FNA was performed with a 23 gauge needle and a 2 ml syringe using the to-and-fro method without aspirator and local anesthesia. Acquired cells were deposited on glass slides and were stained according to the standard Papaniciolaou stain method. Cytology was evaluated by three experienced cytopathologists. Cytological results were classified into inadequate sampling, negative, atypical and positive for metastasis.

3. Sentinel lymph node biopsy

In patients with negative axillary US, SLNB was performed without US-FNA. In patients with negative or inadequate FNA result, SLNB was performed. Patients were given between three and four injections of 30 MBq (0.8 mCi) Tc 99m-antomony trisulfide colloid in 1.0 ml saline in the subareolar and intradermal area. After injection, anteroposterior and lateral views were obtained using a large field of view dual-head camera for confirming presence of SLN. In the operating room, radioactive LNs were

detected using a gamma probe (Navigator Gamma Guidance system, USSC) and were checked for residual radioactivitiy after surgery. In patients with positive pathologic results on SLNB, ALND was performed.

4. Final Reference Standard

Among the 382 total patients, 236 underwent mastectomy and 146 underwent breast conserving surgery. For axillary staging, 102 patients underwent SLNB only, 58 underwent ALND only, and 222 underwent both SLNB and ALND. On the basis of pathologic reports of ALND or SLNB, 129 patients had metastatic ALNs and 253 patients showed no axillary metastasis. Of the 35 patients who underwent chemotherapy, all underwent ALND afterwards. Among patients who received chemotherapy, 25 showed positive findings of ALNs, while 10 were negative for ALNs on final pathologic results. We regarded these 10 patients as complete responders to neoadjuvant chemotherapy.

5. Statistics

The accuracy of US and US- FNA were correlated with final pathologic reports of ALN. When only SLNB was performed, the pathologic report of SLNB was regarded as standard. Isolated tumor cells on final pathologic reports were regarded as negative findings. The T staging and N staging of breast cancer were based on American Joint Committee on Cancer recommendations, 7th edition.

For evaluating accuracy of US-FNA, metastasis and atypical cytological results were regarded as cytological positive results on FNA. Inadequate sampling on FNA was considered a negative result, because an ALN with inadequate sampling would undergo SLNB as an ALN with negative cytology [6, 26, 30]. Patients who had positive cytological results on US-FNA but negative pathology results of ALND after neoadjuvant chemotherapy

were considered as complete responders to neoadjuvant chemotherapy. Using these selection criteria, we calculated true positive (TP), true negative (TN), false positive (FP) and false negative (FN) of axillary US and US-guided FNA of ALN. The results of US and US-guided FNA for ALN were evaluated with respect to sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) as follows: sensitivity, TP/(TP+FN); specificity, TN/(TN+FP); positive predictive value, TP/(TP+FP); negative predictive value, TN/(TN+FN); and accuracy, (TP+TN)/(TP+FP+FN+TN). For comparing the difference of diagnostic accuracy between palpable and non-palpable breast cancer groups, we used McNemar's test (comparison for sensitivity and specificity), GEE (comparison for PPV and NPV), and Chi-square tests (comparison of diagnostic accuracy). Values of p less than 0.05 were considered to be statistically significant. Statistics were performed using commercially available statistical software (SAS version 9.1, SAS Inc., Cary, NC, USA).

III. RESULTS

Patient demographics and tumor characteristics are listed in Table 1. The mean age of the patients was 49.5 years with a range of 26 to 79. The mean size of the tumor was 20.4 mm with a range of 4 -130 mm. A palpable breast mass was the most common clinical manifestation (n=241). The most common tumor type was invasive ductal carcinoma (n=363).

Table 1. Patient demographics and tumor characteristics

Mean age of patients	49.53±10.03
Mean size of primary tumor	20.41±12.90
Clinical manifestation	
palpable breast mass	241
asymptomatic	132
pain	5
discharge	4
Tumor type	
ductal	363
lobular	10
mixed ductal and lobular	4
other*	5
T stage (by AJCC classification)	
Tis	34
T1	168
T2	167
T3	11
T4	2
Pathologic N stage (by AJCC classification)	
0	255
1	100
2	16
3	11

*other: invasive apocrine carcinoma, invasive neuroendocrine cancer, metaplastic carcinoma

*SD: standard deviation

1. Diagnostic performance of axillary US

There were 121 patients who had suspicious ALNs and 261 patients who had benign lymph nodes on axillary US. The sensitivity, specificity, PPV, and NPV of axillary US alone were 56.6% (73/121), 81.0% (205/253), 60.3% (73/121) and 78.5% (205/261), respectively. The overall diagnostic accuracy of axillary US was 72.8% (278/382). Excluding the 10 patients who were complete responders to neoadjuvant chemotherapy from the analysis increased the specificity and PPV of axillary US to 84.4% (205/243) and 65.8% (73/111) .

2. Diagnostic performance upon including US-FNA

For the 121 patients who underwent US-FNA, the cytological results of FNA were positive (n=61), atypical (n=1), negative (n=52) and inadequate (n=7). The adequacy rate of US-FNA was 94.2% (114/121). Of the 7 inadequate cytological results, 6 were finally diagnosed as metastasis by SNLD or ALND. When US-FNA was added with US, the sensitivity, specificity, PPV, NPV and accuracy of adding US-FNA were 39.5% (51/129), 95.7% (242/253), 82.3% (51/62), 75.6% (242/320) and 76.7% (293/382), respectively (Figs. 1-3).

Figure 1. A 52 year-old woman with 2.0 cm invasive lobular carcinoma. US of ipsilateral axilla shows cortical thickening with a round shape, suggesting possible metastasis (arrows). The results of FNA were positive for malignancy, and ALND also revealed metastasis.

Figure 2. A 49 year-old woman with a 2.9 cm invasive ductal carcinoma. Axillary US showed asymmetric cortical thicking, suggesting possible metastasis (arrows). The results of FNA and subsequent SNB for axillary LN were negative for malignancy

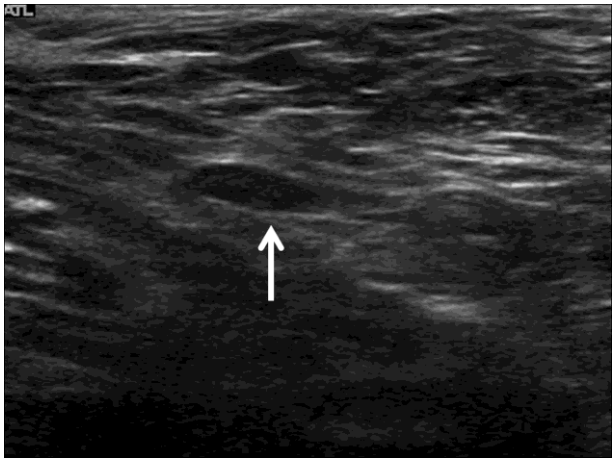

Figure 3. A 57 year-old woman with a 2.5 cm invasive ductal carcinoma. Axillary US showed an oval shaped axillary LN with loss of fatty hilum, suggesting possible metastasis (arrows). The results of FNA were negative for malignancy but SLNB revealed a metastatic lymph node.

With the exception of the ten complete responders, only one false positive FNA was noted, and thus the specificity and PPV of US- FNA were increased to 99.6% (242/243) and 98.1% (51/52). Addition of FNA decreased sensitivity and NPV, whereas specificity and PPV were increased (Table 2). Table 3 shows the diagnostic performance of US and adding US-FNA according to palpability of the primary breast cancer. The palpable cancer group exhibited higher sensitivity of ALN metastasis detection than the nonpalpable cancer group, although the difference was not statistically significant. However, NPV was increased to a statistically significant degree in the nonpalpable breast cancer group compared with the palpable breast cancer group after adding US –FNA.

3. Influence on treatment

Sixty-two patients had positive cytological results on FNA, and thus

unnecessary SLNB was avoided in 16.2% (62/382) of all patients and 51.2% (62/121) of patients who underwent US-FNA.

Table 2. Comparison of diagnostic performances of US and US-FNA in the diagnosis of axillary lymph node metastasis

	US only (%)	**Adding US-FNAB (%)**	**P value**
Sensitivity	73/129 (56.3)	51/129 (39.5)	<0.0001
Specificity	205/253 (81.0)	242/253 (95.7)	<0.0001
Specificity*	205/243 (84.4)	242/243 (99.6)	<0.0001
PPV	73/121 (60.3)	51/62 (82.3)	<0.0001
PPV*	73/111 (65.8)	51/52(98.1)	0.0009
NPV	205/261 (78.5)	242/320 (75.6)	0.0296

*: excluding complete responders to chemotherapy

Table 3. Comparison of diagnostic performances of US and US-FNA in the diagnosis of axillary lymph node metastasis between palpable breast cancers and nonpalpable breast cancers

		Total (n=382)	Palpable (n=241)	Non-palpable (n=141)	p-value
Sensitivity	US only (%)	73/129 (56.6)	54/93 (58.1)	19/36 (52.8)	0.5869
	Adding US-FNA (%)	51/129 (39.5)	38/93 (40.9)	13/36 (36.1)	0.6207
Specificity	US only (%)	205/253 (81)	116/148 (78.4)	89/105 (84.8)	0.202
	Adding US-FNA (%)	242/253 (95.7)	139/148 (93.9)	103/105 (98.1)	0.129
Specificity*	US only (%)	205/243 (84.4)	116/140 (82.9)	89/103 (86.4)	0.4514
	Adding US-FNA (%)	242/243 (99.6)	139/140 (99.3)	103/103 (100)	>0.9999
PPV	US only (%)	73/121 (60.3)	54/86 (62.8)	19/35 (54.3)	0.3859
	Adding US-FNA (%)	51/62 (82.3)	38/47 (80.9)	13/15 (86.7)	>0.9999
PPV*	US only (%)	73/111 (65.8)	54/78 (69.2)	19/33 (57.6)	0.2369
	Adding US-FNA (%)	51/52 (98.1)	38/39 (97.4)	13/13 (100)	>0.9999
NPV	US only (%)	205/261 (78.5)	116/155 (74.8)	89/106 (84.0)	0.0778
	Adding US-FNA (%)	242/320 (75.6)	139/194 (71.7)	103/126 (81.8)	0.0398

*: excluding complete responders to chemotherapy

IV. DISCUSSION

Although SLNB is less invasive than ALND and has the potential to improve preoperative staging, SLNB has several disadvantages such as anesthetic risk, inconvenience for some patients to undergo a two-stage surgery, and some complications such as seroma formation, lymphedema, sensory nerve injury, and limitation in the range of shoulder motion [9]. If ALN metastasis was identified by pre-operative status, unnecessary SLNB could be avoided, allowing patients to undergo one-stage axillary surgery and neoadjuvant chemotherapy directly. Therefore, more reliable and less invasive methods for preoperative evaluation of ALN should be performed on patients with breast cancer, and SLNB should be performed prudently.

Our study suggests that patients who underwent axillary US with US-FNA had higher specificity and PPV for detecting axillary metastasis compared to patients who underwent US only. However, addition of US-FNA lowered sensitivity compared with axillary US only, because 6 out of the 7 inadequate cytologic results of US-FNA were later identified as metastasis in final pathology. Baruah et al. also reported a lower sensitivity after adding US-FNA (28.5%) compared to axillary US only (54.0%), which was due to regarding nine inadequate cytologic results as negative results [32]. Likewise, a study by Kuenen-Boumeester showed a higher sensitivity of US-FNA in cases where inadequate cytologic reports were excluded (57.0%) rather than when they were regarded as negative results (47.1%) [26].

In both the present study and previous reports, the sensitivity and NPV after adding US-FNA have not been high enough to omit SLNB. Thus, several authors have recommended that patient who have negative cytology on US-FNA be subjected to SLNB because of the false negative rate of US-FNA and non-visualization of micrometastasis on axillary US [5, 6, 13, 14, 17, 32, 33]. The frequency of inadequate sampling was about 5.7% on our study,

which is comparable with a prior study performed at our institution (4.5%) [34] and is much lower than of the rates reported by Kuenen-Boumeester (26.8%) and Baruah (12.2%) [26, 33]. This difference may be due to experience of radiologists and pathologists, as well as specimen preparation technique.

Recently, Baruah et al. showed the influence of tumor grade and size of breast cancer on axillary US and US-FNA [33]. In their study, the sensitivity of axillary US and US-FNA was increased in patients with a high grade of breast cancer and tumors 20mm or greater ($p < 0.0005$). Furthermore, US-FNA was more sensitive for detecting LN metastasis in patients with larger primary cancers because LN metastasis tends to be higher in groups with larger breast cancers [35]. Their study evaluated the relationship between sensitivity of US-FNA and pathologic size of primary breast cancer; however, we consider the influence of palpability of primary breast cancer on diagnostic performance of US and US-FNA in clinical practice to be very important. Therefore, we compared diagnostic performance of US and US-FNA according to the palpability of breast cancer. In our study, the sensitivity of US alone and with US-FNA was increased in the palpable breast cancer group compared with the non-palpable breast cancer group, although the difference was not statistically significant. However, the NPV of adding US-FNA was increased in the non-palpable breast cancer group compared to the palpable group, the result of which showed that the benign cytologic result of non-palpable breast cancer group had higher predictive value of benign ALN than the palpable breast cancer group.

Previous studies have reported that the rates of patients who may be able to avoid SLNB are between 1~26%, which is a rather broad range [12, 14, 18-22]. In our study, 16.2% of all breast cancer patients could have avoided unnecessary SLNB. Further, our study showed that axillary US and US-guided FNA of ALN in breast cancer patients with clinically negative ALN could be reliable tools for evaluation of axillary metastasis. Therefore,

significant numbers of patients may be able to avoid unnecessary SLNB, and instead quickly undergo ALND or neoadjuvant chemotherapy.

Aside from the complete responders, only one patient who had positive cytological results on FNA showed negative final pathologic findings after chemotherapy. Previous studies have reported that the false-positive rate of US-FNA is between 0 to 1.6% and are likely caused by misinterpretation of cytologic specimens by cytopathologists [17, 26, 31]. The other possibility was incomplete dissection of metastatic ALN, and therefore long-term follow-up of axillary metastasis of this patient will be necessary.

The false negative rate of US and US-FNA for ALN metastasis (8~35.3%) in our study was higher than reported in previous studies [6, 15, 16, 17, 19, 26, 34]. Krishnamurthy et al. reported that discrepancies between negative cytological results of FNA and positive final surgical results are caused by smaller metastatic deposition (<0.5mm) [15]. Likewise, a recent study reported that none of the ALNs among 12.1% (14/116) with micrometastasis in patients with LN metastasis were diagnosed by pre-operative US and FNA [32]. In our study, 17 negative cytological results of FNA, six inadequate FNA samplings, and 55 benign findings of ALN on US were identified as metastatic ALN on final pathologic reports. We did not evaluate the metastatic deposit sizes of axillary lymph nodes, although we did presume that the LNs with false-negative results on US-FNA may have had small metastatic deposits. Another possibility is that FNA of non-sentinel LNs instead of metastatic sentinel LN were performed. In this study, only abnormal axillary LNs at US were aspirated, while lymph nodes that appeared abnormal at US were more likely to be positive at US-FNA. Indeed, some authors have suggested that performing US-FNA in non-suspicious LNs may be beneficial [19, 35]. Specifically, Jain, et al. reported that preoperative ALN metastasis could be detected in seven patients (26% of non-suspicious LNs) with high specificity and PPV (100%) of FNA, by

performing US-FNA in clinically and radiologically non-suspicious LN [19]. Likewise, Koeliker, et al. reported that an increase in the rate of preoperative detection of ALN metastases in three non-suspicious LNs (13.0% of non-suspicious LNs) [35]. To increase the sensitivity of FNA of ALN in breast cancer patients, Kim et al suggested that evaluation of tumor markers (breast cancer antigen 15-3 and carcinoembryonic antigen) in FNA washout could be helpful [34]. To test this hypothesis, further studies with a larger population should be conducted.

Our study has several limitations. First, five different radiologists with varying degrees of experience performed axillary US and US-FNA, and therefore interobserver variability may affect the interpretations of axillary US. Secondly, the palpability of primary breast cancer is subjective, and therefore there was the possibility of bias owing to breast composition and/or tumor location.

V. CONCLUSION

In conclusion, the combination of axillary US and US-FNA is useful in preoperative work-up of breast cancer patients and is valuable in planning the proper management of breast cancer patients.

REFERENCES

1. Wilking N, Rutqvist LE, Carstensen J, Mattsson A, Skoog L. Prognostic significance of axillary nodal status in primary breast cancer in relation to the number of resected nodes. Stockholm Breast Cancer Study Group. Acta Oncol. 1992;31:29-35.
2. Bryan RM, Mercer RJ, Bennett RC, Rennie GC. Prognostic factors in breast cancer and the development of a prognostic index. Br J Surg. 1986;73:267-71.
3. Krag D, Weaver D, Ashikaga T, Moffat F, Klimberg VS, Shriver C, et al. The sentinel node in breast cancer--a multicenter validation study. N Engl J Med. 1998;339:941-6.
4. Banerjee M, George J, Song EY, Roy A, Hryniuk W. Tree-based model for breast cancer prognostication. J Clin Oncol. 2004;22:2567-75.
5. Fraile M, Rull M, Julian FJ, Fuste F, Barnadas A, Llatjos M, et al. Sentinel node biopsy as a practical alternative to axillary lymph node dissection in breast cancer patients: an approach to its validity. Ann Oncol. 2000;11:701-5.
6. Deurloo EE, Tanis PJ, Gilhuijs KG, Muller SH, Kroger R, Peterse JL., et al. Reduction in the number of sentinel lymph node procedures by preoperative ultrasonography of the axilla in breast cancer. Eur J Cancer. 2003;39:1068-73.
7. Goyal A, Newcombe RG, Chhabra A, Mansel RE. Morbidity in breast cancer patients with sentinel node metastases undergoing delayed axillary lymph node dissection (ALND) compared with immediate ALND. Ann Surg Oncol. 2008;15:262-7.
8. Veronesi U, Paganelli G, Galimberti V, Viale G, Zurrida S, Bedoni M, et al. Sentinel-node biopsy to avoid axillary dissection in breast cancer with

clinically negative lymph-nodes. Lancet. 1997;349:1864-7.
9. Purushotham AD, Upponi S, Klevesath MB, Bobrow L, Millar K, Myles JP, Duffy SW. Morbidity after sentinel lymph node biopsy in primary breast cancer: results from a randomized controlled trial. J Clin Oncol. 2005;23:4312-21.
10. Mustonen P, Farin P, Kosunen O. Ultrasonographic detection of metastatic axillary lymph nodes in breast cancer. Ann Chir Gynaecol. 1990;79:15-8.
11. Oruwari JU, Chung MA, Koelliker S, Steinhoff MM, Cady B. Axillary staging using ultrasound-guided fine needle aspiration biopsy in locally advanced breast cancer. Am J Surg. 2002;184:307-9.
12. Yang WT, Ahuja A, Tang A, Suen M, King W, Metreweli C. High resolution sonographic detection of axillary lymph node metastases in breast cancer. J Ultrasound Med. 1996;15:241-6.
13. Moore A, Hester M, Nam MW, Brill YM, McGrath P, Wright H, et al. Distinct lymph nodal sonographic characteristics in breast cancer patients at high risk for axillary metastases correlate with the final axillary stage. Br J Radiol. 2008;81:630-6.
14. Verbanck J, Vandewiele I, De Winter H, Tytgat J, Van Aelst F, Tanghe W. Value of axillary ultrasonography and sonographically guided puncture of axillary nodes: a prospective study in 144 consecutive patients. J Clin Ultrasound. 1997;25:53-6.
15. Krishnamurthy S, Sneige N, Bedi DG, Edieken BS, Fornage BD, Kuerer HM, et al. Role of ultrasound-guided fine-needle aspiration of indeterminate and suspicious axillary lymph nodes in the initial staging of breast carcinoma. Cancer. 2002;95:982-8.
16. van Rijk MC, Deurloo EE, Nieweg OE, Gilhuijs KG, Peterse JL, Rutgers EJ, et al. Ultrasonography and fine-needle aspiration cytology can spare breast cancer patients unnecessary sentinel lymph node biopsy. Ann Surg

Oncol. 2006;13:31-5.
17. Holwitt DM, Swatske ME, Gillanders WE, Monsees BS, Gao F, Aft RL, et al. Scientific Presentation Award: The combination of axillary ultrasound and ultrasound-guided biopsy is an accurate predictor of axillary stage in clinically node-negative breast cancer patients. Am J Surg. 2008;196:477-82.
18. Pamilo M, Soiva M, Lavast EM. Real-time ultrasound, axillary mammography, and clinical examination in the detection of axillary lymph node metastases in breast cancer patients. J Ultrasound Med. 1989;8:115-20.
19. Jain A, Haisfield-Wolfe ME, Lange J, Ahuja N, Khouri N, Tsangaris T, et al. The role of ultrasound-guided fine-needle aspiration of axillary nodes in the staging of breast cancer. Ann Surg Oncol. 2008;15:462-71.
20. de Freitas R Jr., Costa MV, Schneider SV, Nicolau MA, Marussi E. Accuracy of ultrasound and clinical examination in the diagnosis of axillary lymph node metastases in breast cancer. Eur J Surg Oncol. 1991;17:240-4.
21. Tate JJ, Lewis V, Archer T, Guyer PG, Royle GT, Taylor I. Ultrasound detection of axillary lymph node metastases in breast cancer. Eur J Surg Oncol. 1989;15:139-41.
22. Bonnema J, van Geel AN, van Ooijen B, Mali SP, Tjiam SL., Henzen-Logmans SC, et al. Ultrasound-guided aspiration biopsy for detection of nonpalpable axillary node metastases in breast cancer patients: new diagnostic method. World J Surg. 1997;21:270-4.
23. de Kanter AY, van Eijck CH, van Geel AN, Kruijt RH, Henzen SC, Paul, MA, et al. Multicentre study of ultrasonographically guided axillary node biopsy in patients with breast cancer. Br J Surg. 1999;86:1459-62.
24. Sapino A, Cassoni P, Zanon E, Fraire F, Croce S, Coluccia C, et al. Ultrasonographically-guided fine-needle aspiration of axillary lymph

nodes: role in breast cancer management. Br J Cancer. 2003;88:702-6.
25. Motomura K, Inaji H, Komoike Y, Kasugai T, Nagumo S, Hasegawa Y, et al. Gamma probe and ultrasonographically-guided fine-needle aspiration biopsy of sentinel lymph nodes in breast cancer patients. Eur J Surg Oncol. 2001;27:141-5.
26. Kuenen-Boumeester V, Menke-Pluymers M, de Kanter AY, Obdeijn IM, Urich D, Van Der Kwast TH. Ultrasound-guided fine needle aspiration cytology of axillary lymph nodes in breast cancer patients. A preoperative staging procedure. Eur J Cancer. 2003;39:170-4.
27. Yang WT, Chang J, Metreweli C. Patients with breast cancer: differences in color Doppler flow and gray-scale US features of benign and malignant axillary lymph nodes. Radiology. 2000;215:568-73.
28. Abe H, Schmidt RA, Sennett CA, Shimauchi A, Newstead GM. US-guided core needle biopsy of axillary lymph nodes in patients with breast cancer: why and how to do it. Radiographics. 2007;27 Suppl 1:S91-9.
29. Topal U, Punar S, Tasdelen I, Adim SB. Role of ultrasound-guided core needle biopsy of axillary lymph nodes in the initial staging of breast carcinoma. Eur J Radiol. 2005;56:382-5.
30. Moon HJ, Kim MJ, Kim EK, Park BW, Youk JH, Kwak JY, et al. US Surveillance of regional lymph node recurrence after breast cancer surgery. Radiology 2009;252:673-81
31. Ciatto S, Brancato B, Risso G, Ambrogetti D. Bulgaresis P, Maddau C, et al. Accuracy of fine needle aspiration cytology (FNAC) of axillary lymph nodes as a triage test in breast cancer staging. Breast Cancer Res Treat. 2007;103:85-91.
32. Swinson C, Ravichandran D, Nayagam M, Allen S. Ultrasound and fine needle aspiration cytology of the axilla in the pre-operative identification of axillary nodal involvement in breast cancer. Eur J Surg Oncol.

2009;35:1152-7
33. Baruah BP, Goyal A., Young P, Douglas-Jones AG, Mansel RE. Axillary node staging by ultrasonography and fine-needle aspiration cytology in patients with breast cancer. British Journal of Surgery 2010; 97:680-3
34. Kim MJ, Park BW, Lim JB, Kim HS, Kwak JY, Kim SJ, et al. Axillary Lymph node metastasis: CA-15-3 and carcinoembryonic antigen concentrations in fine-needle aspirates for preoperative diagnosis in patients with breast cancer. Radiology 2010;254:691-7
35. Koelliker SL, Chung MA, Mainiero MB, Margaret MS, Blake C. Axillary lymph nodes: US-guided fine-needle aspiration for initial staging of breast cancer-correlation with primary tumor size. Radiology 2008;246:81-9.

<ABSTRACT (IN KOREAN)>

유방암 환자에서 수술 전 액와림프절 초음파와 초음파유도하세침검사의 의의

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목적: 수술 전 유방암 환자를 대상으로 액와림프절 전이를 평가하는 데 있어서 초음파와 초음파유도하세침검사의 정확도을 알아봄으로써 그 진단적 의의에 대해 알아 보고 자 한다.

재료 및 방법: 수술 전 액와림프절 초음파를 시행받은 유방암 환자 382명의 환자의 기록을 후향적으로 분석해 보았다. 그 중 121명의 환자가 초음파에서 전이가 의심되어 초음파유도하세침검사를 시행하였다. 초음파 또는 초음파유도하세침검사의 정확도는 세포병리 또는 수술 후 조직병리 결과와 비교하여 나타내고, 진양성, 진음성, 가양성, 가음성을 기록하고 민감도, 특이도, 양성예측도, 음성예측도를 계산하여, 그 결과를 분석하였다.

결과: 382명의 환자 중, 253명의 환자가 수술 후 조직병리 검사에서 액와부 전이가 없었다다. 액와림프절 초음파의 민감도, 특이도, 양성예측도, 음성예측도는 각각 56.6% (73/129), 81.0% (205/253), 60.3% (73/121) and 78.5% (205/261) 였으며 초음파유도하세침검사를 시행한 경우에는 각각 39.5% (51/129), 95.7% (242/253), 82.3% (51/62) and 75.6% (242/320) 였다. 초음파유도하세침검사에서는 전이가

있었으나 신보강화학요법을 시행하여 수술 후 조직병리 검사에서 전이가 없었던 환자를 제외하였을 때, 초음파유도하세침검사를 함께 시행한 경우의 특이도와 양성예측도는 99.6% (242/243)과 98.1% (51/52)로 증가하였다. 이학적검사에서 유방암 종괴가 촉지되는 군과 촉지되지 않는 군 사이의 민감도, 특이도, 양성예측도, 음성예측도는 초음파만 시행했을 경우는 통계학적으로 의미있는 차이가 없었지만 초음파유도하세침검사를 함께 시행한 경우 촉지되지 않는 유방암 종괴를 가지고 있는 군에서 음성예측도가 증가하였다 (p= 0.0398). 수술 전 액와림프절의 평가를 위해 시행한 초음파와 초음파유도하세침검사를 통해 유방암 환자의 16.2% (62/382)에서 불필요한 감시림프절 생검을 피하고 신보강화학요법 또는 액와림프절곽청술을 바로 시행할 수 있었다.

결론: 유방암 환자에서 수술 전 액와림프절 초음파와 초음파유도하세침검사를 시행함으로써 적절한 치료를 시행하는 데 유용한 정보를 제공할 수 있다.

핵심되는 말 : 액와림프절, 초음파, 초음파유도하세침검사, 유방암.

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