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Automated Versus Handheld Breast Ultrasound for Evaluating Axillary Lymph Nodes in Patients With Breast Cancer

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Objective: Automated breast ultrasound (ABUS) is a relevant imaging technique for early breast cancer diagnosis and is increasingly being used as a supplementary tool for mammography. This study compared the performance of ABUS and handheld ultrasound (HHUS) in detecting and characterizing the axillary lymph nodes (LNs) in patients with breast cancer.

Materials and Methods: We retrospectively reviewed the medical records of women with recently diagnosed early breast cancer (≤ T2) who underwent both ABUS and HHUS examinations for axilla (September 2017–May 2018). ABUS and HHUS findings were compared using pathological outcomes as reference standards. Diagnostic performance in predicting any axillary LN metastasis and heavy nodal-burden metastases (i.e., ≥ 3 LNs) was evaluated. The ABUS-HHUS agreement for visibility and US findings was calculated.

Results: The study included 377 women (53.1 ± 11.1 years). Among 385 breast cancers in 377 patients, 101 had axillary LN metastases and 30 had heavy nodal burden metastases. ABUS identified benign-looking or suspicious axillary LNs (average, 1.4 ± 0.8) in 246 axillae (63.9%, 246/385). According to the per-breast analysis, the sensitivity, specificity, positive and negative predictive values, and accuracy of ABUS in predicting axillary LN metastases were 43.6% (44/101), 95.1% (270/284), 75.9% (44/58), 82.6% (270/327), and 81.6% (314/385), respectively. The corresponding results for HHUS were 41.6% (42/101), 95.1% (270/284), 75.0% (42/56), 82.1% (270/329), and 81.0% (312/385), respectively, which were not significantly different from those of ABUS ($P \geq 0.53$). The performance results for heavy nodal-burden metastases were 70.0% (21/30), 89.6% (318/355), 36.2% (21/58), 97.3% (318/327), and 88.1% (339/385), respectively, for ABUS and 66.7% (20/30), 89.9% (319/355), 35.7% (20/56), 97.0% (319/329), and 88.1% (339/385), respectively, for HHUS, also not showing significant difference ($P \geq 0.57$). The ABUS–HHUS agreement was 95.9% (236/246; Cohen's kappa = 0.883).

Conclusion: Although ABUS showed limited sensitivity in diagnosing axillary LN metastasis in early breast cancer, it was still useful as the performance was comparable to that of HHUS.

Keywords: Automated breast ultrasound system; Ultrasound; Axillary lymph node; Diagnostic performance; Breast cancer

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INTRODUCTION

Accurate assessment of the presence and extent of lymph node (LN) metastasis is a key determinant of locoregional stage and appropriate disease management of breast cancer [1]. Axillary LN dissection (ALND) is a traditional method for axillary staging that involves the surgical removal of level I and II axillary LNs [2]. However, ALND was recently replaced by sentinel LN biopsy (SLNB) based on evidence from several prospective randomized trials demonstrating high negative predictive values (NPVs) for the latter, which could reduce the need for ALND and its associated morbidity [3-5]. Moreover, given the results of the ACOSOG Z0011 trial, SLNB is the standard treatment for T1-2 cancer with one or two LN metastases [6]. This trial revealed that women with clinical T1-2 tumors and fewer than three positive sentinel LNs who underwent lumpectomy and breast radiation therapy followed by systemic therapy did not benefit from ALND in terms of local control, disease-free survival, and overall survival [7].

Axillary ultrasonography (US) is the optimal imaging tool for nodal staging, with moderate sensitivity and high specificity [8]. In addition, the added benefit of US-guided biopsy is the increased sensitivity and specificity of axillary US. A previous meta-analysis revealed that combined axillary US and US-guided biopsy had sensitivities of 79.6% and specificities of 98.3% [9]. However, the ACOSOG Z0011 trial [7] suggested that the usefulness of axillary US in women with early breast cancer remains unclear [10,11].

US is commonly used as an adjunct cancer screening method for dense breast tissue. Automated breast US (ABUS) is commonly used owing to its ability to produce reproducible, high-resolution images and reduced dependency on human operators [12]. Supplementing mammography with ABUS screening reportedly results in positive outcomes similar to handheld US (HHUS) screening, including increased invasive cancer detection and reduced interval cancer rates [13,14]. Although ABUS only evaluates a limited area, it still covers the lower axillary regions. Owing to its large field of view, ABUS provides information on the status of axillary LN with suspected metastasis. This study compared the performance of ABUS and handheld ultrasound (HHUS) in detecting and characterizing the axillary LNs in patients with breast cancer.

MATERIALS AND METHODS

Study Population

The initial sample included 603 consecutive patients with breast cancer who underwent preoperative ABUS at our tertiary care academic institution between September 2017 and May 2018. During the study period, ABUS performed on women with recently diagnosed breast cancer covered the same areas as screening. This included both the breast and the lower axillary areas. Additionally, HHUS was performed after ABUS in the axillary area for staging; if suspicious LNs were identified on HHUS, a US-guided biopsy was performed. Subsequently, women with LN metastases were considered candidates for neoadjuvant chemotherapy. Women without available HHUS images for axillary LNs (n = 32), those who underwent neoadjuvant chemotherapy (n = 63), and those with final pathologically confirmed ductal carcinoma in situ only (n = 84) or T3 or higher advanced cancer (n = 47) were excluded. The final sample included 377 women, comprising 385 breasts, including eight bilateral breast lesions (Fig. 1).

This study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by our Institutional Review Board (IRB No. B-2105-683-106), which waived the requirement for written informed consent owing to the retrospective nature of the study.

Image Acquirement of ABUS

All ABUS examinations were performed using the Invenia ABUS system (GE Healthcare, Sunnyvale, CA, USA) by one of the two radiology technologists with extensive US training.

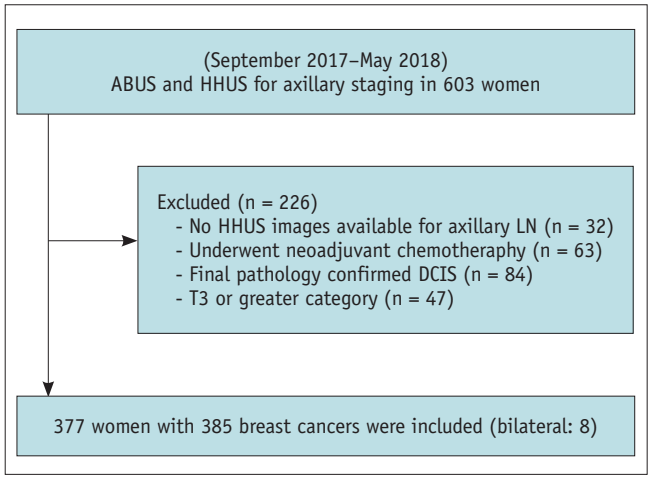

Fig. 1. Flowchart of the study population. ABUS = automated breast ultrasound, HHUS = handheld ultrasound, LN = lymph node, DCIS = ductal carcinoma in situ

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ABUS was continuous, automated, and presented a 6–15 MHz wide-aperture linear probe. The patients were placed in the supine position during the examination, and a sponge was placed beneath their shoulders to evenly spread the breast tissue. Three volumes were obtained for each breast as follows: anteroposterior, covering the central part of the breast with the nipple centered; medial, covering the inner and inferior parts, including inframammary folds, with the nipple in the superior-lateral corner; and lateral, covering the upper and outer parts with the nipple in the inferior-medial corner (Fig. 2) [15]. The lateral view must include the axillary tail and usually starts at the lower axillary fossa; therefore, it includes the lower axillary areas as seen on mammography. In patients with large breasts, additional views were obtained to cover all breast tissues. Volume images were automatically transferred to a dedicated workstation. Volumetric data were obtained in the axial plane with a 0.2-mm slice thickness. Coronal and sagittal images were reconstructed from the axial images. The field of view was set to 15.4 x 17.0 x up to 5 cm from the skin to the chest wall. Multiplanar images (axial, sagittal, and coronal planes) were used for the evaluation. The scan time for a 6-volume bilateral routine is usually 10–15 minutes.

Image Acquirement of HHUS

HHUS was performed after ABUS, specifically for the axillary staging of both axillae. HHUS images were acquired using a linear transducer at a bandwidth of 7–15 MHz (iU22 Ultrasound System, Philips, Bothell, WA, USA; SuperSonic Imagine, Aix-en-Provence, France). All HHUS examinations were performed by one of three breast radiologists (S.M.K., M.J., and B.L.Y.) with 20, 16, and 11 years of experience in breast imaging, respectively.

Imaging Evaluation

Initially, two radiologists (S.M.K. and M.J.) independently reviewed the ABUS and HHUS images. The reviewers were aware that the patients had breast cancer and which side was affected, although they were blinded to the presence of axillary LN metastasis on pathological examination. Two separate US image review sessions were conducted: the first involved a review of HHUS images of axillary LNs, and the second, performed 3 months after the first, involved a review of ABUS volume data using a dedicated workstation. Reviewers first evaluated the presence of identifiable benign-looking or suspicious axillary LNs on ABUS images and then evaluated the LNs based on the following findings: hilum compression or loss, uneven or even cortical thickening > 3-mm, focal hyperechoic cortical change, LN shape (oval, round, or irregular), circumscribed or non-circumscribed LN margins, and presence of extranodal extension [16]. Any of the following US findings were considered abnormal: hilum compression or loss, > 3-mm uneven cortical thickening, > 3-mm cortical thickening, focal hyperechoic cortical change, round or irregular shape, non-circumscribed margin, and extranodal extension of

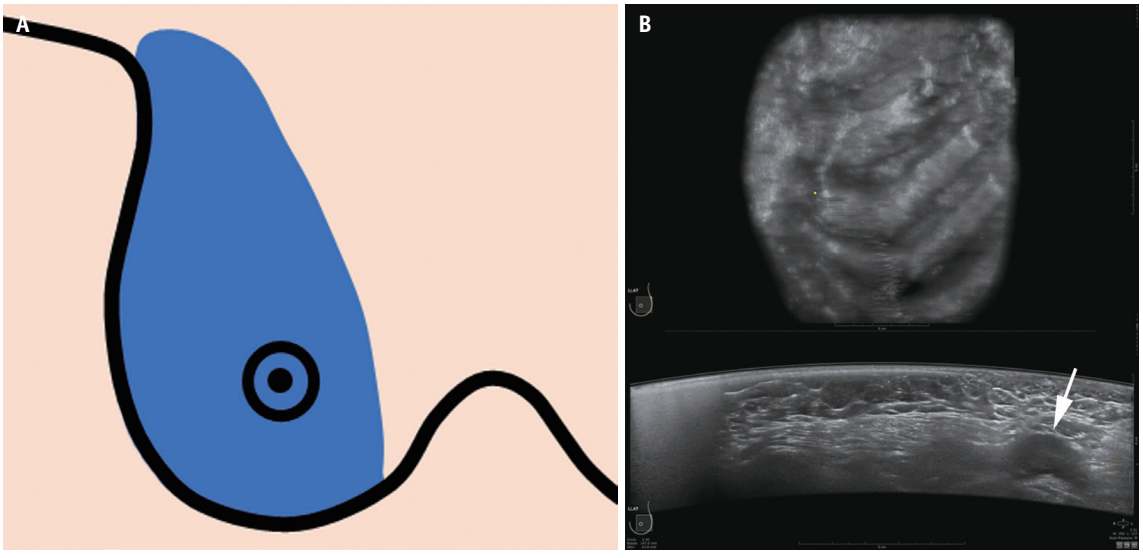

Fig. 2. Diagram and ABUS image of lateral scan. **A:** A blue area indicates the scan range of the lateral scan, which covers the upper and outer parts with the nipple in the inferior-medial corner. **B:** ABUS lateral scan shows a suspicious lymph node (arrow). ABUS = automated breast ultrasound

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axillary LNs [16,17].

After completing their analyses, the radiologists reviewed the images, analyzed the results at the same workstation, and reached a consensus. The consensus results were used for further analyses.

Histopathological Evaluation

LN tissues obtained by ALND and SLNB were sectioned. Five slides were prepared, stained with hematoxylin and eosin, and examined by a pathologist (S.Y.P.) with 21 years of experience. We described the tumor and nodal stages according to the TNM staging system from the seventh edition of the American Joint Committee on Cancer Staging Manual [1]. A nodal stage of N0 (i+) was considered as a negative final pathology. In patients with bilateral cancer, the surgical and histopathological records were reviewed separately for each side. Tumor molecular subtypes were defined as estrogen/progesterone receptor-positive, human epidermal growth factor receptor 2-positive, or triple-negative [18].

Statistical Analysis

Data were analyzed using Excel (version 16.0; Microsoft Corporation, Redmond, WA, USA). Categorical variables were compared between the ABUS identified and non-identified groups using the chi-square or Fisher's exact test; continuous variables were compared using Student's *t*-test.

Diagnostic performance was compared between ABUS and HHUS, including sensitivity, specificity, positive predictive value (PPV), NPV, and accuracy, using the McNemar test or a generalized estimating equation. The ABUS-HHUS agreement for US detection of abnormal LNs was estimated using percentage agreement and kappa statistics. The ABUS-HHUS agreement for the detection of abnormal LNs was based on the presence of abnormal US findings (hilar changes, cortical changes, LN shape, LN margin, cortical echo pattern, or presence of extranodal extension) and was estimated using kappa statistics. The agreement between ABUS and HHUS cortical thickness measurements was assessed using intraclass correlation coefficients. Kappa values < 0.20, 0.21–0.40, 0.41–0.60, 0.61–0.80, 0.81–1 indicated slight, fair, moderate, substantial, and excellent agreement, respectively [19]. The interobserver variability between the two reviewers of ABUS for LN US findings before consensus was estimated using percent agreement, kappa statistics, and intraclass correlation coefficients.

All statistical analyses were performed using STATA (version 14.0; StataCorp, College Station, TX, USA) and open-source R software (version 3.3.2; http://www.R-project.org). $P < 0.05$ indicated statistical significance.

RESULTS

Patient and Lesion Characteristics

The characteristics of 377 patients, 385 breasts, and tumors are shown in Table 1. This study included 317 invasive ductal carcinomas, 23 ductal carcinomas in situ with microinvasion, and 37 malignancies including invasive lobular carcinoma (n = 18), metaplastic carcinoma (n = 2), papillary carcinoma (n = 3), mucinous carcinoma (n = 13), and tubular carcinoma (n = 1). The axillary nodal staging was performed using SLNB (81.2%, 306/377) and ALND (18.8%, 71/377). Among 377 patients, 100 had axillary LN metastases (N1, 81; N2, 13; N3, 6) and 29 had ≥ 3 heavy nodal-burden metastases. Among 385 breasts with cancer, 101 had axillary

Table 1. Patient and tumor characteristics

Variable	Per patient (n = 377)	Per breast (n = 385)
Age, yrs	53.1 ± 11.1 (28–91)	53.0 ± 11.0 (28–91)
Histologic type		
Invasive ductal carcinoma	317 (84.1)	325 (84.4)
Others*	60 (15.9)	60 (15.6)
T category		
T1	263 (69.8)	270 (70.1)
T2	114 (30.2)	115 (29.9)
Surgical methods of axillary nodal staging		
SLNB	306 (81.2)	313 (81.3)
ALND	71 (18.8)	72 (18.7)
N category		
N0	277 (73.5)	284 (73.8)
N1	81 (21.5)	81 (21.0)
N2	13 (3.4)	14 (3.6)
N3	6 (1.6)	6 (1.6)
Heavy nodal-burden metastasis (defined as ≥ 3 LNs)		
Yes	29 (7.7)	30 (7.8)
No	348 (92.3)	355 (92.2)

Data are presented mean ± standard deviation (range) or number of patients or tumors with percentages in parentheses.
*Other histologic types were ductal carcinoma in situ with microinvasion, invasive lobular, mucinous, metaplastic, papillary, and tubular carcinomas.
T = tumor, SLNB = sentinel lymph node biopsy, ALND = axillary lymph node dissection, N = node, LNs = lymph nodes

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LN metastases (N1, 81; N2, 14; N3, 6) and 30 had heavy nodal-burden LN metastases on surgical pathology.

The Presence of Identifiable Axillary LNs on ABUS

Of 385 ipsilateral axillae breast cancer sites, 246 (63.9%, 246/385) had identifiable axillary LNs (average, 1.4 ± 0.8; median, 1; range, 1–8) visualized by ABUS. For ABUS, patients in the identified versus non-identified group were older age (54 ± 11.7 vs. 51.2 ± 9.6 years, $P = 0.011$), higher body mass index (BMI) (24.1 ± 3.4 vs. 23.2 ± 3.4 kg/m^2, $P = 0.007$), and larger T category tumors at the time of surgery (36.6% [90/246] vs. 18% [25/139], $P < 0.001$). The identified versus non-identified group had a significantly higher incidence of LN (36.2% [89/246] vs. 8.6% [12/139], $P < 0.001$) and heavy nodal-burden (12.2% [30/246] vs. 0% [0/139], $P < 0.001$) (Table 2) metastases with significantly higher abnormality detection using HHUS (21.1% [52/246] vs. 2.9% [4/139], $P < 0.001$). Only 3.1% (12/385) of the patients exhibited clinical palpability in the axilla, and no statistically significant differences were observed.

Among the 139 axillae with LNs not identified on ABUS, 12 had axillary LN metastases (8.6%, 12/139; all N1; one LN metastasis; 11; two LNs metastases; 1) (Table 2, Fig. 3). Ten of the twelve cases not identified by ABUS were not detected by HHUS, all of which had metastases in a single LN, and six had microscopic metastases. In the remaining two cases of metastases detected by HHUS, the LNs were located in the upper axillary region: one with one metastatic LN and the other with two metastatic LNs.

ABUS identified LNs, although they were considered benign, with metastases in 45 cases. Among these cases, 9 had heavy nodal metastases and 36 had less than three LN

Table 2. Characteristics of 385 breast cancers according to LN identification by automated breast ultrasound

Variable	Nonidentified (n = 139)	Identified (n = 246)	Total (n = 385)	*P*
Age, yrs	51.2 ± 9.6	54.0 ± 11.7	53.0 ± 11.1	0.011
BMI, kg/m^2	23.2 ± 3.4	24.1 ± 3.4	23.8 ± 3.5	0.007
Clinical palpability in axilla				0.549
Non-palpable	136 (97.8)	237 (96.3)	373 (96.9)	
Palpable	3 (2.2)	9 (3.7)	12 (3.1)	
T category				< 0.001
T1	114 (82)	156 (63.4)	270 (70.1)	
T2	25 (18)	90 (36.6)	115 (29.9)	
LN metastasis				< 0.001
Yes	12 (8.6)	89 (36.2)	101 (26.2)	
No	127 (91.4)	157 (63.8)	284 (73.8)	
Heavy nodal-burden metastasis				< 0.001
Yes	0 (0)	30 (12.2)	30 (7.8)	
No	139 (100)	216 (87.8)	355 (92.2)	
Estrogen receptor				0.155
Positive	107 (77.0)	204 (82.9)	311 (80.8)	
Negative	32 (23.0)	42 (17.1)	74 (19.2)	
Progesterone receptor				0.509
Positive	95 (68.4)	176 (71.5)	271 (70.4)	
Negative	44 (31.6)	70 (28.5)	114 (29.6)	
HER-2 receptor				0.588
Positive	16 (11.5)	24 (9.8)	40 (10.4)	
Negative	123 (88.5)	222 (90.2)	345 (89.6)	
LN abnormality at handheld US				< 0.001
Yes	4 (2.9)	52 (21.1)	56 (14.6)	
No	135 (97.1)	194 (78.9)	329 (85.5)	

Data are presented as mean ± standard deviation or number of cancers with percentages in parentheses.
LN = lymph node, BMI = body mass index, T = tumor, HER2 = human epidermal growth factor, US = ultrasonography

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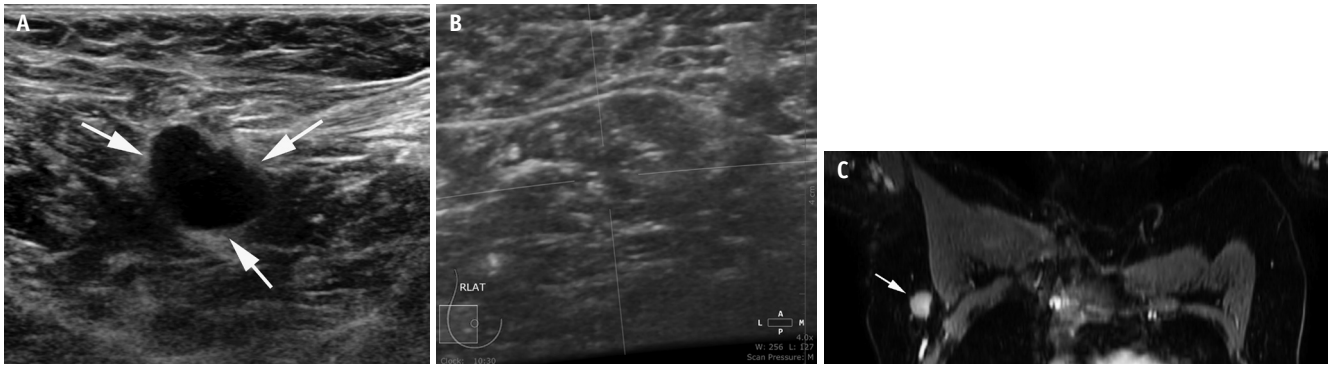
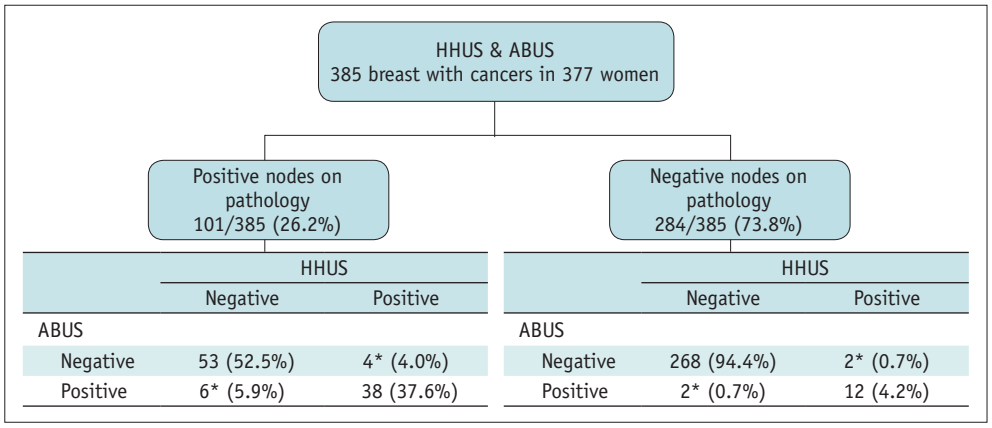


Fig. 3. A 65-year-old woman with recently diagnosed right breast cancer (invasive ductal carcinoma). **A:** Handheld ultrasound showed a suspicious LN with loss of the hilum at level I (arrows). **B:** ABUS showed no suspicious LNs. **C:** Coronal post-gadolinium enhanced T1 weighted MR image shows a highly located LN (arrow) that was not visualized on ABUS. Two metastatic LNs were observed among 18 LNs by axillary dissection. The final anatomical stage was T2, N1. LN = lymph node, ABUS = automated breast ultrasound, T = tumor, N = node



	HHUS	
	Negative	Positive
ABUS		
Negative	53 (52.5%)	4* (4.0%)
Positive	6* (5.9%)	38 (37.6%)

	HHUS	
	Negative	Positive
ABUS		
Negative	268 (94.4%)	2* (0.7%)
Positive	2* (0.7%)	12 (4.2%)

Fig. 4. Results of ABUS and HHUS in relation to any axillary lymph node metastasis at pathology. *Discordant cases between ABUS and HHUS. ABUS = automated breast ultrasound, HHUS = handheld ultrasound

metastases, including 13 micrometastases.

Diagnostic Performance of ABUS and HHUS

The suspicious US findings are presented in Supplementary Table 1. ABUS detected suspicious LNs in 58 axillae (23.6%, 58/246). On ABUS, one suspicious LN was detected in 23 axillae, two in 20 axillae, and three or more in 15 axillae. Metastasis was confirmed in 44 (75.9%, 44/58) of these 58 axillae, including six occurrences of HHUS false negatives (Figs. 4, 5). The remaining 14 (24.1%, 14/58) patients had no metastasis and 10 (71.4%, 10/14) showed suspicious findings on HHUS. HHUS detected suspicious LNs in 56 (14.5%, 56/385) axillae, with confirmed metastasis in 42 (75.0%, 42/56; Fig. 4). Regarding diagnosis of any axillary LN metastasis, the sensitivity, specificity, PPV, NPV, and accuracy were 43.6% (44/101), 95.1% (270/284), 75.9% (44/58), 82.6% (270/327), and 81.6% (314/385), respectively, for ABUS and 41.6% (42/101), 95.1% (270/284), 75.0% (42/56), 82.1% (270/329), and 81.0% (312/385), respectively, for HHUS ($P \geq 0.53$; Table 3).

Of the 58 axillae with suspicious findings detected by ABUS, heavy nodal burden metastasis was confirmed in 21 (36.2%, 21/58), including two HHUS false-negatives (Figs. 5, 6). On ABUS, one suspicious LN with a heavy nodal burden was detected in five axillae, two in eight axillae, and three in eight axillae. The remaining 37 (63.8%, 37/58) patients had no heavy nodal metastases and 31 (83.8%, 31/37) showed suspicious findings on HHUS. Of the 56 axillae with suspicious findings detected on HHUS, heavy nodal burden metastasis was confirmed in 20 patients (35.7%, 20/56). The sensitivity, specificity, PPV, NPV, and accuracy in predicting heavy nodal-burden metastases were 70.0% (21/30), 89.6% (318/355), 36.2% (21/58), 97.3% (318/327), and 88.1% (339/385), respectively, for ABUS and 66.7% (20/30), 89.9% (319/355), 35.7% (20/56), 97.0% (319/329), and 88.1% (339/385), respectively, for

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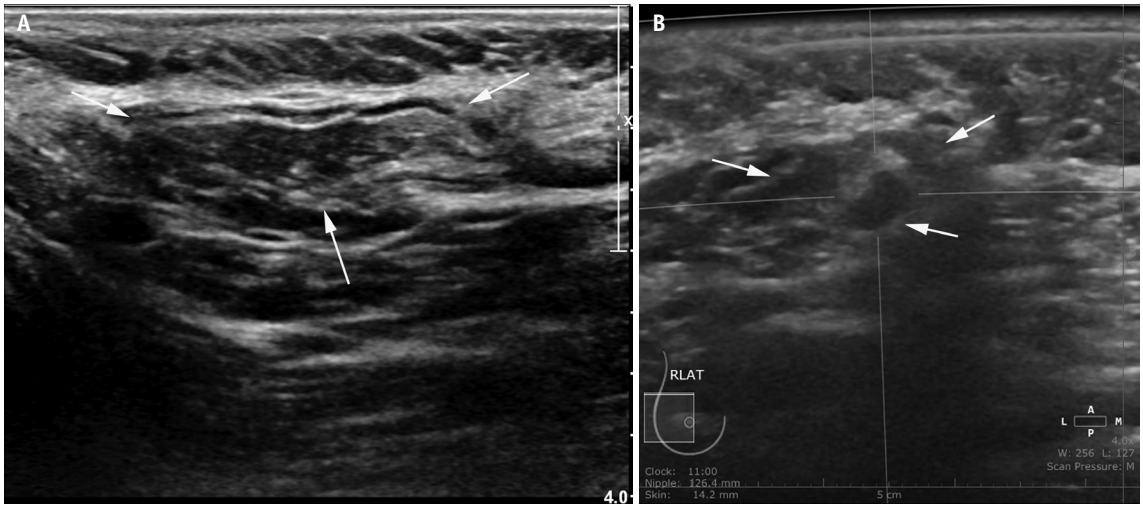
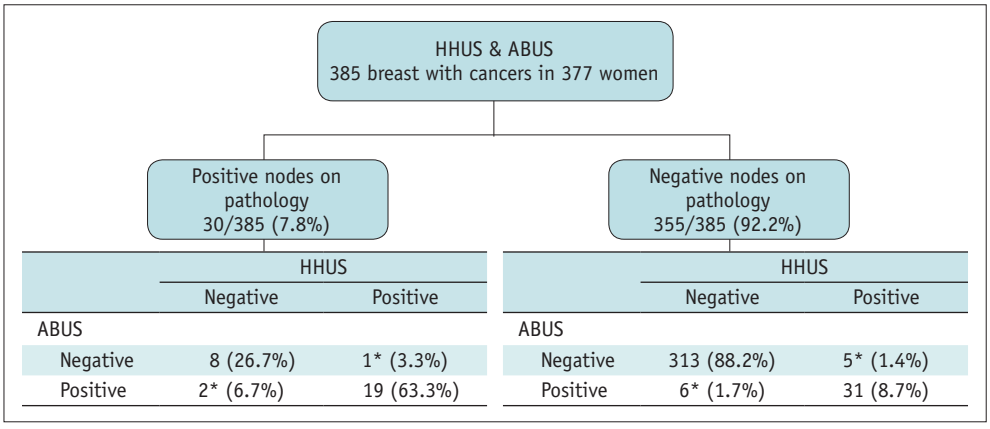


Fig. 5. A 44-year-old woman with recently diagnosed right breast cancer (invasive ductal carcinoma). **A:** Handheld ultrasound shows a normal LN (arrows). **B:** Automated breast ultrasound shows a suspicious LN with uneven cortical thickening and a compressed hilum at level I (arrows). Four metastatic LNs were identified among 24 LNs by axillary dissection. The final anatomical stage was T2, N2. LN = lymph node, T = tumor, N = node



	HHUS	
	Negative	Positive
ABUS		
Negative	8 (26.7%)	1* (3.3%)
Positive	2* (6.7%)	19 (63.3%)

	HHUS	
	Negative	Positive
ABUS		
Negative	313 (88.2%)	5* (1.4%)
Positive	6* (1.7%)	31 (8.7%)

Fig. 6. Results of ABUS and HHUS in relation to heavy nodal axillary lymph node metastasis at pathology. *Discordant cases between ABUS and HHUS. ABUS = automated breast ultrasound, HHUS = handheld ultrasound

HHUS ($P \geq 0.57$) (Table 3).

Agreement between ABUS and HHUS

In the group with ABUS-identified LNs, the ABUS–HHUS agreement rate for detecting suspicious LNs in the 246 axillae was 95.9% (236/246, kappa = 0.883). The kappa values were excellent for the LN cortex echo pattern and cortical change, substantial for hilar change and extranodal extension, and moderate for shape and margin (Table 4). The intraclass correlation coefficient agreement of the LN cortical thickness between ABUS and HHUS was 0.88 (Supplementary Fig. 1).

The interobserver agreement rate between the two reviewers for suspicious LN detection in 246 axillae using ABUS was 88.6% (218/246, kappa = 0.681). The kappa values were excellent for extranodal extension, and substantial for hilar change, shape, margin, echo pattern, and cortical change (Supplementary Table 2). The intraclass correlation coefficient agreement of LN cortical thickness between the two reviewers was 0.79.

DISCUSSION

ABUS is increasingly used as an initial imaging tool for early breast cancer diagnosis. However, the inability to assess the axilla is a disadvantage of ABUS and can lead to false negatives. In our study, LNs were not identified in 36.1% (139/385) of patients, more commonly in patients with low BMIs. Owing to the convex contour of the lateral chest curvature, a slender body shape might lead to less

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Table 3. Diagnostic performance of ABUS and HHUS (n = 385)

Performance parameter	LN metastases (1 or more)		*P*	Heavy nodal burden (3 or more)		*P*
	HHUS	ABUS		HHUS	ABUS	
Sensitivity	41.6 [42/101] (31.9–51.8)	43.6 [44/101] (33.7–53.8)	0.75	66.7 [20/30] (47.2–82.7)	70.0 [21/30] (50.6–85.3)	1.00
Specificity	95.1 [270/284] (91.9–97.3)	95.1 [270/284] (91.9–97.3)	1.00	89.9 [319/355] (86.2–92.8)	89.6 [318/355] (85.9–92.6)	1.00
PPV	75.0 [42/56] (63.1–84.0)	75.9 [44/58] (64.3–84.6)	0.77	35.7 [20/56] (27.1–45.3)	36.2 [21/58] (27.9–45.5)	0.86
NPV	82.1 [270/329] (79.5–84.4)	82.6 [270/327] (79.9–84.9)	0.53	97.0 [319/329] (95.1–98.2)	97.3 [318/327] (95.3–98.4)	0.57
Accuracy	81.0 [312/385] (76.8–84.8)	81.6 [314/385] (77.3–85.3)	0.78	88.1 [339/385] (84.4–91.1)	88.1 [339/385] (84.4–91.1)	1.00

Data are % [numerator/denominator] (95% confidence interval).
ABUS = automated breast ultrasound, HHUS = handheld ultrasound, LN = lymph node, PPV = positive predictive value, NPV = negative predictive value

Table 4. Kappa agreement of ultrasound findings of suspected lymph node metastasis between automated breast ultrasound and handheld ultrasound (n = 246)

Variable	Kappa value
Echo pattern	1.00
Cortical change	0.81
Hilar change	0.80
Extranodal extension	0.71
Shape	0.55
Margin	0.43

coverage of the axillary area on lateral ABUS. Despite this limitation, we observed a LN identification rate on ABUS of 63.9% (246/385), which was higher than that reported for routine mammography (25%–50%) [20]. Mammography is the recommended modality for local staging; however, both mammography and ABUS have limitations in visualizing axillary LNs, resulting in underestimation of the true incidence of axillary LN metastasis. When LNs were not identified on ABUS, only 8.6% (12/139) of the cases showed metastasis; interestingly, all had < 3 LN metastases. Among the 12 metastatic LNs not identified using ABUS, 10 were not detected using HHUS with a single metastatic LN, including six microscopic metastases. Many cases included small metastatic foci that were difficult to detect even with HHUS because of their limited extent, leading to false negatives. The remaining two patients with one or two metastatic LNs in the upper axillary region that were not detected by ABUS were detected by HHUS.

Despite its limited axillary LN identification, ABUS has a diagnostic performance similar to that of HHUS in predicting both LN metastasis and heavy nodal burden metastasis. US is the primary method for the preoperative evaluation of axillary metastasis, with an excellent ability to characterize LN morphology and guide LN sampling. In our study, the sensitivity and specificity of ABUS and HHUS for predicting LN metastasis were comparable to those reported in previous studies [21-23]. Furthermore, a meta-analysis demonstrated a sensitivity of 26.4%–75.9% and a specificity of 88.4%–98.1% for axillary US in detecting nonpalpable LNs when morphological characteristics were used to determine positivity [8].

Moreover, the sensitivity and specificity of ABUS in predicting heavy nodal metastases were statistically similar to those of HHUS and those previously reported [17,24]. Among the diagnostic performance metrics, the NPV of ABUS was the highest, similar to that of HHUS and comparable to that previously reported (93%) by Luo et al. [25]. This high NPV for heavy nodal burden metastases has implications in axillary management. Kim et al. [26] reported that preoperative axillary US can help select patients at minimal risk of non-sentinel LN metastasis for whom ALND can be avoided.

For LN US characterization, we used the same criteria for both HHUS and ABUS to compare and enable evaluation agreement and further research on HHUS. However, the compression power can vary between HHUS and ABUS; therefore, the US findings may differ. In 246 axillary LNs identified by ABUS, ABUS–HHUS agreement was excellent for detecting suspicious LNs, LN cortex echo pattern, and cortical thickness change; substantial for hilar change and extranodal extension; and moderate for shape and margin. The intraclass correlation coefficient for cortical thickness

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was excellent. To the best of our knowledge, no study has evaluated the interobserver agreement between ABUS and HHUS on LN characterization, although previous studies evaluating breast masses showed slight agreement on margin; fair agreement on shape, orientation, and posterior features; moderate agreement on echogenicity; and moderate and excellent agreement on the Breast Imaging Reporting and Data System (BI-RADS) category [14,27]. In our study, the interobserver agreement was substantial to excellent for LNs on US findings, in line with previous studies showing moderate to substantial agreement in various US BI-RADS mass descriptors [28] and HHUS studies evaluating the number of abnormal LNs and their shapes [29,30]. Most false-positive LNs showed suspicious US findings on both ABUS and HHUS; a reactive change in LN may lead to false-positive findings.

Our study has some limitations. First, this was a retrospective study; therefore, a selection bias should be considered. Additionally, technical variations may exist among the radiologists who performed imaging evaluations. To overcome this limitation, the two reviewers retrospectively reviewed all images to reach a consensus; however, only the stored static images were accessible for HHUS. Second, we did not correlate node-to-node imaging findings with pathological findings. Third, we strictly studied the agreement between these two methods, and the inter-observer agreement among multiple radiologists requires further evaluation. Furthermore, owing to the exclusion of patients who underwent preoperative neoadjuvant chemotherapy, more suspicious LNs might have been excluded and fewer cases with a heavy nodal burden might have been included in this study, possibly influencing the generalizability of our results. Finally, because ABUS presents a limited field of view of the axillary area, our ability to generalize the findings for the evaluation of the entire axillary area may be influenced. However, further studies are needed to confirm this hypothesis.

Although our findings indicate that the overall diagnostic performance of ABUS and HHUS is similar, the use of ABUS for axillary staging remains debatable. HHUS should be considered before ABUS for clinically palpable LNs. Furthermore, more than one-third of axillary LNs in recently diagnosed breast cancer sites were not identified using ABUS. When LNs were successfully identified by ABUS, their characterization was possible, with a diagnostic performance and good interobserver agreement similar to those of HHUS. Therefore, when suspicious LNs are identified using ABUS, clinicians should consider a US-guided biopsy and evaluate the entire axillary area using HHUS.

In conclusion, although ABUS showed limited sensitivity in diagnosing axillary LN metastasis in early breast cancer, it was still useful as the performance was comparable to that of HHUS.

Supplement

The Supplement is available with this article at https://doi.org/10.3348/kjr.2023.0100.

Availability of Data and Material

The datasets generated or analyzed during the study are available from the corresponding author on reasonable request.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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