RESEARCH ARTICLE

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Significance of Shear Wave Elastography and B-Mode Ultrasound in Assessing Axillary Lymph Nodes in Patients with Breast Cancer

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Abstract

Objectives: The purpose of this study was to investigate the potential benefits of including shear wave elastography (SWE) testing alongside B-Mode ultrasonography (US) in identifying morphologic abnormalities in individuals diagnosed with breast cancer involving axillary lymph nodes (ALNs).

Methods: Fifty-seven patients with breast cancer whose ALN spread was investigated were included in this study. Lymph nodes were evaluated using B-Mode US to determine cortical thickness, absence of fatty hilum, presence of a non-hilar blood supply, and a long axis to short axis ratio greater than two. The same patients were evaluated using SWE. Following the assessment of SWE, a core biopsy of the lymph nodes was performed using US guidance.

Results: A biopsy was performed in 57 patients. A total of 45 patients exhibited lymph node metastases, whereas the remaining 12 patients exhibited reactive lymph node hyperplasia. The Emax of the cortex exhibited a higher degree of specificity than the cortical thickness (81.8% vs. 72.7%). The specificity was found to be equal (90.9%) between the combination of Emax of the cortex and cortical thickness, as well as between at least two B-Mode US characteristics.

Conclusion: In conclusion, SWE is valuable for distinguishing between metastases and reactive hyperplasia in individuals exhibiting suspicious features on B-Mode US of ALNs.

Keywords: Shear wave elastography, SWE, elastography, sonography, breast cancer, axillary lymph nodes

Introduction

Breast cancer is a prevalent form of cancer among women worldwide and is the leading cause of cancer-associated mortality.[1] The evaluation of recurrences and metastases is frequently conducted through the investigation of axillary lymph nodes (ALNs).[2] The evaluation of ALN has significant predictive value in the context of breast cancer. The preoperative ALN status is a crucial benchmark for clinical staging and the formulation of treatment strategies for breast cancer.[3,4]

Ultrasonography (US) is currently the imaging technique of choice for evaluating the axilla.[5] In ALN, the presence of a round ALN, a long-axis-to-short-axis ratio of 2, cortical thickness of >3 mm, and an obliterated fatty hilus are indicative of metastatic ALNs.[6] Axillary US has a sensitivity ranging from 35% to 82% and specificity ranging from 73% to 97.9%.[7,8] Despite being an invasive procedure, US-guided core needle biopsy has demonstrated remarkable sensitivity and specificity for detecting metastases.[9,10] Due to the invasive nature of biopsy, a non-invasive imaging examination is required to predict the presence of metastatic ALNs.

US, a non-invasive modality referred to as elastography, can yield significant insights into the stiffness properties of lesions.[11,12] US elastography has the capability to objectively evaluate variations in stiffness between benign and malignant lymph nodes.[13,14] Shear wave elastography (SWE) has been the subject of numerous studies. Recent elastographic investigations examining ALNs have revealed that the precision of subcutaneous US may exhibit variability as a result of anatomical irregularities inside the axillary cavity, the deep positioning of the lymph node, and the reliance on the technique by the user.[15] Nevertheless, there is a scarcity of research on the identification of metastatic ALNs in individuals diagnosed with breast cancer.[16] Chang et al.[17] found that although SWE has limited sensitivity in the evaluation of ALNs, the simultaneous application of US and SWE was useful for lymph node evaluation. The determinant is the cortical thickening of the lymph nodes. Both benign reactive hyperplasia and nodal metastases often show cortical thickening on US. Several studies have been conducted to compare the diagnostic efficacy of SWE techniques with B-Mode US features.[16-19] Nevertheless, metastatic lymph nodes frequently have dubious morphological characteristics. Hence, it is our contention that the integration of SWE with B-Mode US characteristics

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can provide advantageous outcomes in real-world applications. The primary objective of this study was to investigate the potential benefits of including SWE testing alongside B-Mode US for identifying morphologic abnormalities in individuals diagnosed with breast cancer involving ALNs.

Methods

The Erzincan Binali Yıldırım University Clinical Researches Ethics Committee, 16.05.2024, EBYU KAEK 2024.05-1.2356093-113. approved the study, and informed consent was obtained. The study was initiated after obtaining written informed consent from the patients.

Study Population

The research was carried out prospectively. The study comprised individuals who were diagnosed with breast cancer by fine needle aspiration biopsy and those with suspicious ALNs on US. The study omitted ALNs that were anatomically deep and suspected of metastasis due to the absence of a clear evaluation in SWE. Furthermore, those diagnosed with ALN-producing conditions of non-malignant nature, such as granulomatous or lymphoproliferative diseases, were not included in the study. In total, 65 patients with breast cancer were assessed for potential metastases in the lymph nodes using axillary US-guided biopsy. Of the 65 patients, eight were excluded from the study because their lymph nodes were located at a deep anatomical level. Consequently, the study incorporated the remaining 57 individuals for the purpose of ALN examination.

B-Mode US

All patients were evaluated by a radiology physician with 15 years of experience in breast radiology using a 3.5- or 5-MHz real-time US device (Samsung RS85 Prestige, South Korea). Lymph nodes at the axillary level with diffuse cortex thickening or asymmetrical lymph nodes up to 3 mm in thickness were considered suspicious for metastasis. Lymph nodes with increased cortical thickness (>6.7 mm) were selected for B-Mode US-guided evaluation. Lymph nodes were evaluated using B-Mode US to determine cortical thickness, absence of fatty hilum, presence of a non-hilar blood supply, and a long axis to short axis ratio greater than 2.

Shear Wave Elastography

The same patients were evaluated using SWE. localization of the lymph nodes was observed in the central region of the SWE window (Figures 1, 2). The probe remained stationary until the color maps reached a state of stability and photographs were obtained. the typical range of the elastography map was reduced from 180 kPa until more challenging regions within the lymph node became visible. Quantitative SWE features were placed in the hardest regions of the cortex and hilus. A region of interest (ROI) of 1 mm was used to analyze several non-overlapping lymph nodes characterized by a thin cortex

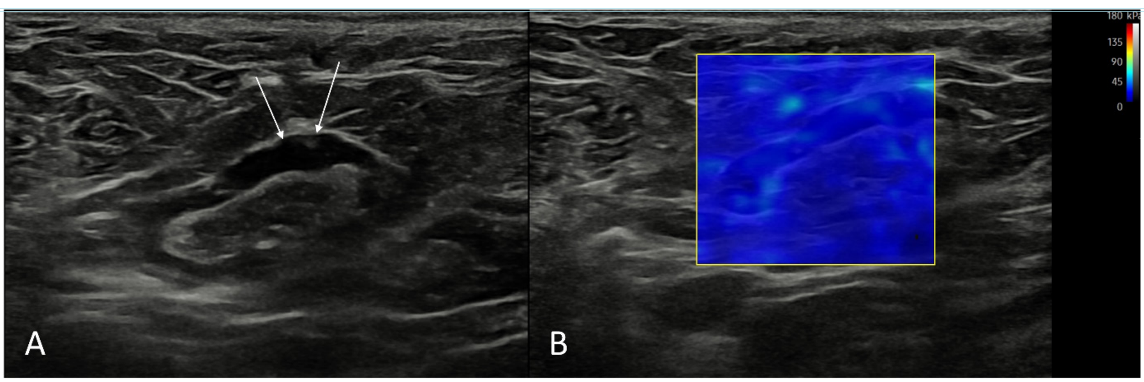

Figure 1. A 57-year-old female patient diagnosed with breast cancer. A) B-Mode ultrasound image of the right axillary lymph node showing focal mild cortical thickening (arrows) is present. B) Shear wave elastography image of the same lymph node showing no color coding indicative of tissue stiffening is observed (rectangle). Core biopsy pathological findings indicated a reactive lymph node. Elastographic measurement values are not numerically presented in this figure

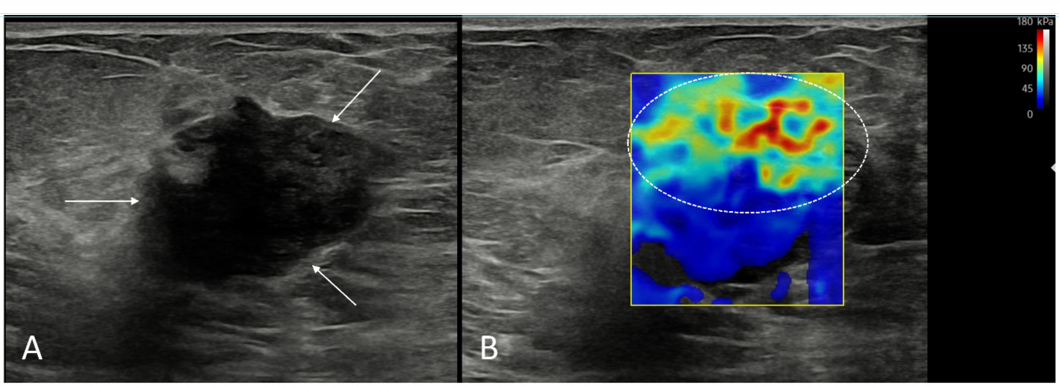

Figure 2. A 54-year-old female patient diagnosed with breast cancer and axillary metastasis. A) In the B-Mode ultrasound image of the left axillary pathological lymphadenopathy (arrows), findings include diffuse thickening of the cortex, absence of the fatty hilum, and a long-axis to short-axis ratio greater than two. B) In the shear wave elastography image of the same pathological lymph node, color coding indicative of tissue stiffening is observed (circle). Elastographic measurement values are not numerically presented in this figure

and clear hilus. Three ROI values were created using this method, and the parameter with the highest reading was selected. The parameters Emax (highest elasticity value), Emin (lowest elasticity value), Emean (average elasticity value), and ESD (standard deviation of elasticity) were evaluated in this study.

Biopsy

Following the assessment of SWE, a core biopsy of the lymph nodes was performed using US guidance. Pathological findings from the biopsied lymph nodes were utilized as a benchmark to assess the diagnostic efficacy of B-Mode US and SWE. In this investigation, the pathologist was unaware of the evaluation outcomes of B-Mode US and SWE.

Statistical Analysis

For data analysis, Statistical Package for the Social Sciences version 20.0 for Windows was used. The normality of the data distribution was assessed using the Kolmogorov-Smirnov test. Categorical variables were evaluated using the chi-square test, whereas parametric variables were analyzed using the Mann-Whitney U test. Additionally, receiver operating characteristics analysis was conducted to determine the sensitivity and specificity. In all evaluations, a p value 0.05 was considered statistically significant.

Results

Table 1 presents the demographic and clinical characteristics of the 57 study patients. The mean age of the 57 patients was 48.1±10.1 years. One of these patients was male, and the others were female. Twenty-seven (47.4%) of the 57 patients were postmenopausal. Patients described a palpable breast mass that lasted a mean of 6.0±0.9 months when they visited the clinic. The upper outer quadrant was the most common site of breast mass in 33 (57.9%) of the 57 patients. It was also shown that the luminal subtype was the most common subtype, affecting 20 (35.1%) patients.

Axillary US and US-guided Biopsy

A total of 312 ALNs, all located on the same side, were identified as suspects of metastasis using axillary US in a cohort of 57 patients. The average number of suspicious lymph nodes per patient was 4. Among the 57 individuals included in the study, 30 (52.6%) exhibited level 1, 19 (33.3%) displayed level 2, 5 (8.7%) displayed level 3, 2 (3.5%) displayed intermammary lymph nodes, and 6 (10.5%) displayed supraclavicular suspicious lymph nodes.

A biopsy was performed in 57 patients. A total of 45 patients exhibited lymph node metastases, whereas the remaining 12 patients exhibited reactive lymph node hyperplasia.

Diagnostic Performance of the SWE

The elasticity value of the cortex was assessed in 57 ALNs during the assessments conducted on the ALNs. Similarly, the elasticity value of the hilus was examined in 37 lymph nodes where the fatty hilus was intact. In the metastatic lymph nodes, the median values of all parameters related to SWE (Emax, Emin, Emean, and ESD) were obtained for both the cortex and hilus. Nodes exhibited a much higher prevalence of hyperplasia than reactive hyperplasia, as indicated in Table 2.

Table 3 presents the diagnostic efficacy of the max, min, and Emean values for the cortex. Three indicators possess significant diagnostic efficacy in differentiating metastatic lymph nodes from reactive

Table 1. Demographic and clinical characteristics of the study group (n=57)

Variable	Number of patients n (%)
Age, years, mean±SD	48.1±10.1
Gender	
Female	56 (98.3)
Male	1 (1.7)
Menstrual status	
Pre-menopausal	29 (50.1)
Post-menopause	27 (47.4)
Not applicable (male)	1 (1.7)
Symptoms	
Breast lump	57 (100)
Mastalgia	12 (21)
Nipple retraction	5 (8.7)
Nipple discharge	2 (3.5)
Duration of symptoms, months, mean±SD	6.0±0.9
Location of the breast mass (dial)	
Upper outer	37 (64.9)
Upper interior	5 (8.7)
Lower outer	6 (10.5)
Bottom interior	5 (8.7)
Central	4 (7)
T staging	
cT2	24 (42.1)
cT3	14 (24.5)
cT4b	16 (28)
cT4c	3 (5.2)
N staging	
cN1	36 (63.1)
cN2a	8 (14)
cN3a	6 (10.5)
cN3b	2 (3.5)
cN3c	5 (8.7)
M staging	
B.C	49 (85.9)
M1	8 (14)
Histological subtype	
Invasive carcinoma	54 (94.7)
Mucinous carcinoma	3 (5.2)
Molecular subtype	
Luminal	22 (38.59)
HER2/neu	15 (26.3)
Basal	20 (35)

SD: Standard deviation

hyperplasia. Although the area under the curve (AUC) was maximum for max, the difference between Emin and Emean was not significant (p=0.73 and p=0.40, respectively). The optimal threshold values for max, min, mean, and ESD of the cortex, which can effectively differentiate metastatic from reactive hyperplasia, were 14.9, 12.2, 13.3, and 1 kPa, respectively. Owing to the obliteration of the fatty hilus in some ALNs, the diagnostic power of SWE could not be fully evaluated in all ALNs.

Table 2. Comparison of quantitative shear wave elastography parameters and B-Mode ultrasound features of lymph nodes according to pathological status (n=57)

Parameter	Nodal status at the core biopsy		p value
	Metastasis	Reactive hyperplasia	
SWE of the cortex	**n=45**	**n=12**	
Emax (kPa)	25.1 (13.8-44.7)	12.9 (11.2-15.3)	0.001
Emin (kPa)	21.45 (11.2-37.1)	10.5 (8.2-10.9)	0.002
Emean (kPa)	24.15 (13.5-42.7)	11.9 (9.2-12.8)	0.001
ESD (kPa)	1.7 (1.4-2.4)	0.95 (0.87-1.9)	0.03
SWE of the hilus	**n=27**	**n=10**	
Emax (kPa)	31.9 (18.8-44.6)	14.9 (9.5-18.1)	0.004
Emin (kPa)	29.5 (17.1-41.2)	8.5 (8.4)-14	0.004
Emean (kPa)	32.6 (19-42.9)	12.4 (8.1-15.8)	0.002
ESD (kPa)	1.9 (1.2-3.2)	0.95 (0.76-1.6)	0.008
B-Mode US features	**n=45**	**n=12**	
Cortical thickness in mm	11.55 (8.5-12.2)	7 (5.6-7.7)	<0.001
Absence of fatty hilum	40 (88.8%)	5 (41.6%)	0.004
Non-hilar blood flow	32 (71.1%)	4 (33.3%)	0.01
Round shape	14 (31.1%)	0	0.05

Each value is depicted as median (interquartile range).
SWE: Shear wave elastography, US: Ultrasonography

Table 3. Diagnostic performance of quantitative SWE and B-Mode US of axillary lymph nodes according to the pathological status of the lymph nodes (n=57)

Variables	AUC	Cut-off	TP	F.P.	TN	F.N.	Sensitivity, % (95% CI)	Specificity, % (95% CI)	LR+ (95% CI)
SWE of the cortex									
Emax	0.870	14.1 kPa	30	5	11	13	71.7 (56-87)	83.4 (53.6-92.9)	4.3 (1.45-12.1)
Emin	0.832	10.2 kPa	32	4	9	12	74.3 (63.4-85)	83.5 (51.3-92.9)	4.4 (1.6-12.6)
Emean	0.896	12.8 kPa	33	5	9	10	75.7 (63.8-89)	64.2 (54.6-95.7)	4.3 (1.4-11.2)
ESD	0.782	1 kPa	35	8	7	7	82.3 (68.3-90.9)	52.5 (29-80.6)	1.8 (1.3-2.9)
B-Mode US features									
Cortical thickness	0.968	6.4 mm	37	5	10	5	89.5 (75.9-95.8)	72.7 (43.4-90.3)	3.3 (1.7-6.3)
Absence of fatty hilum	-	-	37	4	9	7	82.1 (71.4-92.6)	65.6 (345-84.1)	2.5 (1.6-3.9)
Non-hilar blood flow	-	-	32	5	10	10	74.6 (59.4-80.7)	73.9 (44.8- 92.3)	2.4 (1.4-5.8)
Cortical thickness + effacement of fatty hilum and/or non-hilar blood flow	-	≥6.4 mm	38	3	11	5	88.1 (76.7-94.8)	92.1 (63.4-98.6)	9.6 (1.5-72.4)
Combination of SWE and B-Mode US									
Emax (cortex) + cortical thickness	-	≥14.1 kPa + ≥6.4 mm	30	2	11	14	64.9 (48.1-79.8)	92.9 (64.1-97.2)	7 (1-51.8)
Emax (cortex) + cortical thickness + effacement of fatty hilum and/or non-hilar blood flow	-	≥14.1 kPa + ≥6.4 mm	29	0	14	14	67.5 (51.9-79.6)	100 (75.2-100)	-

AUC: Area under the curve, CI: Confidence interval, FN: False negatives; FP: False positives, LR+: Positive likelihood ratio, kPa: Kilo pascal, SWE: Shear wave elastography, TN: True negatives, TP: True positives, US: Ultrasonography

Diagnostic Power of B-Mode US

Metastatic lymph nodes had a higher prevalence of prominent fatty hilus (32/45) than reactive lymph nodes (4/12) (p=0.004). The prevalence of non-hilar engorgement was higher in cases of metastasis (32 out of 45) than in cases of reactive hyperplasia (4 out of 12) (p=0.01). The round shape of lymph nodes was observed in metastatic lymph nodes (14/45) but not reactive lymph nodes (0/12). Although not observed, the difference was not statistically significant (p=0.05) (Table 2). The B-Mode US of cortical thickness demonstrated the highest sensitivity and specificity, with an AUC of 0.87. A threshold value of 6.4 mm was determined to be the most effective value for differentiating metastatic lymph nodes from reactive hyperplasia, with a sensitivity and specificity of 89.5% and specificity of 72.7%. The combined evaluation of lymph nodes with cortical thickness >6.4 mm, non-cortical blood supply, and fatty hilus resulted in a sensitivity of 89.5% and specificity of 90.9% (Table 3). A comparative analysis was conducted to assess the specificity and sensitivity of the Emax value of the cortex, which is considered the parameter with the highest diagnostic power in SWE, in relation to the B-Mode US features of the ALNs. The Emax of the cortex exhibited a higher degree of specificity than the cortical thickness (81.8% vs. 72.7%). However, its sensitivity was found to be quite low (73.7% to 89.5%). However, the differences were not statistically significant (p=0.61 and 0.08, respectively).

Diagnostic Power of the B-Mode US and SWE

The evaluation utilized a combination of cortical thickness in B-Mode US and the Emax value of the cortex in SWE because these parameters demonstrated the strongest diagnostic power. When the Emax value of the cortex was combined with 14.1> kPa, the specificity of the lymph nodes measured with a cortex thickness >6.4 mm increased (72.7-90.9%) (p=0.27), its sensitivity decreased (89.5%-65.8%) (p=0.01). Similarly, when at least two B-Mode US features (non-hilar blood flow and cortical thickness >6.7 mm) were combined with the Emax value of the cortex, specificity increased (increased from 90.0% to 100%) (p=0.31), and sensitivity decreased (from 89.5% to 65.8%) (p=0.01). The specificity was found to be equal (90.9%) between the combination of Emax of the cortex and cortical thickness, as well as between at least two B-Mode US characteristics. However, the sensitivity was significantly lower (65.8-90.5%) (p=0.01) (Table 3).

Discussion

US-guided biopsy is a widely used technique for evaluating ALNs in individuals diagnosed with breast cancer. However, our study revealed a false-positive result when assessing the cortical thickness of ALNs. Compared with the biopsy results for these lymph nodes, reactive hyperplasia was detected in 12 of 57 lymph nodes (21%). Therefore, additional studies are necessary to evaluate the level of specificity exhibited by US. Therefore, this study aimed to evaluate the diagnostic effectiveness of SWE and US.

To differentiate reactive hyperplasia from metastatic lymph nodes, we assessed lymph nodes exhibiting heightened cortical thickness using a combination of B-Mode US and SWE. Subsequently, we compared these lymph nodes with B-Mode US features to ascertain the practical advantages of SWE.

The most influential criterion for differentiating reactive hyperplasia from metastasis among the B-Mode US features of the ALN was increased cortical thickness. The examined patients exhibited a substantial number of ALNs, with a cut-off value of 6.4 mm. This cut-off value achieved sensitivity of 92% sensitivity and 73.4% specificity. Different cut-off values have been reported in various studies due to differences in patient groups and study environments. Zhu et al.[18] determined that a cortical thickness of 3.5 mm was optimal for predicting metastasis. Using this threshold, they attained a sensitivity of 76% and a specificity of 83%. Seo and Sohn[19] determined that a cortical thickness cut-off value of 4.85 mm is sufficient for predicting metastasis in patients with breast cancer. With this cut-off value, they achieved 82.4% sensitivity and 100% specificity. In the current study, a higher cut-off value was used owing to the large number of ALNs.

The cortex of metastatic lymph nodes exhibited greater hardness in comparison to benign lymph nodes in our study. It was found that the hilus and cortex exhibited higher flexibility. The investigation revealed that the Emax values of the cortex and hilus were elevated in metastatic lymph nodes compared with reactive hyperplasia. This study determined that the Emax value of the cortex exhibited the highest significance in differentiating between metastasis and reactive hyperplasia. This parameter had a sensitivity of 71.7% and a specificity of 83.4% when measured at a pressure of 14.1 kPa. Prior research has demonstrated that the Emax and Emin values of the cortex have significant predictive ability in determining metastasis.[16-20] Prior research used ROI values ranging from 2 to 3 mm to assess the level of hardness. However, in our investigation, we used ROI values below 1 mm. In previous investigations, lymph nodes exhibiting normal cortical thickness of the ALNs were also incorporated into the analysis. However, our study exclusively focused on lymph nodes with augmented cortical thickness. In the current study, the Emax value of the cortex exhibited higher specificity (83.4%) and less sensitivity (71.7%) than the lymph node cortical thickness. However, these findings were not statistically significant. Luo et al.[21] reported that the Emax value of the cortex exhibited higher specificity (88.5% versus 82%) and sensitivity (93.3% versus 91.7%) than the US. Seo and Sohn[19] it was observed that Emax values of the cortex showed comparable sensitivity (82.4% for both factors) compared with US, but decreased specificity (100% vs. 95%). Although no statistical comparison was made in these studies, SWE parameters were shown to have comparable effectiveness to B-Mode US for detecting metastatic lymph nodes. In the present investigation, it was shown that the use of SWE and US exhibited a notable degree of specificity, but was accompanied by a decline in sensitivity in the identification of metastatic lymph nodes. A high specificity of 92.9% was achieved when evaluating a cut-off value of 6.4 in conjunction with cortical thickness, while considering an Emax value of 14.1 kPa for the cortex. When evaluating ALNs using US, the specificity of lymph nodes with few suspicious findings can be increased to 100% by combining these findings with the Emax values of the cortex. Kilic et al.[16] they conducted an ex vivo study and observed that B-Mode US features, including the cortical thickness of the lymph node and long-axis/short-axis ratio, exhibited 100% specificity when evaluated together with the Emax of the cortex. However, their findings revealed a sensitivity of 34%, which is consistent with the results of our study. Kilic et al.[16] in his study, evaluating the cortical thickness and stiffness of the lymph node together resulted in a higher sensitivity of 83%, whereas a sensitivity of 75% was obtained by using each of the US parameters alone.

Additionally, our study compared the diagnostic efficiency of the combination of SWE and US and evaluated the usability of SWE using many US features. When the Emax value of the cortex was compared with the lymph node cortical thickness, it was shown that the combination of the cortical thickness and other US parameters of the lymph node showed similar specificity and better sensitivity. Therefore, the effectiveness of SWE is limited in cases in which many suspicious features are present in the lymph nodes.

Nevertheless, previous studies have indicated that the utilization of SWE can be advantageous in cases in which cortical thickness is the sole characteristic observed in lymph nodes that are deemed worrisome. Fischer et al.[22] investigated the application of SWE in ALNs. The researchers observed that the use of cortex elasticity exhibited superior sensitivity and specificity in distinguishing between metastases and reactive hyperplasia compared with subjective evaluation using B-Mode US or elastography. The sensitivity and specificity values obtained were 95% and 74% for B-Mode US, 85% and 60% for subjective elastography, and 85% and 68% for subjective elastography.

Study Limitations

This study has several limitations. The primary constraint of our study was the limited study population size, which necessitated validation with larger study groups. The evaluation of the effectiveness of quantitative elastography was hindered by the absence of a consistent range across all the lymph nodes assessed. Further studies are required to ascertain the optimal range of elasticity that should be employed for the examination of ALNs. SWE measurements were performed by one researcher because this situation did not allow us to evaluate interobserver agreement and repeatability. Another limitation was that excisional biopsy was not performed in the 12 patients with reactive hyperplasia, as indicated by the core biopsy results, which may not represent the entire lymph node.

Conclusion

In conclusion, the use of SWE is advantageous in distinguishing between metastases and reactive hyperplasia in individuals exhibiting suspicious features on B-Mode US of ALNs. Based on our observations, the simultaneous use of SWE and B-Mode US can provide advantageous results only in cortical-thick lymph nodes.

Ethics

Ethics Committee Approval: Erzincan Binali Yıldırım University Clinical Researches Ethics Committee, 16.05.2024, EBYU KAEK 2024.05-1.2356093-113.

Informed Consent: The study was initiated after obtaining written informed consent from the patients.

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