Cite as: Tunçez HC, Koç AM, Adibelli ZH, Arslan FZ, Argon A, Oğuzdoğan GY: Diagnostic efficacy of ultrasonography, Doppler ultrasonography and elastography in the evaluation of suspected malignant lymph nodes. J Ultrason 2023; 23: e1–e9. doi: 10.15557/JoU.2023.0001

Submitted: 26.06.2022
Accepted: 10.10.2022
Published: 05.01.2023

Diagnostic efficacy of ultrasonography, Doppler ultrasonography and elastography in the evaluation of suspected malignant lymph nodes

Hülya Çetin Tunçez[1], Ali Murat Koç[2], Zehra Hilal Adıbelli[3], Fatma Zeynep Arslan[4], Asuman Argon[4], Gülşen Yücel Oğuzdoğan[5]

[1] *Radiology, Bilecik Training and Research Hospital, Bilecik, Turkey*
[2] *Radiology, Izmir Katip Celebi University Ataturk Training and Research Hospital, Izmir, Turkey*
[3] *Radiology, Izmir Bozyaka Education and Research Hospital, Izmir, Turkey*
[4] *Pathology, Ministry of Health İzmir Bozyaka Training and Research Hospital, Izmir, Turkey*
[5] *Radiology, Basaksehir Cam and Sakura City Hospital, Başakşehir, Turkey*

Corresponding author: Fatma Zeynep Arslan; e-mail: zeynep_a1002@hotmail.com

DOI: 10.15557/JoU.2023.0001

Keywords
ultrasonography; Doppler ultrasonography; elastography; lymph node

Abstract

Aim: In this prospective study, the efficiency of imaging findings was investigated by comparing the histopathological results of lymph nodes with Doppler and ultrasound features and elasticity scores. **Material and method:** A total of 100 cervical or axillary lymph nodes with a suspected malignancy or whose size did not decrease after treatment were examined. In addition to the demographic data of the patients, B-mode ultrasound, Doppler ultrasound, and elastography features of the lymph nodes were evaluated prospectively. The irregular shape, increased size, pronounced hypoechogenicity, presence of micro/macro calcification, short axis/long axis ratio >2, increased size of the short axis, increased cortex thickness, obliterated hilus or increased cortex thickness >3.5 mm were evaluated on ultrasound. Resistivity index, pulsatility index, acceleration rate and time were evaluated for intranodal arterial structures on color. Doppler ultrasound, strain ratio value and elasticity score were recorded on ultrasound elastography. After sonographic examination, patients underwent ultrasound-guided fine needle aspiration cytology or tru-cutting needle biopsy. Histopathological examination results of the patients were compared with the B-mode ultrasound, Doppler ultrasound, and ultrasound elastography. **Results:** When the individual and combined effects of the ultrasound, Doppler ultrasound, and ultrasound elastography were evaluated, the combination of all three imaging methods was found to have the highest sensitivity and the highest overall accuracy (90.4% and 73.9%). As an individual method Doppler ultrasound had the highest specificity (77.8%). B-mode ultrasound was found to have the lowest accuracy (56.7%) both in individual and combined evaluations. **Conclusion:** Addition of ultrasound elastography to the combination of B-mode and Doppler ultrasound findings increases diagnostic sensitivity and accuracy in the differentiation of benign and malignant lymph nodes.

Introduction

Ultrasound elastography (USE) is a modality that makes it possible to interpret the degree of stiffness of body tissues, similarly to the findings obtained by palpation. Malignant tissues are usually harder due to the desmoplastic reaction. Accordingly, a harder tissue pattern and higher velocity values are detected on USE in malignant lesions(1). A recent study found that combining USE with the US examination serves to increase the accuracy of detecting malign lymph nodes(2). In a recent meta-analysis evaluating the diagnostic performance of USE for axillary lymph node metastasis, the authors reported a huge variety among studies. They found that the most important reason for such heterogeneous results included study design and measurements(3). We believe that a reference value and standard measurement methods are necessary. However, recent literature data suggest being careful in the interpretation of USE values in view of great heterogeneity among the researchers(3).

In this prospective study, the efficiency of imaging findings was investigated by comparing the histopathological results of lymph nodes with Doppler and US features and elasticity scores.

Methods

Patient selection

Patients over 18 years of age, presenting with lymph nodes suspected of malignancy in the neck and axilla on US, were evaluated prospectively. In B-mode US, long axis/short axis ratio >2 in the lymph node, >1 cm in the short axis, increased cortex thickness (>2.5 mm), absence of fatty hilus were regarded as a suspicion of malignancy[4–6]. The lymph nodes which were suspicious for malignancy were followed-up for 12 weeks with an appropriate antibiotic therapy. During antibiotic treatment, 875 mg of amoxicillin and 125 mg of clavulanic acid were administered to the patients for 10 days. Subsequently, the reduction in size was monitored, and the lymph nodes suspected of malignancy were re-evaluated 12 weeks later.

The study was conducted prospectively between 2019 and 2020. Patients who did not agree to participate in the study, patients under the age of 18, patients with biopsy contraindications/refusal to biopsy, patients in whom US/biopsy could not be performed, and pregnant or lactating patients were excluded from the study. A total of 10 patients whose biopsy results were unsatisfactory and who met the exclusion criteria were excluded from the study.

Oral and written consents were obtained from the parents of all patients who participated in our study, as necessary. Ethical approval was obtained from the local scientific research ethics committee (decision No. 05, dated 17.01.2019). The study was conducted on the basis of ethical standards outlined in the Declaration of Helsinki of the World Medical Association. All sonographic evaluations were performed by two radiologists who are specialized in this field of radiology.

Tab. 1. Elasticity scoring

Pattern 1	No stiff area within the lesion
Pattern 2	The percentage of stiff area is less than 45%
Pattern 3	The percentage of stiff area is greater than 45%
Pattern 4	The lesion is mostly stiff
Pattern 5	The lesion is completely stiff

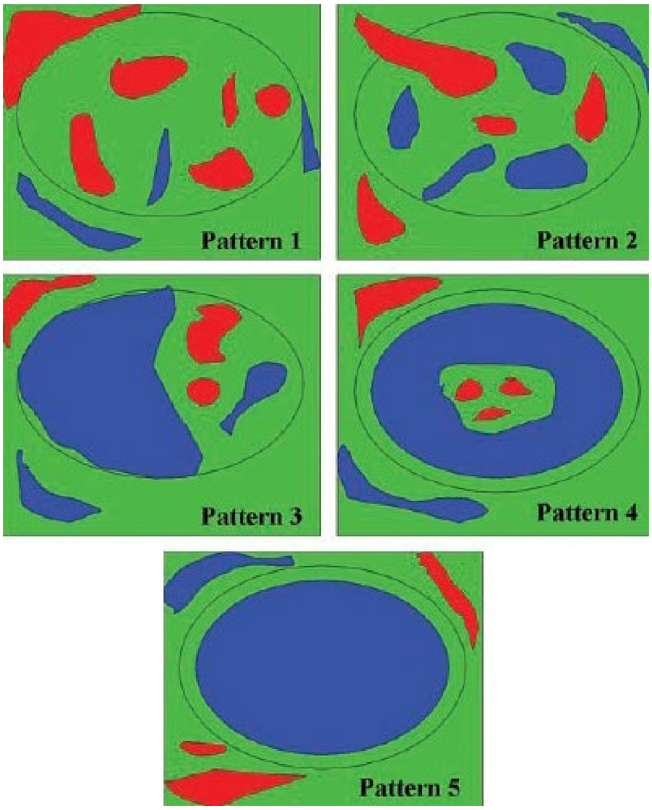

Fig. 1. *Schematic display of elasticity patterns with USE*

Sonographic evaluation

The lymph nodes of the patients were evaluated using a 6–13 Mhz linear probe with an ultrasound device (Hitachi HI VISION) with B-mode US, Doppler US and strain USE features. All radiological examinations were performed by a radiologist with 8 years' experience in the field of sonographic evaluation. The patients were placed in the supine position, and mild manual compression was applied at short intervals to the lymph node in the perpendicular position on the strain elastographic examination. In B-mode US, the features of lymph nodes suspicious for malignancy (i.e. irregular shape, increased size, pronounced hypoechogenicity, presence of micro/macro calcification, short axis/long axis ratio >2, increased size of the short axis, increased cortex thickness, obliterated hilus or increased cortex thickness >3.5 mm) were described as abnormal[5,6]. Resistivity index (RI), pulsatility index (PI), and acceleration rate and time were evaluated for intranodal arterial structures on color Doppler US, and the strain ratio value and elasticity scores were recorded on USE. The strain ratio value was calculated as the ratio of the lymph node examined to the elasticity values of the adjacent muscle tissue for the lymph nodes in the neck and axilla[5,6]. In the axilla, it was accepted as the ratio of the elasticity values of the adipose tissue adjacent to the lymph node[5]. In the calculation of the strain ratio value, an examination area (region of interest, ROI) was as large as possible to represent that part. Reference ROI values were obtained by measuring from the reference tissue in the same image as the study area. The ratio of the reference ROI to the first ROI was calculated. The size of the ROI cursor was adjusted for each lesion according to the lesion size. The ROI cursor was placed on the stiffest part according to the color map. The mean strain ratio value obtained by measuring the lesions at least twice was included in the study[6]. After the sonographic examination, the patients underwent an ultrasound-guided fine needle aspiration cytology or tru-cutting needle biopsy. For fine-needle aspiration biopsy of the lymph node, a 21-gauge needle and a 10 ml disposable injector were preferred. Histopathological examination results were used as reference standards. In order to evaluate the adequacy of the gray-scale findings, vascularity features and elasticity of the lymph nodes in predicting the pathology results, the cases were classified as benign or malignant by two radiologists who were blind to the histopathology results of the patients, based on the current literature on the subject (Tab. 1, Fig. 1). A short axis diameter ≥1 cm, or a long/short axis ratio was <2, round shape and presence of abnormal hilus were considered as malignant features. On Doppler US**,** detecting blood supply outside of the hilus (peripheral or both central and peripheral blood supply), RI >0.7 and PI >1.4 were regarded as malignant (Fig. 2)[5,6].

Elasticity patterns were determined on USE. Pattern 1 was described as no stiff area within the lesion. If the percentage of stiff area was

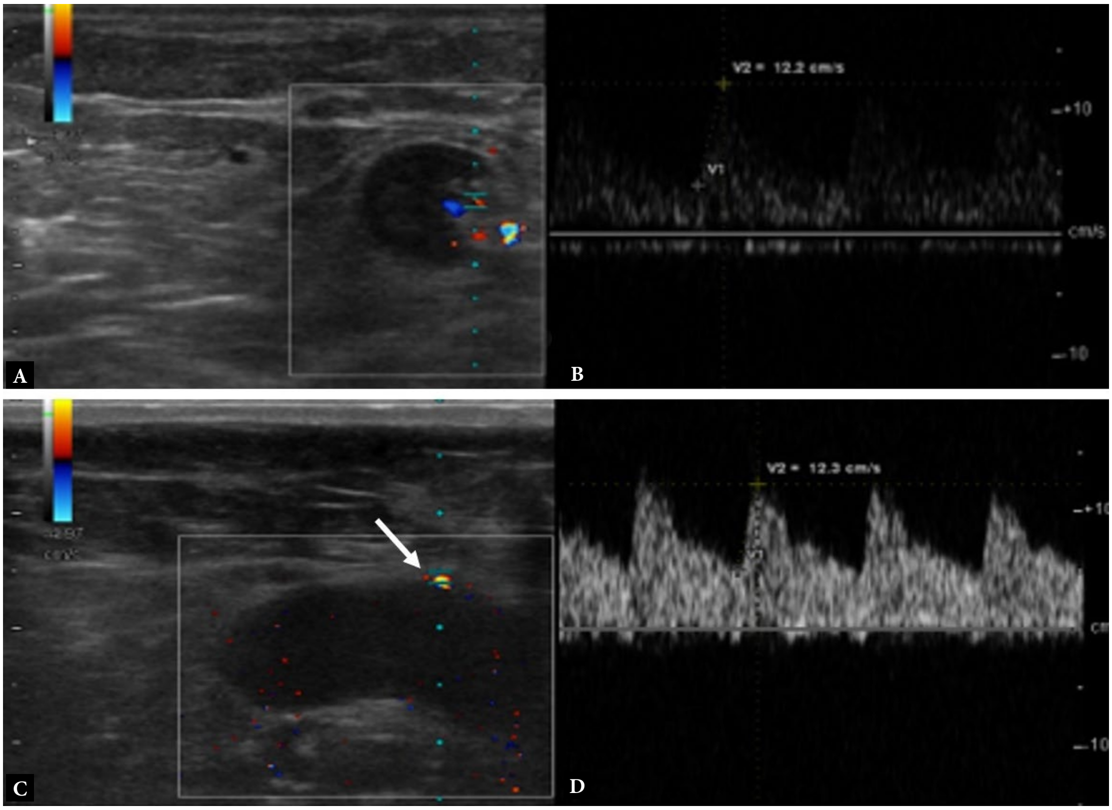

Fig. 2. *On Doppler US,* **A.** *color and* **B.** *spectral Doppler examination of the lymph node with hilar blood supply is shown. On Doppler US,* **A.** *color and* **B.** *spectral Doppler examination of obliterated hilus lymph node with peripheral blood supply and asymmetric cortical thickness is seen*

less than 45%, it was considered as Pattern 2. If the percentage of stiff area was greater than 45%, it was classified as Pattern 3. If the lesion is mostly stiff and containing minimal soft area, it was considered as Pattern 4. If the lesion was completely stiff, it was considered as Pattern 5. Patterns 1 and 2 were considered as benign, while patterns 3,4 and 5 were classified as malignant. When the elastographic measurements were evaluated quantitatively, the lymph nodes with an SR value of >1.5 were recognized as malignant, in accordance with the threshold values found in similar studies in the literature. The USE results were compared with the sonographic interpretations of benign-malignant.

Statistical analysis

Statistical analysis of the data was performed using IBM SPSS Statistics version 24. Pearson chi-squared test and Fisher's exact test were applied for comparison of categorical data between the groups; since continuous data were not normally distributed (Kolmogorov-Smirnov $p < 0.05$), Mann-Whitney U statistical analyses were used for comparisons between the groups. The predictive power of the imaging methods for pathology results was evaluated by ROC analysis. *P*-value <0.05 was considered statistically significant.

Results

In this study, a total of 100 lymph nodes of 96 patients aged between 32 and 86 years were evaluated ultrasonographically. The pathology results of 10 patients were described as non-diagnostic pathology, two patients were re-biopsied, but they were not included in the study because of insufficient results. Of all the patients, 79 (92%) were female, and 7 (8%) were male with a mean age of 53.7 years. Of the lymph nodes, 76 (84.5%) were located in the axilla and 14 (15.5%) were located in the cervical region. Three of 14 cervical lymph nodes were found to be malignant, and 51 of 76 axillary lymph nodes were found to be malignant. A statistically significant difference was found between the groups according to localization ($p = 0.001$). In total, 36 (40%) of the cases were found to be benign, and 54 (60%) were found to be malignant histopathologically.

B-mode US findings

The morphological difference (round, ovoid) between the benign and malign lymph nodes was statistically significant ($p = 0.021$). The presence of fatty hilus was found to be statistically significant in the diagnosis of benign lymph nodes ($p = 0.022$). Lymph nodes with prominent fatty hilum were found to be benign with 75.93% sensitivity, 45.22% specificity, and 64.4% accuracy. The US features of the examined lymph nodes are summarized in Tab. 2.

The long axis lengths of the examined lymph nodes ranged from 8 mm to 50 mm, while the short axis lengths varied from 5 mm to 27 mm. The ratio of long axis to short axis was between 0.88 and 4. The mean of the short axis was 9.36 ± 2.93 mm in the benign group and 13.45 ± 6.15 mm in the group of malignant lymph nodes. The average long axis to short axis ratio was 2.17 ± 0.59 in the benign group and 1.86 ± 0.53 in the malignant group, and the differences between the short axis length and the long axis/short axis ratio were

Tab. 2. Ultrasonographic features of the examined lymph nodes according to their pathological diagnosis

		Pathological diagnosis				X^2	*p*
		Benign		Malignant			
		n	%	*n*	%		
Shape	Round	2	5.6	13	24.1	5.333	***0.021***
	Ovoid	34	94.4	41	75.9		
Hilum	Normal fatty hilum	17	47.2	13	24.1	5.213	***0.022***
	Abnormal obliterated hilum	19	52.8	41	75.9		
Cortical necrosis	No	28	77.8	46	85.2	0.811	0.368
	Yes	8	22.2	8	14.8		
Margin	Regular	36	100.0	50	92.6	2.791	0.147
	Irregular	0	0.0	4	7.4		
Edema within the adjacent tissues	No	34	94.4	53	98.1	0.92	0.561
	Yes	2	5.6	1	1.9		
Echogenicity	Hypoechoic	34	94.4	54	100.0	2.900	0.163
	Isoechoic	2	5.6	0	0.0		

n – number of lymph nodes, *p*-value less than 0.005 considered as significant

statistically significant ($p = 0.002$ and ($p = 0.019$). No statistically significant difference was found in terms of long axis and benign-malignant distinction ($p > 0.005$).

When predicting the pathology outcome by ROC analysis for the power of B-mode US data, the threshold value calculated for the short axis value, with 43.4% sensitivity and 88.9% specificity, was 13 mm. The Area Under Curve (AUC) value was found to be 69.7%, and it was statistically significant ($p < 0.001$). The threshold for the long axis/short axis ratio was found to be ≤1.46, with 24.5% sensitivity and 100% specificity. The AUC value was calculated as 64.7%, and it was statistically significant ($p = 0.011$). The AUC values calculated for the long axis were not statistically significant in estimating the pathology results ($p < 0.05$).

Color Doppler US findings

On Doppler ultrasound examination, 55 (61.1%) lymph nodes showed central (hilar) blood supply, 28 (31.1%) showed peripheral blood supply, and 7 (7.8%) had both central and peripheral (anarchic) blood supply. Of the 36 lymph nodes that were found to be histopathologically benign, 28 (77.8%) had central blood, 7 (19.4%) had peripheral blood, and 1 (2.8%) had both central and peripheral blood supply. Of the 54 malignant lymph nodes, 27 (50%) showed central blood supply, 21 (38.9%) had peripheral, and 6 (11.1%) had both central and peripheral blood supply. Sensitivity was 50%, specificity was 77.78%, and accuracy was calculated as 61.1%. There was a statistically significant difference between the groups in terms of blood supply patterns on Doppler US ($p = 0.033$).

On Doppler examination, RI was found to be in the range of 0.52–1.79, while PI was shown to be between 0.70 and 87. The acceleration rate ranged from 0.10 to 3.55 ms, while the acceleration time ranged between 32 and 421 ms. The RI value was 0.75 ± 0.15 and 0.78 ± 0.28 in benign and malignant cases, respectively, while the PI value was 3.75 ± 14.28 and 1.56 ± 0.64, respectively. The acceleration rate was 0.58 ± 0.58 and 0.62 ± 0.41 in the benign and malignant groups, respectively, and the acceleration time was 160.64 ± 57.36 and 160.78 ± 60.39, respectively. No statistically significant difference was found in terms of RI, PI, acceleration rate and acceleration time, and differentiation between benign and malignant lymph nodes ($p < 0.005$).

Based on the threshold values found in the ROC analysis for the power of Doppler data in estimating the pathology result, the AUC values calculated to predict the pathology outcome of RI, PI, acceleration rate and acceleration time were not found to be statistically significant ($p < 0.05$).

USE findings

In the elastographic examination, the strain ratio ranged between 0.42 and 5.9. While the mean strain ratio value was 1.52 ± 0.98 in patients with benign histopathological results, it was 2.04 ± 1.21 in malignant patients, and the difference was found to be statistically significant ($p = 0.009$).

In the ROC analysis performed for the power of USE data (SR value) to predict the pathology outcome, the threshold value was calculated as 1.21, with a sensitivity of 77.8% and a specificity of 52.8%. The AUC value was found to be 66.3% and was statistically significant ($p = 0.006$).

In addition, elasticity patterns were evaluated by USE. Patterns 1 and 2 were considered benign, while patterns 3, 4 and 5 were considered malignant. A total of 47 (87%) of 54 patients who were found to be malignant histopathologically had patterns 3, 4 and 5, while 20 (55%) of 36 patients found to be benign had patterns 1 and 2. The accuracy rate was 77.8%, and the *p*-value was <0.0001. It was thus statistically significant.

When the imaging methods and histopathological results were compared, 24 (44.4%) of 54 pathologically malignant patients were interpreted as malignant by B-mode US, and 32 (58.5%) were evaluated as malignant by Doppler US; 37 (68.5%) of these patients on USE, 35 (64.2%) of them on B-mode and Doppler US, 48 (88.7%) of them on Doppler US and USE, and 49 (90.4%) of them on all three imaging modalities were interpreted as malignant. In the Kappa fit analysis, the consistency between the histopathology results and the results determined by oppler US, USE, double and triple methods was found to be statistically significant ($p < 0.05$). The compatibility of pathology results and B-mode results was not statistically significant ($p < 0.05$) (Tab. 3, Fig. 3).

When the individual and combined effects of B-mode, Doppler US and USE in differentiating lymph nodes were evaluated, the method with the highest sensitivity was the combination of all three imaging

Tab. 3. Kappa analysis results for the compatibility of pathology results with B-mode, Doppler US and US elastography results

		Pathological diagnosis				Total		Kappa value	*p*
		Benign		Malignant					
		n	%	*n*	%	*n*	%		
B-mode US	Benign	27	75.0	30	55.6	57	63.3	0.177	0.061
	Malignant	9	25.0	24	44.4	33	36.7		
	Total	36	40.0	54	60.0	90	100.0		
Doppler US	Benign	28	77.8	22	41.5	50	56.2	0.341	***0.001***
	Malignant	8	22.2	32	58.5	40	43.8		
	Total	36	40.0	54	60.0	90	100.0		
US elastography	Benign	21	58.3	17	31.5	38	42.2	0.266	***0.012***
	Malignant	15	41.7	37	68.5	52	57.8		
	Total	36	40.0	54	60.0	90	100.0		
B-mode US + Doppler US	Benign	26	72.2	19	35.8	45	50.0	0.350	***0.001***
	Malignant	10	27.8	35	64.2	45	50.0		
	Total	36	40.0	54	60.0	90	100.0		
Doppler US + US elastography	Benign	18	50.0	6	11.3	24	27.0	0.409	***0.000***
	Malignant	18	50.0	48	88.7	66	73.0		
	Total	36	40.0	54	60.0	90	100.0		
B-mode US + Doppler US + US elastography	Benign	18	50.0	5	9.6	23	26.1	0.428	***0.000***
	Malignant	18	50.0	49	90.4	67	73.9		
	Total	36	40.0	54	60.0	90	100.0		
US – ultrasonography									

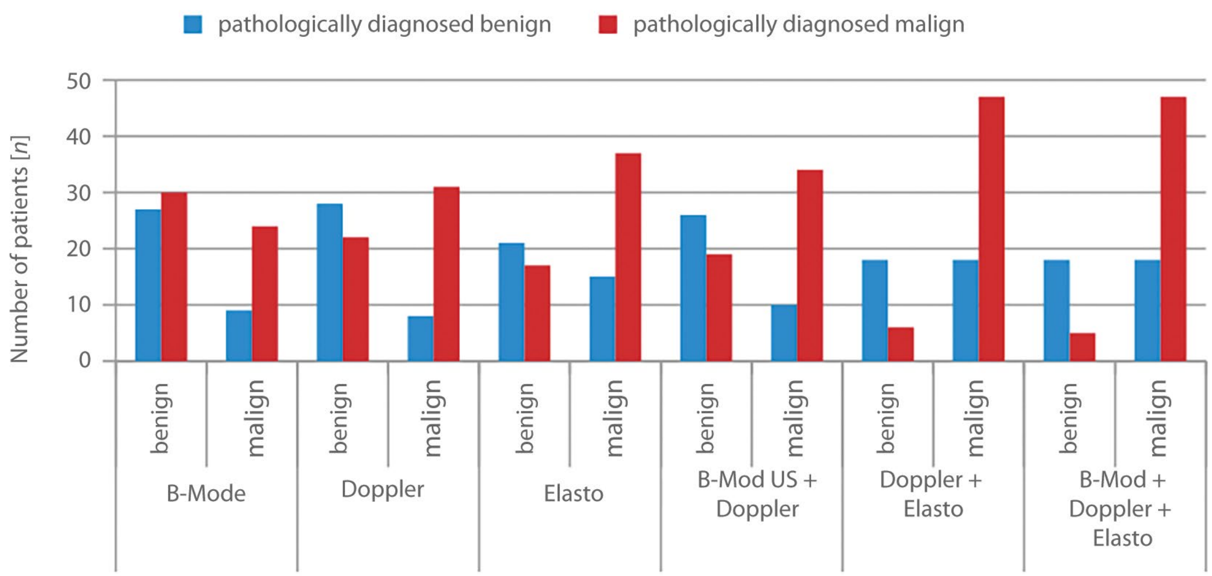

Fig. 3. *Visual representation of the distribution of pathology results and interpretations for different imaging methods*

methods (90.4%), while the modality with the highest specificity was Doppler US (77.8%). The examinations with the highest overall accuracy were the combination of all three methods (73.9%), while the examination with the lowest accuracy was B-mode US (56.7%) (Tab. 4).

A ROC analysis for the power of imaging methods in predicting the outcome of pathological results was performed. The AUC value calculated for the predictive power of the pathology results of the B-mode US results was not statistically significant (p <0.05). The AUC values calculated for the predictive power of the pathology results of the imaging methods and their combinations were found to be statistically significant (p <0.05).

The criteria that were found to be statistically significant among the B-mode findings were the short axis length and the long axis/short axis ratio. When the effects of their elastographic strain ratio value and their dual combinations were evaluated, the association of short axis and strain ratio was found in 48 (88.9%) of 54 malignant patients, while the association of the long axis/short axis and strain ratio was found in 45 (83.3%). The findings were statistically significant (p <0.001).

The threshold values found in the ROC analysis for the power of imaging methods in predicting the pathology results of the cervical lymph nodes; 33 mm for the long axis, 14 mm for the short axis, and 2.21 for the long axis/short axis ratio were calculated (Tab. 5). While the sensitivity of short axis and USE is 100% in predicting the pathological outcome in the cervical region, the rate is lower (88%) in the axilla. The accuracy of the short axis length-long axis/short axis ratio and their strain ratio as well as their binary combinations were found to be higher in the axillary region than in the cervical region.

The threshold values found in the ROC analysis for the power of imaging methods in predicting the pathology results in the axilla; long axis: 24 mm, short axis: 10 mm, long axis/short axis ratio: 1.46, RI: 0.76, PI: 1.26, acceleration speed: 0.41, acceleration time: 136, SR value calculated as 1.75; the AUC values calculated for the long axis, short axis, PI and USE (SR value) were found to be statistically significant (p <0.05) (Fig. 4, Tab. 6).

Discussion

Benign axillary lymph nodes are typically smaller than 2 cm in maximal size, and their parenchymal cortical thickness is less than 2.5 mm[7]. Unlike axillary lymph nodes, the normal short-axis in benign cervical nodes varies according to the levels in the neck; in general, the short axis diameter in axial plane should be <10 mm for cervical lymph nodes. Even the presence of lymph nodes in some parts of the neck, such as the medial retropharyngeal area, is pathological[8].

Although the specific criteria distinguishing benign lymph nodes from malignant lymph nodes have not been determined precisely, various threshold values have been reported in the literature for the short axis of the lymph node: 5 mm, 8 mm, and 10 mm[9]. In our study, the threshold value of 13 mm for the short axis of all lymph nodes showed 88.9% specificity in predicting malignant lymph nodes.

Tab. 4. ROC analysis results for the power of imaging methods in predicting pathological diagnosis

	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Area under the curve	Confidence interval (95%)	*P*-value	Accuracy
B-mode US	44.4	75.0	72.7	47.4	0.597	0.489–0.699	0.108	56.7
Doppler US	58.5	77.8	79.5	56.0	0.681	0.574–0.776	***0.002***	66.3
US elastography	68.5	58.3	71.2	55.3	0.634	0.526–0.733	***0.027***	64.4
B-mode US + Doppler US	64.2	72.2	77.3	57.8	0.682	0.575–0.777	***0.002***	67.4
Doppler US + US elastography	88.7	50.0	72.3	75.0	0.693	0.587–0.787	***0.001***	73.0
B-mode US + Doppler US + US elastography	90.4	50.0	72.3	78.3	0.702	0.595–0.795	***0.001***	73.9

Tab. 5. ROC analysis results for the power of imaging methods in predicting the pathology result of cervical lymph nodes

	Threshold value	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Area under the curve	Confidence interval (95%)	*P*-value
Long axis	>33	33.3	100.0	100.0	84.6	0.515	0.242–0.781	0.947
Short axis	>14	66.7	90.9	66.7	90.9	0.742	0.447–0.932	0.232
Long axis/short axis ratio	≤2.21	100.0	54.6	37.5	100.0	0.788	0.494–0.954	***0.040***
Resistive index	>0.76	100.0	54.6	37.5	100.0	0.742	0.447–0.932	0.102
Pulsatility index	>1.34	100.0	54.6	37.5	100.0	0.697	0.402–0.906	0.180
Acceleration rate	>0.41	100.0	54.6	37.5	100.0	0.727	0.432–0.923	0.106
Acceleration time	>181	0.0	63.6	0.0	70.0	0.53	0.255–0.793	0.848
Elastography (strain ratio)	>1.96	66.7	81.8	50.0	90.0	0.576	0.292–0.826	0.758

Tab. 6. ROC analysis results for the power of imaging methods in predicting the pathology result of axillar lymph nodes

	Threshold value	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Area under the curve	Confidence interval (95%)	*P*-value
Long axis	>24	40.0	88.0	87.0	42.3	0.642	0.523–0.749	***0.023***
Short axis	>10	54.0	84.0	87.1	47.7	0.73	0.615–0.826	***0.000***
Long axisshort axis ratio	≤1.46	24.0	100.0	100.0	39.7	0.624	0.504–0.733	0.060
Resistive index	>0.76	52.9	80.0	84.4	45.5	0.621	0.503–0.730	0.055
Pulsatility index	>1.26	66.7	60.0	76.2	48.4	0.639	0.518–0.748	***0.036***
Acceleration rate	>0.41	66.7	52.0	72.7	44.8	0.573	0.452–0.688	0.295
Acceleration time	≤136	39.6	84.0	82.6	42.0	0.531	0.410–0.649	0.656
Elastography (strain ratio)	>1.75	47.1	88.0	88.9	44.9	0.688	0.571–0.789	***0.003***

When the lymph nodes are evaluated as round and ovoid according to their shape, the threshold value for the long axis/short axis ratio in malignant lymph nodes was found to be 2 in several studies[10]. In our study, malignant lymph nodes were found to have more rounded morphology and were found to be significant in accordance with the literature ($p = 0.021$) Apart from the literature data, we found that a threshold for the long axis/short axis ratio ≤1.46 showed almost 100% specificity. Our remaining gray-scale US findings of the lymph nodes were in accordance with the literature.

In studies performed according to vascular distribution patterns on Doppler US, hilar blood supply was observed in normal and reactive lymph nodes, while peripheral and mixed (hilar + peripheral) blood supply was seen in malignant lymph nodes[11–14]. However, the study by Ying *et al*. found that while peripheral blood supply was observed in metastatic lymph nodes, hilar vascular structures were also preserved in lymphomatous lymph nodes, and there was a tendency for both hilar and peripheral blood supply[15].

In some studies on lymph nodes performed with USE, the strain ratio value was measured, while in others the elasticity score was calculated. In our study, the cut-off value was calculated as 1.21, with 77.8% sensitivity and 52.8% specificity, in the ROC analysis performed for the strain ratio value measured with USE, and it was found to be statistically significant ($p = 0.006$). The accuracy rate was found to be 66.3%. In the study by Acu *et al*., the threshold value for the strain ratio was calculated as 1.7, while the accuracy rate was found to be 64.1%[16]. In the study by Lyshchik *et al*., the threshold value was found to be 1.5 and when all diagnostic criteria were evaluated, it was concluded that SR had the highest accuracy of 92%[17]. The accuracy rate was found to be 89% in the study by Alam *et al*., with USE associated with a sensitivity of 92.8%, a specificity of 53.4%, and a threshold of 1.5[18]. In the study by Zhao *et al*., the threshold value was found to be 1.98[19]. In a paper published by Furukawa *et al*., a four-pattern elasticity scoring was applied to evaluate metastatic lymph nodes of head and neck squamous cell carcinoma[20].

In the scoring system; in pattern 1; 80% or more of the lymph node in the section is red or green (soft), in pattern 2; 50–80% is red or green, pattern 3; 50–80% is blue, pattern 4; 80% or more of the lymph node is blue (stiff). However, a threshold pattern for sensitivity and specificity between benign and malignant lymph nodes was not defined in this scoring system[20]. Alam *et al*. evaluated the accuracy of the combination of USE and B-mode US and USE separately for the differentiation of benign and malignant lymph nodes, and compared their superiority to B-mode US[18]. The elasticity scoring system developed by Alam *et al*. consists of five patterns: pattern 1; no or very small stiff area, pattern 2; stiff area <45%, pattern 3; stiff area >45%, pattern 4; peripheral stiff, central soft, and pattern 5 show a completely stiff lymph node. Patterns 2 and 3 were determined as thresholds for the malignant-benign differentiation with 83% sensitivity, 100% specificity, and 89% accuracy[18]. In another study, the same scoring system was used for USE, revealing that 87.9% of benign lymph nodes were pattern 1 or 2, and 50% of malignant lymph nodes were pattern 3 or 4[21]. In the study of Lenghel *et al*., elasticity scoring was divided into 8 patterns and the threshold in the benign-malignant differentiation was determined between 3–4 patterns[22]. In our study, a 5-pattern scoring system was used for elasticity patterns, and pattern 2 was adopted as the threshold. Considering the elasticity score in distinguishing benign and malignant lymph nodes, the sensitivity was calculated at 87%, specificity at 55.5%, positive predictive value at 88.6%, and negative predictive value at 74% in our study. The accuracy rate was 77.8%.

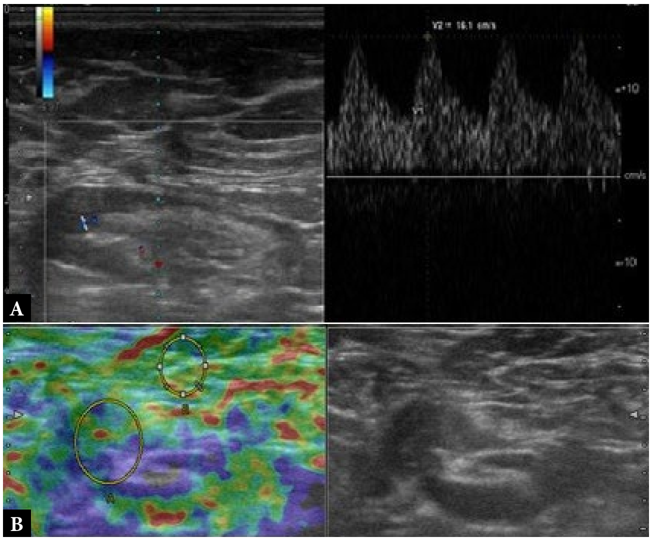

Fig. 4. *A 48-year-old female patient was diagnosed with a BI-RADS 5 mass in the breast, and biopsy was planned from the suspicious axillary lymph node. Hilar blood supply was observed in the ovoid lymph node with a fatty hilum and asymmetrically increased cortical thickness (***A***). The strain ratio was determined as 2.06 on USE, and the elasticity pattern was determined as 3 (***B***). The pathology result was reported as malignant cytology*

In our study, sensitivity was found to be high, while sspecificity was found to be lower. When the superiority of B-mode US, Doppler US and USE to each other in differentiating lymph nodes is evaluated; in all studies, combination with USE was shown to increase sensitivity and specificity levels[23]. In the study by Taylor *et al*. on axillary lymph nodes in patients with breast cancer, both sensitivity and specificity of elasticity scoring were found to be higher than B-mode US (90%, 86% versus 76% and 78%, respectively)[24]. Considering the SR value, while sensitivity was quite high in USE, specificity was found to be significantly low. In our study, the method with the highest sensitivity was found to be the combination of all three methods (90.4%), while USE (68.5%) had the highest sensitivity in individual evaluations. Doppler US with the highest specificity (77.8%) and the examination with the highest overall accuracy were found to be the combination of all three methods (73.9%). Doppler US (66.3%) had the highest overall accuracy in individual evaluations. B-mode US (56.7%) was found to have the lowest accuracy in the stand-alone and combined evaluations. The results showed that USE increased the sensitivity and decreased the specificity in the differentiation of benign-malignant lymph nodes. Regardless of the method, when all criteria were evaluated statistically, the association of short axis- the strain ratio value and long axis/short axis ratio-SR value was found to be the most statistically significant. The combination of short axis length and the strain ratio value was the combination characterized by the highest sensitivity (88.8%).

Regarding the limitations of the study, the reason for the high number of female patients and axillary lymph nodes was thought to be the fact that patients with suspected breast cancer were referred to our clinic and included in the study. Another disadvantage is that the compression load applied with free-hand USE is not standardized and may, therefore, cause some inter-observer and inter-patient variability in the same observer.

Another important limitation of our study was that we examined the lymph nodes in both cervical and axillary regions within the same study. There are significant differences in lymph nodes located in both regions in terms of size and adjacent fatty and muscle tissues. Histopathological results were obtained with tru-cut or fine-needle biopsy. This may result in imprecise results for processes that are actually malignant, such as some lymphomas.

In our study, USE was evaluated semiquantitatively. In addition to USE, performing B-mode US and Doppler US enabled a comparison of elastographic findings with sonographic findings. Shape, short axis, long axis/short axis ratio and hilum status were found to be statistically significant in B-mode US.

Conclusion

USE is a highly sensitive imaging method in the differentiation of benign and malignant lymph nodes, and when combined with B-mode US and Doppler US findings, it makes a significant contribution to the diagnosis. With an increased use of USE, the diagnostic accuracy will improve, and the number of unnecessary biopsies will decrease.

Conflict of interest

The authors do not report any financial or personal connections with other persons or organizations which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

Author contributions

Original concept of study: HCT, AMK, ZHA. Writing of manuscript: ZHA, FZA. Analysis and interpretation of data: AMK, ZHA. Final approval of manuscript: GYO. Collection, recording and/or compilation of data: AA.

References

1. Giambini H, An KN: Ultrasound elastography for hand soft tissue assessment. Hand Clin 2022; 38(1): 119–128. doi: 10.1016/j.hcl.2021.08.013.
2. Ng WL, Omar N, Ab Mumin N, Ramli Hamid MT, Vijayananthan A, Rahmat K: Diagnostic accuracy of shear wave elastography as an adjunct tool in detecting axillary lymph nodes metastasis. Acad Radiol 2022; 29 Suppl 1: S69–S78. doi: 10.1016/j.acra.2021.03.018.
3. Huang XW, Huang QX, Huang H, Cheng M-Q, Tong W-J, Xian M-F *et al.*: Diagnostic performance of quantitative and qualitative elastography for axillary lymph node metastasis in breast cancer: a systematic review and meta-analysis. Front Oncol 2020; 10: 552177. doi: 10.3389/fonc.2020.552177.
4. Togawa R, Binder LL, Feisst M, Barr RG, Fastner S, Gomez C *et al.*: Shear-wave elastography as a supplemental tool in the assessment of unsuspicious axillary lymph nodes in patients undergoing breast ultrasound examination. Br J Radiol 2022; 95: 20220372. doi: 10.1259/bjr.20220372.
5. Pehlivan M, Gurbuz MK, Cingi C, Adapinar B, Değirmenci AN, Acikalin FM *et al.*: Diagnostic role of ultrasound USE on lymph node metastases in patients with head and neck cancer. Braz J Otorhinolaryngol 2019; 85: 297–302. doi: 10.1016/j.bjorl.2018.01.002.
6. Acu L, Oktar SÖ, Acu R, Yücel C, Cebeci S: Value of ultrasound USE in the differential diagnosis of cervical lymph nodes: A comparative study with B-mode and color Doppler sonography. J Ultrasound Med 2016; 35: 2491–2499. doi: 10.7863/ultra.15.09019.
7. Dialani V, James DF, Slanetz PJ: A practical approach to imaging the axilla. Insights Imaging 2015; 6: 217–229. doi: 10.1007/s13244-014-0367-8.
8. Lan M, Huang Y, Chen CY, Han F, Wu SX, Tian L *et al.*: Prognostic value of cervical nodal necrosis in nasopharyngeal carcinoma: analysis of 1800 patients with positive cervical nodal metastasis at MR imaging. Radiology 2015; 276: 536–344. doi: 10.1148/radiol.15141251.
9. Hu M, Xia C, Zhou Y, Yu F, Zhu Q, Zhao H: Ultrasound surveillance of abnormal cervical lymph nodes in patients with papillary thyroid carcinoma after surgery. J Ultrasound Med 2021; 40: 29–37. doi: 10.1002/jum.15369.
10. Prativadi R, Dahiya N, Kamaya A, Bhatt S: Chapter 5 Ultrasound characteristics of benign vs malignant cervical lymph nodes. Semin Ultrasound CT MR 2017; 38: 506–515.
11. Lee S, Lee JY, Yoon RG, Kim JH, Hong HS: The value of microvascular imaging for triaging indeterminate cervical lymph nodes in patients with papillary thyroid carcinoma. Cancers 12; 2839. doi: 10.3390/cancers12102839.
12. Karagülle M, Arslan FZ, Şimşek S, Öncü S, Pamuk GG, Öncü M *et al.*: Investigation of the effectiveness of microvascular Doppler ultrasound and Q-pack in the discrimination of malign thyroid nodules from benign. Ultrasound Q 2022. doi: 10.1097/RUQ.0000000000000590.
13. Abdelgawad EA, Abu-samra MF, Abdelhay NM, Abdel-Azeem HM: B-mode ultrasound, color Doppler, and sonoelastography in differentiation between benign and malignant cervical lymph nodes with special emphasis on sonoelastography. Egypt J Radiol Nuclear Med 2020; 51: 1–10.

14. Arslan FZ, Altunkeser A, Körez MK, Aksoy N, Bayramoğlu Z, Karagülle M: The importance of superb microvascular imaging for the differentiation of malignant breast lesions from benign lesions. Eur J Breast Health 2021; 18: 48–54. doi: 10.4274/ejbh.galenos.2021.2021-6-1.

15. Ying M, Ahuja A, Brook F, Metreweli C: Power Doppler sonography of normal cervical lymph nodes. J Ultrasound Med 2000; 19: 511–517. doi: 10.7863/jum.2000.19.8.511.

16. Acu L, Oktar SÖ, Acu R, Yücel C, Cebeci S: Value of ultrasound elastography in the differential diagnosis of cervical lymph nodes: a comparative study with B-mode and color Doppler sonography. J Ultrasound Med 2016; 35: 2491–2499. doi: 10.7863/ultra.15.09019.

17. Lyshchik A, Higashi T, Asato R, Tanaka S, Ito J, Hiraoka M *et al.*: Cervical lymph node metastases: diagnosis at sonoelastography – initial experience. Radiology 2007; 243: 258–267. doi: 10.1148/radiol.2431052032.

18. Alam F, Naito K, Horiguchi J, Fukuda H, Tachikake T, Ito K: Accuracy of sonographic elastography in the differential diagnosis of enlarged cervical lymph nodes: Comparison with conventional B-mode sonography. Am J Roentgenol 2008; 191: 604–610. doi: 10.2214/AJR.07.3401.

19. Zhao Q-L, Xia X-N, Zhang Y, He J-J, Sheng W, Ruan L-T *et al.*: Elastosonography and two-dimensional ultrasonography in diagnosis of axillary lymph node metastasis in breast cancer. Clin Radiol 2018; 73: 312–318. doi: 10.1016/j.crad.2017.09.013.

20. Furukawa MK, Furukawa M: Diagnosis of lymph node metastases of head and neck cancer and evaluation of effects of chemoradiotherapy using ultrasonography. Int J Clin Oncol 2010; 15: 23–32. doi: 10.1007/s10147-009-0017-1.

21. Tan R, Xiao Y, He Q: Ultrasound USE. Its potential role in assessment of cervical lymphadenopathy. Acad Radiol 2010; 17: 849–855. doi: 10.1016/j.acra.2010.03.014.

22. Lenghel LM, Bolboaca SD, Botar-Jid C, Baciut G, Dudea SM: The value of a new score for sonoelastographic differentiation between benign and malignant cervical lymph nodes. Med Ultrason 2012; 14: 271–277. doi: 10.1016/j.acra.2010.03.014.

23. Tang G-X, Xiao X-Y, Xu X-L, Yang H-Y, Cai Y-C, Liu X-D *et al.*: Diagnostic value of ultrasound elastography for differentiation of benign and malignant axillary lymph nodes: a meta-analysis. Clin Radiol 2020; 75: 481.e9–481.e16.

24. Taylor K, O'Keeffe S, Britton PD, Wallis MG, Treece GM, Housden J *et al.*: Ultrasound USE as an adjuvant to conventional ultrasound in the preoperative assessment of axillary lymph nodes in suspected breast cancer: a pilot study. Clin Radiol 2011; 66: 1064–1071. doi: 10.1016/j.crad.2011.05.015.