Kamel et al. *SECI Oncology* 2024(3):262-269

Quantitative and Qualitative Assessment of Superficial Lymph Nodes by B-mode Ultrasound, Color Doppler and Sono Elastography

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Abstract:

Background: Large number of patients with superficial lymphadenopathy undergo biopsy to differentiate benign and malignant lymph nodes (LNs). Although high accuracy of high-resolution sonography approaches differentiating benign and malignant lymph nodes, Ultrasound elastography (USE) explains that pathological changes are linked to changes in tissue stiffness or elasticity. We suggest the application of elastography may decrease using of invasive maneuvers for low-risk LN and improve the selection of LN with high malignant probability. The aim of our study is to evaluate the diagnostic accuracy of B-mode Ultrasound, color Doppler, elastography, and their combination to differentiate benign and malignant LNs.
Methods: This was a prospective study included 70 patients with enlarged superficial LNs ranging in age from 3 to 82 years old. Using high frequency probes at 9L / ML6-15 MHz from GE Medical Systems, all patients underwent ultrasound, color Doppler scans, and elastography. Patients were subjected to fine needle aspiration cytology, core biopsy, or excisional biopsy according to patient's condition, with histopathological examination.
Results: Based on strain elastography (SE); malignant lesions had strain elastography score 3 and 4 compared to benign lesions (92.3%) had strain elastography score 1 and 2, the difference was statistically significant (p-value < 0.001). The mean strain ratio ± standard deviation (SD) of benign lesions was 0.84 ± 0.34, the mean strain ratio ± SD of malignant lesions was 2.91±1.05. The difference was statistically significant (p-value < 0.001). Based on shear wave elastography (SWE), 79.5% of malignant lesions had rim and undetermined shear wave color pattern compared to all benign lesions had homogenous and nodular shear wave color pattern, the association was statistically significant (p-value < 0.001). The mean maximum stiffness and maximum velocity were statistically significantly higher among the malignant lesions (p-value < 0.001).
Conclusion: Elastography is a non-invasive technique that provides a great promise in distinguishing reactive from malignant lymphadenopathy. Sensitivity can be enhanced when used in conjunction with Doppler and grayscale US. In comparison to greyscale ultrasonography, strain and shear wave elastography provides quantitative and quantitative information on LNs with good diagnostic accuracy differentiating benign and malignant ones.

Keywords: Ultrasound; Elastography; Superficial Lymphadenopathy.

Received: 2 May 2024
Accepted: 14 July 2024

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Introduction:

Using grayscale, color Doppler, and power Doppler in high-resolution ultrasound gives a precise, sensitive, and targeted approach to distinguish between benign and malignant lymph nodes. When compared with cross-sectional modalities like computed tomography (CT), positron emission tomography (PET), and magnetic resonance imaging (MRI), ultrasound is less expensive, noninvasive, and requires no intravenous contrast. It can also characterize nodes smaller than 5 mm, define nodal internal architecture in exquisite detail, and allow free rotation of the scanning plane to precisely determine size dimensions of the lymph node.[1]

Imaging studies have become very important in the diagnosis of lymph node disorders. When it comes to youngsters, US is typically the first and only approach used because CT-scanning is less desirable due to the radiation risk for growing people, while MRI frequently requires general anesthesia for younger children. When deciding whether to proceed along with an invasive maneuver, US can provide an array of data that will help establish a diagnosis.[2]

Since the pathological alterations are typically linked to changes in tissue stiffness or elasticity, elastography, a newly developed diagnostic technology, can add information to standard ultrasonographic findings using two techniques: Strain elastography and Shear wave elastography. Physical tissue displacement is measured by strain elastography in a direction parallel to the applied normal stress. Shear waves can be created in a parallel or perpendicular direction using a dynamic, high-intensity, short-duration acoustic pulse. The velocity of these shear waves can be used to estimate the elasticity of the tissue in terms of the absolute elastic modulus.[3]

This study aims to assess the diagnostic performance of elastography, color Doppler, and sonography alone and in combination for the purpose of distinguishing benign from malignant superficial lymphadenopathy.

Patients and Methods:

Our prospective study enrolled patients presented with superficial lymphadenopathy in the period from 2021 to 2023. 70 patients with enlarged superficial lymph nodes ranging in age from 3 to 82 years old referred to the diagnostic and interventional radiology department at South Egypt Cancer Institute and Assiut University hospitals, from the medical oncology, radiotherapy, nuclear medicine, or surgical oncology clinics. The study was approved by the local research ethical committee at the Faculty of Medicine - Assiut University and registered at Clinical Trials.Gov by registration code: NCT04561999

Every patient underwent US examination, color Doppler scan, and USE utilizing elastography and B-mode ultrasonography on ultrasound machine (LOGIQ S8, GE Medical Systems) with 9L MHz high frequency probe for shear wave elastography and ML6-15 MHz high frequency probe for strain elastography. Patients were subjected to FNAC, core biopsy, or excisional biopsy according to patient’s condition, followed by histopathological examination.

Inclusion criteria:

Patients presented with enlarged superficial lymph nodes by clinical examination.

Exclusion Criteria:

Patients who previously receive any medical treatment or chemo or radiotherapy and patients who previously underwent FNAC or biopsy.

Preparation:

No specific preparation is needed.

Gray scale B-mode ultrasound;

The following data collected; Lymph node size (short axis, long axis, long to short axis “L/S” ratio), shape and, margins of lymph node (i.e., well defined, ill-defined, and matted), presence or absence of hilum and presence of echogenic foci.

Doppler ultrasound;

The following data collected; The presence or absence of vascularity either hilar, peripheral, or mixed (peripheral and hilar). The resistivity index (RI) and pulsatile index (PI). Wave form (high or low resistive waveform).

Ultrasound Elastography;

1) Strain Elastography:

In order to obtain a high-quality graph with consistently high (almost flat, plateau-like) peaks and freeze the image for analysis and measurement, the lymph node is subjected to repeated light pressure followed by decompression along the radiation axis until nearly the same color distribution is obtained in multiple consecutive images. A region of interest (ROI) box is used to measure the strain on the lymph node and the surrounding soft tissue (muscle). The percentage of high elasticity was used to get an elasticity score of four points. The elastography color bar indicates stiff lesions as blue and soft lesions as red as described by Muhi et al. and ACU et al. [4], [5] According to this system, LNs were classified to:

- Score 1 was achieved when less than 10% of the LN was blue-colored and the majority of the node was red.
- Score 2: elastography that showed 10%–50% of the area as blue, with the majority being red and green.
- Score 3: mainly composed of green and blue (50–90%).
- Score 4 denotes a rigid node that is primarily (>90%) blue in color.

As the technique is operator dependent, the ratio of normal surrounding soft tissue to lymph node strain (strain ratio or strain index) is calculated at least 2 times for each lymph node and saved.[5]

2) Shear Wave Elastography:

Because SWE doesn't require manual compression, it can minimize interference from subjective factors as described by V. Romeo et al and L. Chami et al. The probe is positioned vertically on the skin and applied with little force. At the moment of acquisition, the following color patterns are prospectively accessed [6], [7]:

- Homogeneous blue pattern: The entire elasticity map, which includes the LN and its surroundings, has a uniformly soft blue tone.
- Nodular pattern: The lesion can be visibly distinguished from the surrounding tissue by

showing empty, uncolored regions or by being firmer or softer than the surrounding tissues.

- Rim pattern: A yellow to red rim of stiffer tissue surrounds the LN, and the LN may show empty areas or hues distinct from the surrounding tissue.
- Undetermined pattern: the entire lesion is crisscrossed by soft and stiff, regions, possibly void regions and none of the previous patterns can be seen.

Rather than averaging all readings or assessing the node as a whole using a single large reading, we chose one reading with the highest value for further investigation since the nodes might have displayed focal spatial heterogenicity as a result of partial tumor cell invasion, we repeated the procedures three times to measure the intra-observer reproducibility. In the highest quality regions, shear wave velocity SWV is measured using the same fixed dimension ROI in the stiffest area within the LN. The highest velocity is defined as SWV max. [6]

Statistical Analysis:

Data entry and cleaning was done using Excel program. Data was analyzed using IBM SPSS (Statistical Package of Social Sciences) statistical software, version 22. Numeric data was checked for normality using Sharpiro-wilk tests of normality. Quantitative data was expressed as mean ± standard deviation (SD) and compared using Mann–Whitney U test.

Qualitative data was expressed as frequencies and percentages and was compared using chi-square test. Accuracy of different parameters used in the diagnosis of the nature of lymphadenopathy was assessed using receiver operator characteristics (ROC) curve. Level of significance was kept at 95% and hence, p-value was considered significant if ≤ 0.05.

Ethical consideration:

Verbal consent is obtained from patients included in this study. Approval of ethical committee at faculty of medicine- Assiut University is obtained, code:17101353 at 21-2-2021.

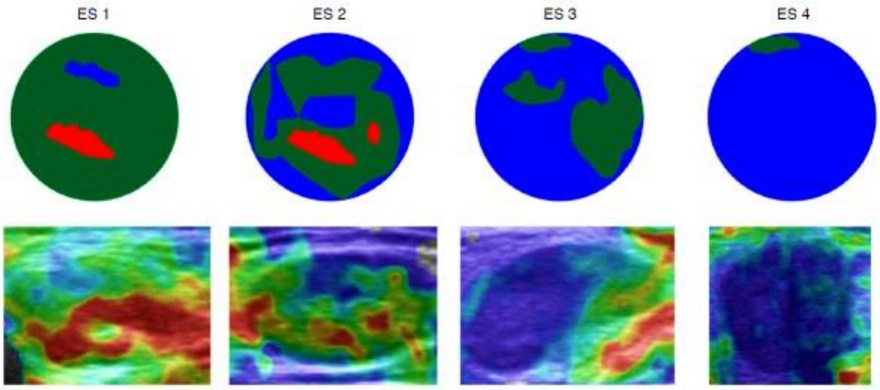

Fig.1: schematic diagram for elasticity score of LNs

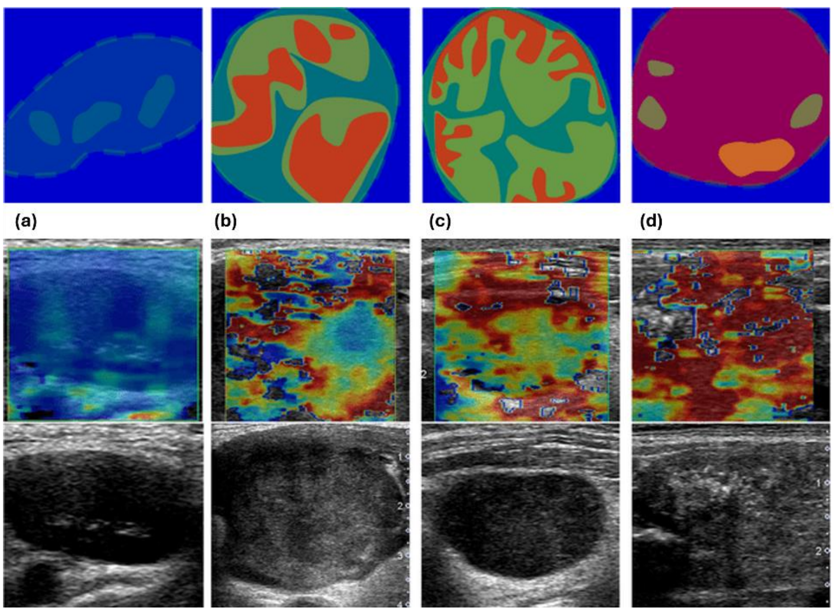

Fig.2: schematic diagram for shear wave elastography color pattern of LNs

Results:

Mean age of the enrolled patient's ± SD was 43.94 ± 17.04. Out of the studied patients 74.3% were females. The most frequent sites for lymphadenopathy were cervical (78.6%) and axillary (14.3%)

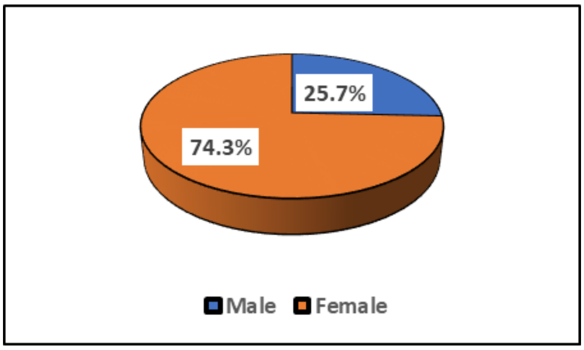

Fig.3: Sex distribution among the studied patients

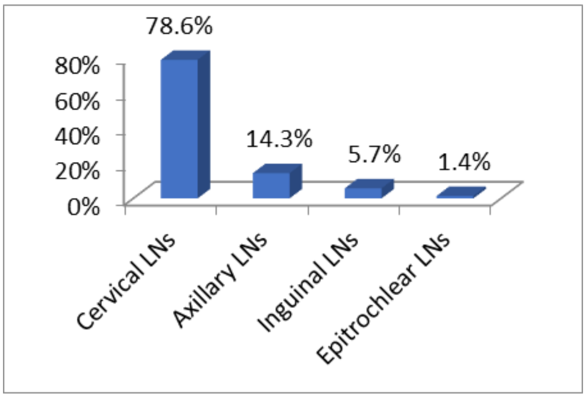

Fig.4: Sites of lymphadenopathy among the studied patients

Table 1: Type and result of histopathology among studied patients

Variables	No. (%) (N=70)
Type of histopathology	
FNAC	47 (67.1%)
TCNB	14 (20%)
Excisional biopsy	9 (12.9%)
Histopathologic diagnosis	
Benign lesions	26 (37.2%)
• Reactive lymphoid hyperplasia	22 (31.5%)
• Tuberculous lymphadenitis	4 (5.7%)
Malignant lesions	44 (62.8%)
• Metastasis	33 (47.1%)
• Lymphoma	11 (15.7%)

Gray scale B-mode US;

The mean short axis diameter, mean long axis diameter were significantly higher in malignant lesions. Mean long /short axis diameter ratio was significantly higher in benign lesions. Majority (92.3%) of benign lesions was oval, while majority (84.1%) of malignant lesions was rounded, the association was statistically significant (p-value < 0.001). All benign lesions had well-defined smooth outline while 77.3% of malignant lesions had well-defined smooth outline, the association was statistically significant (p-value=0.03). The hilum was lost in majority (93.2%) of malignant lesions compared to 0% of benign lesions, the association was statistically significant (p-value < 0.001). At cutoff point ≤1.78, long/ short axis ratio had 79.55 % sensitivity and 88.46 % specificity in differentiating benign and malignant lymphadenopathy.

Doppler Ultrasound:

The central, peripheral and mixed vascular pattern were present in 32.9%, 30% and 30% of the patients. At cutoff point < 0.77, resistive index had 95.24% sensitivity and 100% specificity in differentiating benign and malignant lymphadenopathy. At cutoff point < 1.3, pulsatile index had 97.62% sensitivity and 95.62 % specificity in differentiating benign and malignant lymphadenopathy. Almost all malignant lesions had peripheral and mixed vascular pattern with high resistive waveform compared to all benign lesions had central vascular pattern with low resistive wave form, the difference was statistically significant (p-value < 0.001). The mean resistive index ± SD of benign lesions was 0.58 ± 0.09, the mean resistive index ± SD of malignant lesions was 0.94 ± 0.32. The difference was statistically significant (p-value < 0.001).

The mean pulsatility index ± SD of benign lesions was 1.12 ± 0.8, the mean resistive index ± SD of malignant lesions was 1.94 ± 0.54. The difference was statistically significant (p-value < 0.001).

Strain Elastography:

40% and 25.7% of the patients had strain elastography score 3 and 4. Mean strain ratio ± SD was 2.14±1.33.

All malignant lesions had strain elastography score 3 and 4 compared to majority of benign lesions (92.3%) had strain elastography score 1 and 2, the difference was statistically significant (p-value < 0.001). The mean strain ratio ± SD of benign lesions was 0.84 ± 0.34, the mean strain ratio ± SD of malignant lesions was 2.91±1.05. The difference was statistically significant (p-value < 0.001). At cutoff point < 2, elasticity score had 100% sensitivity and 92.3% specificity in differentiating benign and malignant lymphadenopathy. At cutoff point < 1.5, strain ratio had 97.7% sensitivity and 96.2 % specificity in differentiating benign and malignant lymphadenopathy.

Shear Wave Elastography:

35.7% and 32.9% had homogenous and undetermined color pattern respectively.

Mean of maximum stiffness ± SD was 5.94±2.11. Mean of maximum velocity ± SD was 121.34±68.28.

At cutoff point < 90 kPa, maximum stiffness had 95.5% sensitivity and 100% specificity in differentiating benign and malignant lymphadenopathy. At cutoff point < 5.4 m/s, maximum velocity had the same sensitivity and specificity in differentiating benign and malignant lymphadenopathy.

Using ultrasonography, Doppler, and SE: the sensitivity was 100%, specificity was 92.3%, PPV was 95.7%, NPV was 100%, false positive was 7.7%, false negative was 0.0% and the accuracy was 97.1% (p-value <0.001).

Using ultrasonography, Doppler, and SWE: the sensitivity was 100%, specificity was 88.5%, PPV was 93.6%, NPV was 100%, false positive was 11.5%, false negative was 0.0% and the accuracy was 95.7% (p-value <0.001).

Elasticity score had the highest sensitivity (100%) differentiating benign and malignant lymphadenopathy, while resistive index, maximum stiffness and maximum velocity had the highest specificity (100%) differentiating benign and malignant lymphadenopathy.

Table 2: Comparison between the significant diagnostic parameters accuracy in diagnosis the nature of lymphadenopathy:

	Sensitivity	Specificity	PPV	NPV	Accuracy
RI	95.24%	100%	100%	92%	97.1%
PI	97.62%	95.62%	97.62%	95.62%	96.92%
ES	100%	92.3%	95.7%	100%	97.1%
SR	97.7%	96.2%	97.7%	96.2%	97.1%
Maximum stiffness	95.5%	100%	100%	92.6%	95.7%
Maximum velocity	95.5%	100%	100%	92.6%	95.7%

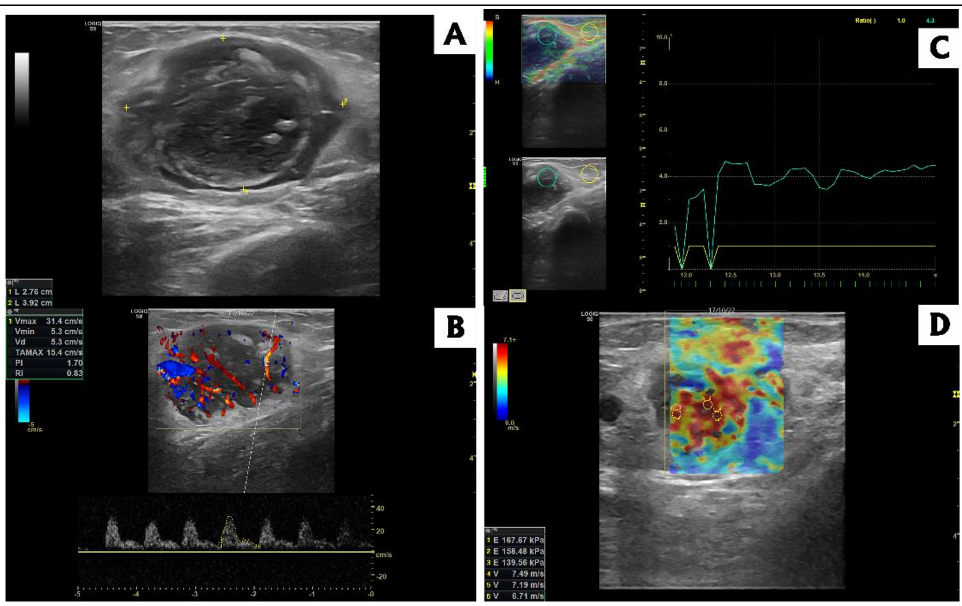

Fig. 5. A 63-year-old female patient presented with right epitrochlear swelling.
(A) By gray scale ultrasound: Right epitrochlear well defined irregular outline round lesion with lost hilum and multiple echogenic foci with long/short axis diameter ratio 1.4 **(B) By color Doppler ultrasound:** Mixed (central and peripheral) vascularity with RI 0.83 and PI 1.7 **(C) By strain elastography:** Score-4 and strain ratio 4.3 **(D) By shear wave elastography:** Nodular pattern with maximum stiffness 167.67 kPa and velocity 7.49m/s. **Pathological result revealed:** follicular center cell lymphoma GI.

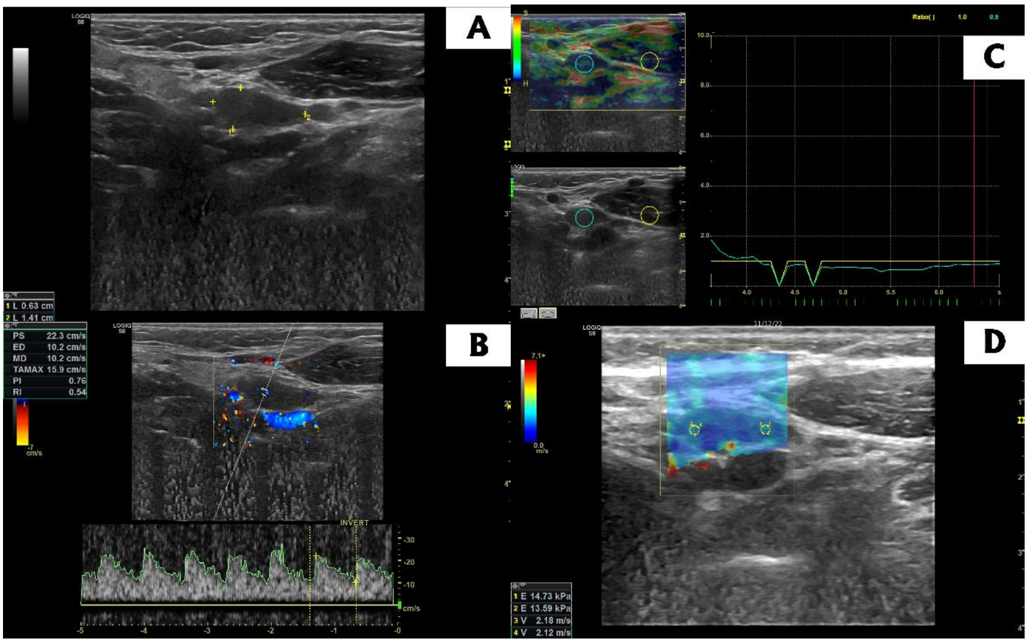

Fig. 6. A 40-year-old female patient with history of CLL presented with enlarged left cervical LN. **(A) By gray scale ultrasound:** Left cervical well defined oval LN with preserved central hilum and long/short axis diameter ratio 2.24 **(B) By color Doppler ultrasound**: Central (hilar) vascularity with RI 0.54 and PI 0.76 **(C) By strain elastography:** Score-2 and strain ratio 0.9 **(D) By shear wave elastography:** Homogenous blue pattern with maximum stiffness 14.73 kPa and velocity 2.18 m/s**. Pathological result revealed:** reactive lymphoid hyperplasia.

Discussion:

As a non-invasive imaging technique, sono-elastography may be able to play a role in the distinction between benign and malignant LNs by reducing the total number of needless biopsies. Elastography evaluations can be broadly divided into qualitative and quantitative categories. [8]

In our study, 70 patients (18 male and 52 female) with 70 enlarged superficial LNs (pathologically proven 26 benign and 44 malignant).

In our study, using the gray scale ultrasound alone, the cut off value of long/short axis ratio was 1.78 with sensitivity of 79.55%, specificity 88.46%, PPV 92.1%, NPV 71.9% and accuracy 82.9%.

Our cut off value was lower than cut off value of Dawoud et al., [9] and Acu et al. [5] studies, where the cut off value was 2 with sensitivity, specificity, PPV, NPV and accuracy were 77.78%, 73.3%, 89.74%, 53.38% and 76.67% respectively for Dawoud et al., [9] study and lower accuracy (55.9%) for Acu et al. [5] study.

In our study, the cut off value of RI was 0.77 with sensitivity 95.24%, specificity, PPV, NPV, accuracy of 100%, 100%, 92% and 97.1% respectively. While the cut off value of PI was 1.33 with sensitivity, specificity, PPV, NPV and accuracy were 97.62%, 95.62%, 97.62%, 95.62% and 96.92% respectively.

Our cut off point was nearly similar to cut off point reported by Prativadi et al., [10], Zaidan et al., [11].

Zaidan et al., [11] study was performed on 81 patients (45 males and 36 females) with cervical lymphadenopathy. The cut off value of RI was 0.71 with sensitivity 90% and specificity 95.1% while the cut off value of PI was higher (1.73) with sensitivity 92.5% and specificity 93.7%

Prativadi et al., [10] study obtained 0.7 as a cut of point value for RI and 1.4 for PI with sensitivity 86% and 80% and specificity 70% and 86% respectively.

The calculated sensitivity of strain elastography, as regard strain ratio, in differentiation between benign and malignant LNs was 97.7%, specificity, PPV, NPV and accuracy was 96.2%, 97.7%, 96.2% and 97.1% respectively (Significant at P<0.001) with a cut off value of 1.5 when considering elasticity score 3 and 4 as malignant lesion and elasticity score 1 and 2 as benign lesion.

In our study, we suggested a cut off value of 1.5 as described, similar to cut off value proposed by Moharram et al.,[8] and Lyschik et al. [12], lower than cut off value proposed by Muhi et al., [4] and Acu et al. [5].

Moharram et al.,[8] study was performed on sample size lower than our study (30 patients: 17 male and 13 female) with 75 cervical LNs (25 benign and 50 malignant) with 92% specificity, 86% sensitivity, 95.5% PPV, 76.6% NPV and 88% accuracy using 7.5-MHz superficial linear probe (Toshiba Japan, Aplio 500 Ultrasound systems).

Lyschik et al. [12] study was performed on sample size lower than our study (43 patients: 22 male and 21 female) with 141 neck LNs (60 metastatic and 81 metastatic free) with 98% specificity, 85% sensitivity, 96% PPV, 90% NPV and 92% overall accuracy using a 7.5-MHz linear probe (Siemens Medical Systems).

Muhi et al. [4] study was performed on sample size lower than our study (45 female patients with 45 axillary LNs), compared to 70 male and female patients and different groups of lymph nodes in our study. The elasticity score ratio is referenced to the axillary fat. In our study, the surrounding muscle was the reference. They suggested a higher cut off value (2.1) with 100% sensitivity but lower specificity of 66.7%, and 100% NPP using a linear transducer 9L-D (2-8MHz with FOV 44mm) of a GE health care sonographic machine (LOGIQ S8 XD clear 2.0). 101

ACU et al. [5] study was performed on 168 patients with 220 neck LNs. The stain index cut off value was accepted as (1.7) with 71.6% sensitivity, 76.5% specificity, 57.1% PPV, 86% NPV and 75% accuracy using a linear transducer 13-8MHz (Hitachi medical system) with the size of the ROI box was adjusted to calculate the stiffness of the entire lymph node. In our study we adjust a ROI of the lymph node with the same size of the ROI of the surrounding muscles.

In our study the sensitivity of SE was higher when used combined with gray scale US and Doppler (100%) than when used alone (97.7%). The sensitivity, specificity, PPV, NPV, false positive, false negative and accuracy when used alone were 97.7%, 92.3%, 95.6%, 96%, 7.7%, 2.3& and 95.7% respectively. While the sensitivity, specificity, PPV, NPV, false positive, false negative and accuracy when used combined with other modalities were 100%, 92.3%, 95.7%, 100%, 7.7%, 0% and 97.1% respectively.

The sensitivity, specificity, PPV, NPV and accuracy of combined US, Doppler and UE were higher than that of Acu et al. [5] study that were (62.7%, 86.9%, 67.7%, 84.2% and 79.6%)

In our study, the maximum stiffness cut off point of shear wave elastography was 90 kPa with calculated sensitivity, specificity, PPV, NPV and accuracy was 95.5%, 100%, 100%, 92.6% and 95.7% respectively and the corresponding maximum velocity cut off point 5.5m/s when considering that most of malignant lesions had rim and undetermined color pattern and most of the benign lesions had homogenous and nodular color pattern. This cut off point is higher than Choi et al.,[13]

Choi et al. [13] study was performed on sample size lower than our study (15 patients: 8male and 7female) with 67 cervical lymph nodes with cutoff level of 19.44 kPa with accuracy, sensitivity and specificity were 94%, 91% and 97% respectively using Aixplorer ultrasound system with a frequency range of 4 to 15 MHz.

In our study the sensitivity of SWE was higher when used combined with gray scale US and Doppler (100%) than when used alone (95.5%). The sensitivity, specificity, PPV, NPV, false positive, false negative and accuracy when used alone were 95.5%, 96.2%, 97.7%, 92.6%, 3.8%, 4.5% and 95.7% respectively. While the sensitivity, specificity, PPV, NPV, false positive, false negative and accuracy when used combined with other modalities were 100%, 88.5%, 93.6%, 100%,11.5%, 0.0% and 95.7% respectively.

Our study has two points of strength, large sample size in comparison to other previous studies that was forementioned & our study was carried upon multiple groups of LNs (cervical, inguinal & axillary LNs) not only confined on single group.

Study limitations: Lower quality scores were obtained for hard lesion at SWE. Since pixels containing minute or microscopic necrotic changes inside the metastatic nodes can create signal void artifact, it makes since to use the maximum value of Swe rather than mean value to prevent underestimating stiffness in necrotic areas. Elastogram with poor quality the result of nearby vessels pulsations.

Conclusion:

Elastography is a non-invasive technique that provides a great promise in distinguishing reactive from malignant lymphadenopathy. Sensitivity can be enhanced when used in conjunction with Doppler and grayscale US. In comparison to greyscale ultrasonography, strain and shear wave elastography provides quantitative and quantitative information on LNs with good diagnostic accuracy differentiating benign and malignant ones.

List of abbreviations

CT: computed tomography
MRI: Magnetic Resonance Imaging
PET: positron emission tomography
PI: pulsatile index
RI: resistivity index
ROC: receiver operator characteristics
US: Ultrasound scan

References:

[1] Dudea SM, Lenghel M, Botar-Jid C, et al. Ultrasonography of superficial lymph nodes: Benign vs. malignant. Med Ultrason. 2012 Dec;14(4):294-306.

[2] Qureshi FG, Newman KD. Lymph Node Disorders. Pediatric Surgery, 7th ed. 2012: 737–743.

[3] Ying M, Bhatia KS, Lee YP, et al. Review of ultrasonography of malignant neck nodes: greyscale, Doppler, contrast enhancement and elastography. Cancer Imaging. 2014 Jan 6;13(4):658-69.

[4] Muhi AM, Kamal AM, Dawood SN, et al. The Role of Strain Elastography in Evaluating Borderline Axillary Lymph nodes. AL-Kindy Coll Med J 2022; 18(1):68-72.

[5] Acu L, Oktar SÖ, Acu R, et al. 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 Nov;35(11):2491-2499.

[6] Romeo V, Stanzione A, D'Auria D, et al. COVID - 19 vaccine - induced lymphadenopathies: incidence, course and imaging features from an ultrasound prospective study. J Ultrasound. 2022 Dec;25(4):965-971.

[7] Chami L, Giron A, Ezziane M, et al. Quantitative and Qualitative Approach for Shear Wave Elastography in Superficial Lymph Nodes. Ultrasound Med Biol. 2021 Aug;47(8):2117-27.

[8] Moharram MA, El Maboud NMA, Ahmed HAE. Evaluation of the role of sono-elastography in diagnosis of enlarged cervical lymph nodes. Egypt J. Radiol Nucl Med 2017; 48(2): 381–91.

[9] Dawoud MM, Nagy HA, Allam AA. Role of strain elastosonography, B mode and color duplex ultrasonography in differentiation between benign and malignant axillary lymph nodes. Egypt J Radiol Nucl Med 2018; 49(2):485–91.

[10] Prativadi R, Dahiya N, Kamaya A, et al. Chapter 5 Ultrasound Characteristics of Benign vs Malignant Cervical Lymph Nodes. Semin Ultrasound CT MR. 2017 Oct;38(5):506-15.

[11] Ali SD, Zaidan TF, Al-Janab F. Role of high-resolution colored-doppler ultrasound in the differentiation between benign and malignant cervical lymphadenopathy. J Pharm Sci Res 2018; 10(12): 3223–27.

[12] Lyshchik A, Higashi T, Asato R, et al. Cervical lymph node metastases: diagnosis at sonoelastography--initial experience. Radiology. 2007 Apr;243(1):258-67.

[13] Choi YJ, Lee JH, Lim HK, et al. Quantitative shear wave elastography in the evaluation of metastatic cervical lymph nodes. Ultrasound Med Biol. 2013 Jun;39(6):935-40.