DOI: https://doi.org/10.53350/pjmhs20221611894

ORIGINAL ARTICLE

Diagnostic Accuracy of Elastography to Differentiate Between Malignant and Benign Lymph Nodes of Neck and Head Region Taking Histopathology as Gold Standard

HINA BAIG[1], MUHAMMAD SHAFIQ UL AZAM[2], AYSHA AKRAM[3], ASIM ALI[4], AISHA ASIM[5], RABIA YOUNAS[6]
[1]*Specialist Registrar, Diagnostic Radiology Mardan Medical Complex, Mardan*
[2]*Registrar Specialist Radiologist, King AbdulAziz Airbase Armed Forces Hospital- Dhahran Saudi Arabia*
[3]*Associate Professor Paediatric Radiology, Children Hospital and University of Child Health Sciences, Lahore*
[4]*Consultant Radiologist, Diagnostic Radiology, Nishter Medical University, Multan*
[5]*Associate Professor, Diagnostic Radiology, Al-Nafees Medical College & Hospital Islamabad*
[6]*Senior Registrar Diagnostic Radiology, Fazaia Ruth Pfau Medical College Karachi.*
Corresponding author: Muhammad Shafiq ul Azam, Email: drmsa78@hotmail.com

ABSTRACT

Background: The analysis of superficial lymphadenopathy in the cervical, axillary, and inguinal regions is vital in planning therapy for patients. Elastography is a technique currently being used for the evaluation of lymph nodes by means of evaluating tissue elasticity. In medical practice, shear wave-based and strain elastography techniques are being utilized. Strain elastography can be used to assess types of elasticity. Colors inside and around the nodes are estimated in the first place and then a 4-5 scale scoring system is used to score them visually. The present study aimed to assess the diagnostic accuracy of elastography in distinction between malignant and benign lymph nodes of the neck and head region, taking histopathology as the gold standard.

Methods: This study was carried out on ninety-six (96) patients of either gender with lymph nodes in the head and neck region admitted to Children Hospital and University of Child Health Sciences Lahore and Mardan Medical Complex. Patients with proven histopathology and gone through surgery in the head and neck region were excluded from the study. Each patient was subjected to the high-resolution elastography with a 7.5 MHz linear array probe. A consultant radiologist performed the elastography in the presence of the researcher and noted the lymph node types. The histopathology report was compared with the findings of elastography.

Results: High-resolution elastography was conducted on each patient enrolled in this study and their results were categorized into two distinct groups' namely positive elastography and negative elastography. In the positive group, malignant lymph node diagnoses were supported in 51 patients by elastography. Out of which 46 were true positive cases and 5 were false-positive cases with no malignant histopathology. Similarly, in elastography, negative patients, only 3 cases were false negative and 42 cases were true negative. The overall diagnostic precision, specificity, negative predictive value, positive predictive value, and sensitivity of elastography was found to be 92%, 89.10%, 92.80%, 89.40%, and 94%, respectively, in order to differentiate malignant lymph nodes from benign lymph nodes in the neck and head region, taking histopathology as the gold standard.

Conclusions: The present study demonstrated that elastography is a favorable and invasive technique for the diagnosis and differentiation of malignant lymph nodes from benign lymph nodes with high diagnostic accuracy. It may help in selecting surgical procedures for lymph nodes in the neck and head region.

Keywords: Elastography, Sensitivity, Malignant Lymph Nodes.

INTRODUCTION

The lymph node (LN) is an oval-shaped lymphatic system organ that is linked through lymphatic vessels and is extensively distributed in the stomach, armpit, and all across the body[1-3]. Immune cells like T and B, are primarily located at lymph nodes. The immune system requires lymph nodes for proper functioning as these serve as filters for cancer cells and other foreign particles. Toxicity, mainly caused by the kidneys and liver, is not treated by the lymph nodes. These have clinical importance as well. Various disorders and infections cause lymph nodes to become bloated or inflamed, ranging from trivial infections of the throat to deadly types of cancers[4]. In the cancer stage, the lymph nodes are at a very critical state, which defines the best procedure to be employed and decides the diagnosis. In case of bloating, swelling, or expansion, lymph nodes can become tender, firm, or hard[5]. LN patient's evaluation with different underlying diseases is critical for the diagnosis of effective treatment and patient's prognosis. Although the most effective process of differentiating malignant and benign LNs is considered to be fine-needle aspiration (FNA), it is considered an intrusive method that is prone to analytic unreliability and sampling errors[6]. Its false-negative rate has been reported to be between 12.5% and 25% [7, 8].

Various approaches, like magnetic resonance imaging, computed tomography, and ultrasound, are different imaging modalities to differentiate between malignant and benign lymph nodes, but their ability to differentiate benign and malignant LNs is limited[9]. Since malignant LNs are more rigid than usual underlying tissues, calculating the elasticity of tissues can be useful for the differential prognosis of multiple pathological adaptations. The two clinically used types of elasticity are shear wave (SWE) and strain elasticity. First, the colors outside and within the nodes are measured and visually graded on a 4–5 scale scoring system. In the second place, specific regions are targeted and some reference regions are also identified. Lastly, elastography dynamically measures the strain ratio. The risk of malignancy of the LNs is higher when the strain ratio is higher. A previous study reported that prevalence of lymph nodes was 40.65% with elastography sensitivity 88% and precision 93%[10]. Another study found that the sensitivity and precision of stain electrography was 100% and 80.2% respectively[11]. Several previous research evaluated the precision of this modality for the distinction of malignant and benign LNs. Its specificity and sensitivity ranged from 50-96% and 79% to 100% respectively[12, 13]. The purpose of the present research was to examine the average precision of elastographic technique for the distinction of malignant and benign lymph nodes in the neck and head region.

METHODS AND MATERIALS

This study has been carried out on ninety-six (96) patients of either gender with LNs in the neck and head region admitted to Children Hospital and University of Child Health Sciences Lahore and Mardan Medical Complex, Mardan from January 2022 to June 2022. Study protocol was approved by research and ethical committee. Patients with palpable lymph nodes and had disease since 3 months were enrolled. Patients with prior history of proven histopathology and surgery were excluded. Each patient was subjected to elastography with a 7.5 MHz linear array probe of high resolution. A consultant radiologist performed the elastography in

the presence of the researcher and noted the lymph node type. The histopathology report was compared with the findings of elastography. Sample size was calculated based on prevalence of lymph nodes 40.5%[13] taking 95% CI, absolute precision 10%, and specificity 6.5%. Consequent to informed consent, every patient was subjected to strain high-resolution ultrasound elastography with a 7.5 MHz linear array probe. A specialized radiologist, with experience of at least years, performed this strain ultrasound elastography in every patient under the examination of the researcher and benign or malignant lymph nodes of each operation were noted.

SPSS version 26 was used for data analysis. Qualitative variables such as gender, lymph nodes were expressed as frequency and percentages. Quantitative variables such as age, disease duration, and lymph node size were described as mean and standard deviation. The diagnostic accuracy, NPV, PPV, specificity, and sensitivity of elastography were calculated using a 2×2 contingency table for the distinction of malignant and benign lymph nodes. Post-stratification was done to see the effect modifiers such as gender, age, size of nodes, and disease duration were controlled. Diagnostic accuracy was also calculated after the stratification.

RESULTS

The overall mean age range was 41.06±6.67 years (28-68 years). About 86 (90.1%) were in the range of 28-50 years. Of these 96 patients, 46 (44.16%) were female and 50 (48%) were male with a 1:1 male-to-female ratio (Figure 1). The mean disease period was 9.05±3.41 months. The mean nodule size was 4.76±1.51 cm. All patients underwent elastography supported the malignant lymph nodes diagnosis in 51 patients. In 46 (true positive) cases where 5 (false positive) had no malignant lymph nodes reported on histopathology. Similarly, in elastography negative patients, 3 and 42 were found to be the false and true negative cases, respectively, as Table 1 describes. The overall diagnostic precision, specificity, negative predictive value, positive predictive value, and sensitivity of elastography was found to be 92%, 89.10%, 92.80%, 89.40%, and 94%, respectively, in order to differentiate malignant lymph nodes from benign lymph nodes in the neck and head region, taking histopathology as a gold standard.

Table 1: Patient's distribution based on histopathology report

	Positive Histopathology	Negative Histopathology	P-value
Positive Elastography	46 (TP)	5 (FP)	0.001
Negative Elastography	3 (FN)	42 (TN)	0.001

*TP True positive, FP False positive, FN False negative, TN True negative

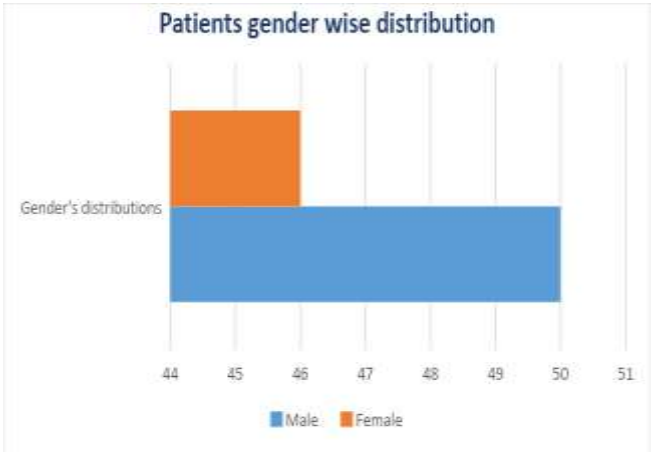

Figure 1: Patient's gender-wise distributions

Table 2: Diagnostic accuracy stratification w.r.t disease duration

	Positive Histopathology	Negative Histopathology	P-value
Disease duration≤ 12 months N= 74			
Positive Elastography	34 (TP)	3 (FP)	0.001
Negative Elastography	2 (FN)	35 (TN)	0.001
Disease duration≥ 12 months N=22			
Positive Elastography	9 (TP)	2 (FP)	0.001
Negative Elastography	2 (FN)	9 (TN)	0.001

Table 3: Stratification of diagnostic accuracy w.r.t lymph nodes size

	Positive Histopathology	Negative Histopathology	P-value
Size of nodule ≤5 cm N=66			
Positive Elastography	27 (TP)	3 (FP)	0.001
Negative Elastography	3 (FN)	33 (TN)	0.001
Size of nodule >5 cm N=30			
Positive Elastography	18 (TP)	1 (FP)	0.001
Negative Elastography	00 (FN)	11 (TN)	0.001

DISCUSSIONS

Populations are widely encountered by benign lymph nodes usually. Depending upon the population and used methods, the widespread presence rate of lymph nodes may differ. Reports are present that found the gradual increase in their prevalence[14]. Previous neck and head radiation, iodine deficiency, advanced age, and female gender can be some risk factors for lymph nodes in the neck and head region. According to reports, the presence of lymph nodes was detected to be 8-65%, 19-35%, and 2-6% by autopsy data, ultrasonography, and palpation, respectively[15]. Differential diagnosis can help in providing information on different stages of malignant LNs and may help to differentiate benign diseases from malignancies. The real significant prognostic factor in malignancies is to know the status or stage of the LNs because it helps manage metastatic diseases[16]. For this reason, decision-making on a clinical basis requires a correct and early distinction between malignant and benign lymph nodes.

The present study detected high sensitivity and specificity for both elastography scoring systems and SR. It can show that the odds of obtaining positive results in diseased rather than non-diseased individuals by means of elastography is high. Another study[17] reported 95% and 84% specificity and sensitivity, respectively. Even using the same threshold could lead to variations in the subjective interpretation of the pattern of the colors. The high precision of the elastography in the distinction between malignant and benign lymph nodes is still suggested by the pooled results as suggested by previous study[18].

The overall diagnostic precision, specificity, negative predictive value, positive predictive value, and sensitivity of elastography was found to be 92%, 89.10%, 92.80%, 89.40%, and 94%, respectively, in order to differentiate malignant lymph nodes from benign lymph nodes in the neck and head region, taking histopathology as the gold standard. Stratifications are done based on the time duration and size of lymph nodes. Encouraging results were found in the meta-analysis of 8 studies of 2010 which included 639 cases of thyroid nodes. The overall average specificity and sensitivity of 90% and 92% with confidence intervals of 85-95% and 88-96%, respectively, was recorded with remarkable heterogeneity in specificity was shown in different researches[19, 20].

The inferior performance was shown in the results of elastography; negative predictive value (NPV) and sensitivity of 79.1% and 65.4% as compared to the US features on grayscale i.e, NPV and sensitivity of 94.7% and 91.7%, respectively, for this reason, the authors reported the unreliable use of SE in the recommendation of FNAB[21].

According to Bae et al. study conducted to evaluate the different effects of a physician's experiments when he tries to differentiate malignant and benign lymph nodes with the help of elastography and told of inferior specificity of an inexperienced physician as compared to an experienced one[22] Zhao et al. reported in another study for inter-observer agreement, the lowest Cohen's kappa coefficient for the echogenicity score (0.83) and the highest Cohen's kappa coefficient for the strain ratio measurements (0.95)[23].Three independent operators were present in their studies.

Mahmoud et al. reported the principle on which the real-time USE is grounded that is under compression the harder or rigid parts of the tissues take more time in deforming as compared to the softer ones, which allows determining the maximum diameter of tissues with the help of conventional ultrasound showing indeterminate results. A 4-5 elasticity score of malignancy was highly predictive with an accuracy, specificity, and sensitivity of 90.20%, 89.47%, and 90.63%, respectively [24].

Garg et al. reported 83.7% accuracy of USE in detecting thyroid cancer with NPV, PPV, specificity, and sensitivity of 98.2%, 55.2%, 81%, and 94.1%, respectively[25]. Another study conducted on the evaluation of 58 and 89 malignant and benign cases who went through thyroidectomy and came with findings of 89% and 93% of specificity and sensitivity, respectively, considering 2 to be the cutoff value for elastography score. The results and findings of this study showed that when compared to color Doppler US and US, more accurate findings were provided by elastography. Kiliçarslan et al reported that when combined with the high-resolution US, elastography showed better diagnostic performance and they found the accuracy, NPV, PPV, specificity, and sensitivity of elastography as 86.7%, 90.5%, 71.4%, 85.5%, 75.4%, respectively[26].

Wang et al. conducted their study on 132 cases with 40 malignant and 92 benign nodes, using elastography, he reported that 34 of 40 malignant nodes got score of 3 or 4 and 77 of 92 benign nodes got 1 or 2 score (92.7% NPV, 69.3% PPV, 83.7% specificity, 85% sensitivity)[27]. In another study, Ozkan et al. reported their evaluation of 69 benign and 17 malignant nodes and found the accuracy, NPV, PPV, specificity, and sensitivity of elastography as 83.7%, 98.2%, 55.2%, 81%, and 94.1%, respectively[28]. Leyla et al. performed an evaluation of 23 nodes and reported in results that 88% of malignant nodes got score 3-4 and 78% of benign nodes got 1-2. The study reported the accuracy, NPV, PPV, specificity, and sensitivity of elastography as 82%, 91%, 72%, 78%, and 88%, respectively[29]. Furthermore, Onol et al carried out a prospective evaluation of 97 patients and reported the specificity and sensitivity of elastography as 91.7% and 97.3%, respectively. The study reported that nodes with ≥2 strain ratio were likely to be suspected as malignant[30].

CONCLUSIONS

The present study demonstrated that elastography is a favorable and non-invasive technique for the diagnosis and differentiation of malignant lymph nodes from benign lymph nodes with high diagnostic accuracy. It may help in selecting surgical procedures for lymph nodes in the neck and head region.

REFERENCES

1. Vineela E, Sakalecha AK, Narayanrao Suresh T. Role of Sonoelastography in Differentiating Benign From Malignant Cervical Lymph Nodes and Correlating With Pathology. Cureus. 2022 Mar 9;14(3):e22984.
2. Tan PW, Goh T, Nonomura H and Tan BK. Hilar vessels of the submandibular and upper jugular neck lymph nodes: anatomical study for vascularized lymph node transfer to extremity lymphedema. Ann Plast Surg 2016; 76: 11723.
3. Ng, W.L.; Omar, N.; Ab Mumin, N.; Ramli Hamid, M.T.; Vijayananthan, A.; Rahmat, K. Diagnostic Accuracy of Shear Wave Elastography as an Adjunct Tool in Detecting Axillary Lymph Nodes Metastasis. Acad. Radiol. 2022, 29, S69–S78.
4. Wei, C.; Li, C.; Szewczyk-Bieda, M.; Upreti, D.; Lang, S.; Huang, Z.; Nabi, G. Performance Characteristics of Transrectal Shear Wave Elastography Imaging in the Evaluation of Clinically Localized Prostate Cancer: A Prospective Study. J. Urol. 2018, 200, 549–558.
5. Li, D.-D.; Xu, H.-X.; Guo, L.-H.; Bo, X.-W.; Li, X.-L.; Wu, R.; Xu, J.-M.; Zhang, Y.-F.; Zhang, K. Combination of two-dimensional shear wave elastography with ultrasound breast imaging reporting and data system in the diagnosis of breast lesions: A new method to increase the diagnostic performance. Eur. Radiol. 2016, 26, 3290–3300.
6. Sigrist, R.M.S.; Liau, J.; Kaffas, A.E.; Chammas, M.C.; Willmann, J.K. Ultrasound Elastography: Review of Techniques and Clinical Applications. Theranostics 2017, 7, 1303–1329.
7. Youk, J.H.; Son, E.J.; Kim, J.-A.; Gweon, H.M. Pre-Operative Evaluation of Axillary Lymph Node Status in Patients with Suspected Breast Cancer Using Shear Wave Elastography. Ultrasound Med. Biol. 2017, 43, 1581–1586..
8. Dietrich, C.F.; Bamber, J.; Berzigotti, A.; Bota, S.; Cantisani, V.; Castera, L.; Cosgrove, D.; Ferraioli, G.; Friedrich-Rust, M.; Gilja, O.H.; et al. EFSUMB Guidelines and Recommendations on the Clinical Use of Liver Ultrasound Elastography, Update 2017 (Long Version). Ultraschall Med. 2017, 38, e16–e47. [CrossRef]
9. Davis, L.C.; Baumer, T.G.; Bey, M.J.; Holsbeeck, M.V. Clinical utilization of shear wave elastography in the musculoskeletal system. Ultrasonography 2019, 38, 2–12.
10. Seo, M.; Sohn, Y.-M. Differentiation of benign and metastatic axillary lymph nodes in breast cancer: Additive value of shear wave elastography to B-mode ultrasound. Clin. Imaging 2018, 50, 258–263.
11. Kim, H.J.; Choi, I.H.; Jin, S.-Y.; Park, H.K.; Byun, D.W.; Suh, K.; Yoo, M.H. Efficacy of Shear-Wave Elastography for Detecting Postoperative Cervical Lymph Node Metastasis in Papillary Thyroid Carcinoma. Int. J. Endocrinol. 2018, 2018, 9382649.
12. Luo, S.; Yao, G.; Hong, Z.; Zhang, S.; Wang, W.; Zhang, J.; Zhang, Y.; Wu, J.; Zhang, L.; Cheng, H.; et al. Qualitative Classification of Shear Wave Elastography for Differential Diagnosis Between Benign and Metastatic Axillary Lymph Nodes in Breast Cancer. Front. Oncol. 2019, 9, 533.
13. Yang, J.-R.; Song, Y.; Jia, Y.-L.; Ruan, L.-T. Application of multimodal ultrasonography for differentiating benign and malignant cervical lymphadenopathy. Jpn. J. Radiol. 2021, 39, 938–945.
14. Chen, B.-B.; Li, J.; Guan, Y.; Xiao, W.-W.; Zhao, C.; Lu, T.-X.; Han, F. The value of shear wave elastography in predicting for undiagnosed small cervical lymph node metastasis in nasopharyngeal carcinoma: A preliminary study. Eur. J. Radiol. 2018, 103, 19–24.
15. Page, M.J.; McKenzie, J.E.; Bossuyt, P.M.; Boutron, I.; Hoffmann, T.C.; Mulrow, C.D.; Shamseer, L.; Tetzlaff, J.M.; Akl, E.A.;
16. Brennan, S.E.; et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. BMJ 2021, 372, n71.
17. Chami, L.; Giron, A.; Ezziane, M.; Leblond, V.; Charlotte, F.; Pellot-Barakat, C.; Lucidarme, O. Quantitative and Qualitative Approach for Shear Wave Elastography in Superficial Lymph Nodes. Ultrasound Med. Biol. 2021, 47, 2117–2127.
18. Lo, W.C.; Hsu, W.L.; Wang, C.T.; Cheng, P.W.; Liao, L.J. Incorporation of shear wave elastography into a prediction model in the assessment of cervical lymph nodes. PLoS ONE 2019, 14, e0221062.
19. Suh, C.H.; Choi, Y.J.; Baek, J.H.; Lee, J.H. The diagnostic performance of shear wave elastography for malignant cervical lymph nodes: A systematic review and meta-analysis. Eur. Radiol. 2017, 27, 222–230.
20. Wang, R.Y.; Zhang, Y.W.; Gao, Z.M.; Wang, X.M. Role of sonoelastography in assessment of axillary lymph nodes in breast cancer: A systematic review and meta-analysis. Clin. Radiol. 2020, 75, 320.e1–320.e7.
21. Huang, X.-W.; Huang, Q.-X.; Huang, H.; Cheng, M.-Q.; Tong, W.-J.; Xian, M.-F.; Liang, J.-Y.; Wang, W. 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.
22. Bae, S.J.; Park, J.T.; Park, A.Y.; Youk, J.H.; Lim, J.W.; Lee, H.W.; Lee, H.M.; Ahn, S.G.; Son, E.J.; Jeong, J. Ex Vivo Shear-Wave Elastography of Axillary Lymph Nodes to Predict Nodal Metastasis in Patients with Primary Breast Cancer. J. Breast Cancer 2018, 21, 190–196.

23. Zhao, Q.; Sun, J.-W.; Zhou, H.; Du, L.-Y.; Wang, X.-L.; Tao, L.; Jiang, Z.-P.; Zhou, X.-L. Pre-operative Conventional Ultrasound and Sonoelastography Evaluation for Predicting Axillary Lymph Node Metastasis in Patients with Malignant Breast Lesions. Ultrasound Med. Biol. 2018, 44, 2587–2595.
24. Mahmoud, O.M.; Khedrawy, M.E.-M.; Megally, H.I.; Mohamed, M.F.; Allam, M.T. Fine-needle aspiration cytology versus core needle lymph node biopsy in axillary staging of breast cancer. Egypt. J. Radiol. Nucl. Med. 2022, 53, 219.
25. Garg, S.; Rohilla, M.; Srinivasan, R.; Bal, A.; Das, A.; Dey, P.; Gupta, N.; Gupta, P.; Rajwanshi, A. Fine-Needle Aspiration Diagnosis of Lymphoma Based on Cytomorphology Alone: How Accurate is it?—A Cyto-Histopathology Correlative Study. J. Cytol. 2021, 38, 164–170.
26. Kiliçarslan, A.; Do ˘gan, M.; Süngü, N.; Karakök, E.; Karabekmez, L.; Akyol, M.; Do ˘gan, H.T. Can Cutting-Needle Biopsy Be an Alternative to Excisional Biopsy in Lymph Node Pathologies? Türk Patoloji Dergisi 2017, 1, 235–239.
27. Wang, B.; Guo, Q.; Wang, J.-Y.; Yu, Y.; Yi, A.-J.; Cui, X.-W.; Dietrich, C.F. Ultrasound Elastography for the Evaluation of Lymph Nodes. Front. Oncol. 2021, 11, 3133.
28. Ozkan MB, Bilgici MC, Eren E, Caltepe G, Yilmaz G, Kara C, et al.. Role of Point Shear Wave Elastography in the Determination of the Severity of Fibrosis in Pediatric Liver Diseases With Pathologic Correlations. J Ultrasound Med: Off J Am Inst Ultrasound Med (2017) 36(11):2337–44. 10.1002/jum.14277.
29. Leyla A, Suna Özhan O, Rusen A. Value of Ultrasound Elastography in the Differential Diagnosis of Cervical Lymph Nodes. J Ultrasound Med (2016) 35:2491–9. 10.7863/ultra.15.09019.
30. Onol S, Ozkaya O. Diagnostic Value of Real-Time Elastography in Diagnosing Lymph Node Metastasis of Skin Cancer. Cureus (2020) Oct 17 12(10):e10997. 10.7759/cureus.10997.