See discussions, stats, and author profiles for this publication at: https://www.researchgate.net/publication/351408248

Ultrasound, endoscopic ultrasound elastography, and the strain ratio in differentiating benign from malignant lymph nodes

Article · May 2021



Arab Journal of Gastroenterology 19 (2018) 7-15



Contents lists available at ScienceDirect

Arab Journal of Gastroenterology

journal homepage: www.elsevier.com/locate/ajg



Ultrasound, endoscopic ultrasound elastography, and the strain ratio in differentiating benign from malignant lymph nodes



Arab Journal of GASTROENTEROLOGY

Hussein Okasha^a, Shaimaa Elkholy^{a,*}, Mohamed Sayed^a, Mohamed El-Sherbiny^a, Ramy El-Hussieny^b, Emad El-Gemeie^c, Waleed Al-Nabawy^d, Moustafa Saeed Mohamed^a, Yahia Elsherif^e

^a Internal Medicine Department, Faculty of Medicine, Cairo University, Egypt

^b Internal Medicine at National Hepatology and Tropical Medicine Research Institute (NHTMRI), Egypt

^c Head of the Pathology Department, National Cancer Institute, Cairo University, Egypt

^d Internal Medicine Department, Faculty of Medicine, Beni-suef University, Beni-Suef, Egypt

^e Liver Unit, El Manial Specialized Hospital, Tropical Medicine Department, Faculty of Medicine, Cairo University, Cairo, Egypt

ARTICLE INFO

Article history: Received 29 January 2017 Accepted 30 January 2018

Keywords: EUS Elastography Strain Ratio US Lymphadenopathy

ABSTRACT

Background and study aims: Endoscopic ultrasound elastography (EUS-elastography), or sonoelastography, has emerged in the past 2 decades as a qualitative method of estimating tissue stiffness. Strain elastography allows for semi-quantitative measurements of the average elasticity of a lesion, and previous studies have proposed the strain ratio (SR) for overcoming the limitations of the elasticity score. The main objective of this study is to assess the specificity, sensitivity and predictive values of the SR measured by EUS-elastography in differentiating benign from malignant lymph nodes (LNs). This study also aims to find significant ultrasonographic features other than the SR which could help in predicting LN malignancy.

Patients and methods: This prospective study included 126 Egyptian patients with lymphadenopathy. US and EUS-elastography and the SR were assessed, in addition to detailed sonographic features, including size, longest diameter, shortest diameter, ratio of shortest/longest diameter, echotexture (echogenic or echo-poor) and hilum (lost or preserved).

Results: The SR cut-off value of 4.61 showed a sensitivity and specificity of 89.8% and 83.3%, respectively. This parameter had high positive and negative predictive values of 82.5% and 90.2%, respectively, for predicting malignant LNs. Univariate regression analysis showed that echogenicity, hilum preservation, elastography, the shortest dimension, the ratio of the shortest/longest dimension, ultrasound diagnosis and SR could be potential predictors of the final lymph node diagnosis. Sono-diagnosis depending on echogenicity, the shortest/longest diameter ratio and a preserved hilum in combination was the only predictive parameter in multivariate regression analysis.

Conclusion: EUS-elastography and the SR could be excellent prognostic indices in differentiating benign from malignant lymph nodes if combined with other US features.

© 2018 Pan-Arab Association of Gastroenterology. Published by Elsevier B.V. All rights reserved.

Introduction

Ultrasound (US) is a useful imaging modality in the diagnosis of lymphadenopathy, particularly for diseases that affect superficial lymph nodes (LNs), such as cervical lymphadenopathy [1,2]. The sensitivity and specificity of US are significantly higher when combined with fine needle aspiration and cytology (FNAC) [3]. Endoscopic ultrasound (EUS) has been introduced as a minimally invasive modality for better visualization of inaccessible LNs, such as intra-abdominal and mediastinal LNs [4,5].

EUS-elastography, which is also called sono-elastography, has emerged in the past 2 decades as a non-invasive means of assessing the mechanical properties of tissues [6]. This technique is based on the degree of tissue distortion in response to an external force, so it is used to estimate tissue stiffness [7]. The strain ratio (SR) is considered to be a semiquantitative measure of elastography patterns. This ratio is calculated by comparing the elastography patterns of the targeted LNs to those of a nearby reference tissue [7,8]. Elastography has been used to examine several organs, such as the breast, thyroid, prostate, cervix and liver [9]. Although FNA

https://doi.org/10.1016/j.ajg.2018.01.001

1687-1979/© 2018 Pan-Arab Association of Gastroenterology. Published by Elsevier B.V. All rights reserved.

^{*} Corresponding author at: 531, 3rd division, 5th district, 6 of October city, Cairo, Egypt.

E-mail addresses: shaimaa.elkholy@cu.edu.eg, shuma50082@kasralainy.edu.eg (S. Elkholy).

remains the gold standard for the detection of malignant cells in a LN, with a specificity and a positive predictive value (PPV) approaching 100%, FNA requires a high level of experience and may be associated with many hazards [10]. Many recent studies of the use of EUS-elastography and the SR in assessing LNs showed that this technique is useful for selecting LNs. This approach is diagnostically significant because it targets the most suspicious area of a LN for tissue diagnosis. In the presence of multiple LNs, EUS-elastography can help reduce the number of unnecessary biopsies and hence increase the sensitivity of EUS-FNA [11–13].

Micrometastases may escape detection by EUS-FNA. However, elastography in combination with the SR can assess malignancy-related changes in tissue stiffness, making this technique useful for delineating early circumscribed malignant changes so that surgeons can target the most suspicious area of a LN. Moreover, in cases of negative EUS-FNA or in circumstances in which this procedure is not possible (technical difficulties or interposed vascular structures), EUS-elastography and the SR may be a useful alternative for differential diagnosis [11–13].

The main objective of this study is to assess the specificity, sensitivity and predictive value of the SR measured by EUS or US in the diagnosis of benign and malignant LNs. This study also aims to identify significant ultrasonographic features other than the SR that could help in predicting LN malignancy.

Patients and methods

Study design and population

This prospective study analysed data from 126 Egyptian patients who were referred to the GIT Unit in the Internal Medicine Department of the Faculty of Medicine of Cairo University. The patients included in the study included 71 (56.3%) males and 55 (43.7%) females. The ages of the patients ranged from 6 to 75 years, with a mean (SD) of 50.6 (13) years. The included patients were referred for a LN status assessment between January 2013 and February 2016. Fifty-six (44.4%) patients were referred for TNM staging of a primary tumour, 44 (34.9%) patients had isolated intra-abdominal lymphadenopathy, and 21 (16.7%) and 5 (4%) patients had generalized and isolated mediastinal lymphadenopathy, respectively.

Inclusion criteria

- 1. All patients were referred for US and US-elastography of the LNs for conditions discovered clinically or with other imaging modalities.
- 2. All patients were referred for EUS assessment of the mediastinal or abdominal LNs, either isolated or with associated primary tumours, for TNM staging.

Exclusion criteria

- 1. Patients were excluded if the final diagnosis was not settled, such as in patients with no definite cytopathological diagnosis or patients who were lost to follow-up.
- 2. Patients were excluded if they were unfit for propofol administration or had severe coagulopathy.

Methods in detail

In all patients, US or EUS was performed at the request of the consulting physician, and informed consent was obtained after explaining the procedure to the patient. For confidentiality, the patient names were omitted and replaced with numerical codes.

On the day of the procedure, the patients were subjected to the following:

- A thorough history and clinical examination were completed.
- All patient data were recorded.
- US was performed using a Hitachi EUB-7000 US unit (Hitachi Medical Systems, Tokyo, Japan).
- For patients who underwent EUS, deep sedation with intravenous propofol was administered. An EUS linear array machine (Pentax EG-3830UT Echo-endoscope, HOYA Corporation, PEN-TAX Lifecare Division, Showanomori Technology Center, Tokyo, Japan) connected to a Hitachi EUB-7000 was used.
- For other patients, the target LNs were initially identified, and their detailed sonographic features were assessed, including size, longest diameter, shortest diameter, ratio of shortest/longest diameter, echotexture (echogenic or echo-poor) and hilum (lost or preserved).
- Elastography was then displayed with the B-mode image in a colour scale that ranged from red for components with the greatest elastic strain (i.e., the softest components) to blue for components with no strain (i.e., the hardest components). The elastography scoring patterns were as follows [14]:

Pattern 1: \geq 80% of the cross-sectional area was red or green (i.e., soft).

Pattern 2: ${\geq}50\%$ and <80% of the cross-sectional area was red or green.

- Pattern 3: \geq 50% and <80% of the cross-sectional area was blue. Pattern 4: \geq 80% of the cross-sectional area was blue (i.e., hard).
- The SR was calculated as R₂/R₁; where R₂ represented the elastography of a selected soft (red) reference area outside the target LNs, preferably the gut wall, <u>perinodal tissue or</u> <u>subcutaneous tissue</u>, and R1 represented the elastography of the targeted LNs, as shown in Fig. 1.

Study definitions

- An EUS diagnosis suggestive of malignant or benign lymphadenopathy depended on the presence of ≥2 of the following features:
- Echogenicity (echo-poor for malignancy and echogenic for benign LNs) [15].
- Transverse/longitudinal diameter ratio (>0.5 for malignant and <0.5 for benign LNs) [16].
- Loss of hyperechoic hilum for malignancy and preserved hilum for benign LNs [17]. Fig. 2 shows benign-looking porta hepatis LNs with a small size, an echogenic texture, a flat shape and a hyperechoic hilum.
- Lesions that presented with elastography pattern 1 or 2 were classified as probably benign, while patterns 3 and 4 indicated probable malignancy [9,14]. Fig. 3 shows a malignant-looking cervical LN: rounded in shape and echo-poor, with a lost hilum and an elastography score of 4. Fig. 4 shows EUS-elastography of a peripancreatic malignant LN with a high SR.
- The final gold standard diagnosis was made via FNA, cytopathological examination and immunohistochemistry, if needed, or excision surgical biopsies during resection or surgical exploration. Benign LNs were followed up via sonography or CT scanning for at least 6 months to ensure that they were not increasing in size (i.e., ensuring their benign nature).

Compliance with the study

All patients were compliant with the study.



Fig. 1. EUS grey-scale assessment features of benign-looking porta hepatis LNs, including size, the longest diameter, the shortest diameter, the ratio of the shortest/longest diameter, the echotexture and the hilum.



Fig. 2. EUS-elastography of a benign-looking cervical LN: >80% of the cross-sectional area of the LN was red or green (i.e., soft), with an elasticity score of 1.



Fig. 3. EUS-elastography of a malignant cervical LN, with >80% of the cross-sectional area blue (i.e., hard) and an elasticity score of 4.



Fig. 4. EUS-elastography of a peripancreatic malignant LN with a calculated SR, which was high (6.84).

Patient consent

The protocol was approved by the ethics committee, and informed consent was obtained.

Statistical analysis

All patient data were tabulated using Excel 2010. Data were processed using SPSS version 20 for Windows 2010. All qualitative data were analysed using the chi-square test or the Fischer's exact test, as appropriate. The chi-square test was used to calculate Pearson's chi-square and its P value when both table variables were quantitative. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated. Receiver operating characteristic (ROC) curves were applied to calculate the area under the curve (AUC) and the sensitivity and specificity of the tests used. Cut-off values were calculated. Differences for which P < 0.05 were not considered to be significant, differences for which P < 0.05 were considered to be statistically significant and differences for which P < 0.001 were considered to be highly significant.

Results

Groups of lymph nodes involved in the study: Table 1. shows the various groups of LNs involved. The most frequently encountered LNs were the peripancreatic LNs (42, 33.3%), followed by the porta hepatis LNs (28, 22.2%), the upper deep cervical LNs (19, 15.1%), the celiac LNs (14, 11.1%), the mediastinal LNs (4, 3.26.3%) and others.

Final diagnosis of the lymph nodes: According to the final diagnosis, 59 (46.8%) patients were proved to have malignant LNs, and 67 (53.2%) patients had lymphadenopathy of a benign nature (Table 2).

Ultrasonographic features of the lymph nodes: Table 3 shows the ultrasonographic features of the LNs, including echogenicity, hilum preservation and elastography. The table also shows the dimensions of the LNs; the shortest dimension ranged from 3 to 55 mm, with a mode of 6 and a median (IQR) of 12 (10.25), while the longest dimension ranged from 6 to 60 mm, with a mode of 16 and a median (IQR) of 19 (13). The ratio of the shortest/longest dimension ranged from 0.22 to 1, with a mode of 0.67 and a median (IQR) of 0.63 (0.36). R1 ranged from 0.01 to 1.85, with a mode of 0.01 and a median (IQR) of 0.095 (0.36). R2 ranged from 0.01 to 1.72, with a mode of 0.4 and a median (IQR) of 0.56 (0.43). The

Table 1

Groups of the lymph nodes involved.

Groups of LNs	Number	Percent%
Peripancreatic	42	33.3
Porta hepatis	28	22.2
Upper Deep Cervical	19	15.1
Celiac	14	11.1
Perigastric	7	5.6
Mediastinal	6	4.7
Submandibular	2	1.6
Para rectal	2	1.6
Pretracheal	1	0.8
Submental	1	0.8
Para-aortic	1	0.8
Portocaval	1	0.8
Postauricular	1	0.8
Femoral	1	0.8
Total	126	100

Lymph nodes.

Table 2

Final diagnosis of the lymph nodes.

	Number	Percent%
Malignant	59	46.8
Pancreatic adenocarcinoma	23	18.3
Gastric adenocarcinoma	10	7.9
Cholangiocarcinoma	5	3.9
Papillary adenocarcinoma	4	3.2
Lymphoma	4	3.2
HCC	5	3.9
Thyroid carcinoma	3	2.4
Rectal adenocarcinoma	2	1.6
GB adenocarcinoma	1	0.8
GIST	1	0.8
IPMN	1	0.8
Breast	1	0.8
Oesophageal carcinoma	1	0.8
Ovarian and peritoneal masses	1	0.8
Benign	67	53.2
Inflammatory	58	46
Sarcoidosis	4	3.2
TB	1	0.8
Total	126	100

HCC: hepatocellular carcinoma, GB: gall bladder, GIST: gastrointestinal stromal tumours, IPMN: Intraductal papillary mucinous neoplasm, TB: tuberculosis.

Table 3			
Characteristics	of the lymph	nodes in	the ultrasound.

Characteristics	
Echogenicity [number (%)] Echogenic Echo-poor	65 (52%) 61 (48%)
Hilum preservation [number (%)] Preserved Lost	42 (33.3%) 84 (66.6%)
Elastography [number (%)] 1 2 3 4 Shortest dimension [median(IQR)] Longest dimension [median(IQR)] Shortest/longest [median(IQR)] R ₁ [median(IQR)] R ₂ [median(IQR)] Strain Ratio [median(IQR)]	17 (13.5%) 46 (36.5%) 34 (27%) 29 (23%) 12 (10.25) 19 (13) 0.63 (0.36) 0.095 (0.36) 0.56 (0.43) 15 2 (16)

IQR = inter quartile range.

SR ranged from 0.37 to 114, with a mode of 0.9 and a median (IQR) of 5.2 (16).

Comparison of the ultrasonographic features of benign and malignant lymph nodes using the chi-square test: Table 4 shows that significant differences in echogenicity, hilum preservation and elastography were observed between benign and malignant LNs (all p < 0.0001, chi-square test). The US diagnosis was significantly close to the final diagnosis, as 62 (49.2%) LNs were diagnosed as benign via US, while this number was 67 (53.2%) in the final diagnosis. In addition, US diagnosed 64 malignant LNs (50.8%) while the final diagnosis was 59 malignant LNs (46.8%) (p-value < 0.000 1) (Table 4).

Strain ratio (SR) in benign and malignant lymph nodes: Table 5 shows that significant differences in the shortest dimension, the ratio of the shortest/longest dimension, R1 and the SR were observed between benign and malignant LNs. The table also shows that the SR was significantly higher in the malignant LNs (p < 0.0001, Mann-Whitney test).

Predictive values, sensitivity and specificity of the strain ratio: Table 6 shows the positive and negative predictive values

Table 4

Comparison of the	U/S features	of the lymph	nodes between	both groups	using chi- sau	are

U/S features		Final Diagnosis		Pearson chi square value	Sig (2-sided) P-value	
		Benign Count (%)	Malignant Count (%)			
Echogenicity	Echogenic Echo-poor	57 (85.1%) 10 (14.9%)	9 (15.3%) 50 (84.7%)	61.3	<0.0001	
Hilum	Preserved Lost	40 (59.7%) 27 (40.2%)	2 (3.4%) 57 (96.6%)	42.8	<0.0001	
Elastography	1 2 3 4	17 (25.4%) 39 (58.2%) 9 (13.4%) 2 (3.0%)	0 7 (11.9%) 25 (42.4%) 27(45.8%)	68.1	<0.0001	
U/S diagnosis Total	Benign = 62 (49.2%) Malignant = 64 (50.8%)	59 8 67 (53.2%)	3 56 59 (46.8%)	86.4	<0.0001	

Table 5

Comparisong of lymph node dimensions, R1, R2 and SR between 2 groups (Benign & and malignant) using Mann-Whitney test.

Lymph node characteristics	Final diagnosis	Mean rank	Mann-Whitney U	Asym. Sig (2-tailed) P-value
Shortest dimension	Benign Malignant	48.78 80.21	990	<0.0001
Longest dimension	Benign Malignant	59.04 68.57	1677	0.143
Short/Long	Benign Malignant	46.82 82.44	859	<0.0001
R ₁	Benign Malignant	88.10 35.56	328	<0.0001
R ₂	Benign Malignant	68.83 57.45	1619	0.081
SR	Benign Malignant	38.81 91.54	322	<0.0001

R₁: elastography of the targeted lymph nodes, R₂: elastography of a selected soft (red) reference area outside the target lymph nodes, preferably the gut wall, perinodal tissue or subcutaneous tissue; SR (strain ratio): R₂/R₁.

Table 6

Predictive values of strain ratio.		
Predictive values	Percent	95% CI
Positive predictive value for malignant lymph nodes Negative predictive value for malignant lymph nodes Positive predictive value for benign lymph nodes	82.5% 90.2% 85.8%	71–90.8 80–96.34 75.5– 93.06
Negative predictive value for benign lymph nodes	87.8%	76.3-95.3

of the SR for malignant and benign LNs. The ROC curve analysis of the SR shows a cut-off value of 4.61, with a sensitivity and specificity of 89.8% and 83.3%, respectively (Fig. 5).

Regression analysis for the final diagnosis: Table 7 shows the univariate regression analysis, in which echogenicity, hilum preservation, elastography, the shortest dimension, the ratio of the shortest/longest dimension, US diagnosis, R1 and the SR were potential predictors of the final LN diagnosis. ROC curve analyses were performed for elastography and the ratio of the shortest/longest dimension, as shown in Figs. 6 and 7, respectively. Table 8 shows the multivariate regression analysis, in which the US diagnosis was the only predictor of the final diagnosis.

Discussion

Differentiating benign from malignant LNs according to US or EUS characteristics is difficult and usually necessitates EUSguided FNA for a more accurate diagnosis [18] Elastography is an evolving non-invasive imaging modality that is confined to mea-



suring the stiffness of tissues. Elastography depends on the fact

that when organs are mechanically stressed by either external or

Fig. 5. Receiver operating characteristic (ROC) curve showing the sensitivity and specificity of the strain ratio at a cut-off value of 4.61.

Table 7				
Univariate regression	analysis	to the	final	diagnosis.

Variables	Coefficient	Odd's Ratio (OR)	95% CI	P-value
Hilum preservation	3.7	40.5	9–182	<0.0001
Echogenicity	3.3	29.4	11-78.3	< 0.0001
Elastography	2.43	11.4	5.2-25.2	< 0.0001
Shortest	0.13	1.14	1.07-1.2	< 0.0001
Longest	0.03	1.03	0.99-1.06	0.066
Short/long	5.7	313	31-3079	< 0.0001
U/S diagnosis	4.9	135	34-536	< 0.0001
R ₁	-13	0	0.00-0.002	< 0.0001
R ₂	-0.55	0.57	0.2-1.6	0.284
Strain Ratio	0.23	1.26	1.15-1.38	<0.0001

R₁: elastography of the targeted lymph nodes, R₂: elastography of a selected soft (red) reference area outside the target lymph nodes, preferably the gut wall, perinodal tissue or subcutaneous tissue; SR (strain ratio): R₂/R₁.

100

80

60

40

20

0

0

Sensitivity



Fig. 6. Receiver operating characteristic (ROC) curve showing the sensitivity and specificity of elastography using a 4-point scoring system with a cut-off point of 2.

Fig. 7. Receiver operating characteristic (ROC) curve showing the sensitivity and specificity of the ratio of the shortest/longest dimension at a cut-off level of 0.5.

40

100-Specificity

60

80

100

20

S/L

Sensitivity: 93.2

Specificity: 60.6

Criterion: >0.5

depends on the tissue's elastic properties and can be qualitatively or quantitatively measured using an US machine [19].

Strain elastography allows semiquantitative measurements of the average elasticity of a lesion. Previous studies have proposed using the SR to overcome the limitations of the elasticity score [19]. EUS-elastography in its qualitative and quantitative forms provides complementary data that bolster conventional sonographic imaging, representing a promising technique that allows the differentiation of benign and malignant LNs, [18] in addition to the usual sonographic features of the LNs.

Our results showed that an increased transverse diameter, a lost hilum and echo-poor LNs were significantly more frequent in malignant LNs, as shown in Table 4. This finding was supported by several recent studies [20–22]. This study found that elastography exhibited a strong correlation with the final diagnosis and increased the diagnostic accuracy of B-mode sonography, with a sensitivity of 88.1% and a specificity of 83.3% at a cut-off value >2, as shown in Table 4 and Fig. 6. These findings are consistent with many recent studies that showed that the complementary data added by elastography imaging led to the accurate differentiation of benign and malignant lesions [21,23–26].

In our study, the SR showed promising results for predicting malignant LNs, with a sensitivity and specificity of 89.8% and

83.3%, respectively, at a cut-off level of >4.6 (Fig. 5). For predicting malignant LNs, the SR had a positive predictive value of 82.5% and a negative predictive value of 90.2%. The positive predictive value of the SR for predicting benign LNs was 85.8%, while the negative predictive value of the SR for predicting benign LNs was 87.8% (Table 6). The SR also exhibited a strong correlation with the final diagnosis; the SR was significantly higher in malignant LNs (Table 5, Fig. 4).

Paterson et al. assessed the role of the SR in the nodal staging of oesophageal and gastric tumours, using FNA cytology as the reference standard. Those authors examined 50 LNs, with a SR cut-off value of \geq 7.5 for malignancy. The sensitivity, specificity, PPV, NPV, and accuracy were 83%, 96%, 95%, 86%, and 90%, respectively, in comparison to the values of 22–70%, 64–96%, 61–83%, 57–72%, and 60–75%, respectively, that were obtained for different B-mode EUS criteria [27].

Larsen et al. evaluated the use of EUS, EUS-elastography, the SR, and EUS-FNA in the assessment of LNs associated with upper gastrointestinal tumours, using surgical pathology as a reference. A total of 56 LNs were examined. The sensitivity, specificity, accuracy, PPV, and NPV were 55%, 85%, 73%, 71%, and 74%, respectively, for EUS-elastography; 59%, 82%, 73%, 68%, and 76%, respectively, for elastography; and 55%, 82%, 71%, 67%, and 74%, respectively,

Table 8		
Multivariate	regression	analysis.

Variable	Coefficient	Odds Ratio (OR)	95% CI	P-Value
Echo-texture	0.87	2.4	0.4-13.7	0.33
Elastography	-0.39	0.7	0.16-2.9	0.59
Hilum preservation	0.65	1.9	0.23-16.3	0.54
Shortest dimension	0.028	1.03	0.93-1.13	0.58
Shortest /Longest	0.16	1.2	0.023-60.5	0.93
Strain ratio	0.05	1.05	0.96-1.16	0.27
Sonar diagnosis	3.6	35	3.3-371.8	0.003

for the SR at a cut-off value of 4.5. The sensitivity and specificity of EUS-FNA were 64% and 96%, respectively [28].

In a prospective study, Knabe et al. assessed the ability of EUSelastography (using computer analysis of the images) to improve LN staging in 40 patients with oesophageal malignancy, using histology/cytology as a reference. The sensitivity, specificity, and PPV of EUS-elastography alone were 88.9%, 86.7%, and 86%, respectively, in comparison to 91.3%, 64.7%, and 74%, respectively for the B-mode criteria [29].

Comparing our study with the above 3 studies, in our study, a larger number of LNs (126 LN) were assessed by a single experienced operator. The higher SR cut-off value that was adopted by Paterson et al. [27] yielded a higher specificity; however, this change decreased the test's sensitivity for detecting malignant LNs. Although Larsen et al. [28] and our group used similar cutoff values for the SR, those authors found a markedly decreased sensitivity (55%) and a similar specificity. Knabe et al. [29] assessed a relatively small number of LNs (40 LN) via EUS-elastography using computer analysis of the images without calculating the SR. The results obtained in that study were similar to our results regarding the sensitivity and specificity of EUS-elastography.

Our study corroborates several studies and meta-analyses that confirm the valuable role of qualitative and quantitative elastography (by calculating the SR) in differentiating benign and malignant lesions (e.g., in the breast, thyroid, pancreas and LNs) compared to histopathology [18,19,27,30–32]. However, a few studies reported that the additional strain index is not mandatory and found no additional benefit in differentiating benign from malignant LNs in comparison to the use of 5-point scoring with EUS-elastography alone [33]. Univariate regression analysis showed that echogenicity, hilum preservation, elastography, the shortest dimension, the ratio of the shortest/longest dimension, US diagnosis and the SR could be potential predictors of the final LN diagnosis, as shown in Table 7. Although the SR was significantly higher in the malignant LNs (Table 5, Fig. 4) and was a potential predictor of the final LN diagnosis in univariate regression analysis (Table 7), multivariate regression analysis showed that US diagnosis was the only predictor of the final diagnosis. Thus, elastography and the SR alone without US findings are not sufficient to differentiate benign from malignant LNs. This outcome may be a limitation of this study. Elastography and SR should be added to, rather than used to replace, the US criteria for lymphadenopathy (which include echogenicity, hilum preservation, the shortest dimension, and the ratio of the shortest/longest dimension). Fortunately, all of these measurements, including the SR, can be made during the same examination. This finding also highlights the importance of an efficient and experienced sonographer or endosonographer, who can make the correct diagnosis [34–36].

It is worth mentioning that the present study had some shortcomings, such as the use of elastography and the SR to assess different types of histopathology in malignant LNs (e.g. pancreatic, gastric adenocarcinoma, cholangiocarcinoma) and benign LNs, as the heterogeneity of histopathology may cause variations in the results. Future studies should focus on assessing the role of elastography and the SR in each histopathology, but this type of investigation will require larger numbers of patients. On the other hand, this study has some strengths. This study is the first Egyptian prospective single-centre study with a relatively large number of patients that assesses the role of elastography and the SR in differentiating malignant and benign LNs.

To conclude, EUS-elastography and the SR could be excellent prognostic indices for distinguishing benign from malignant LNs if combined with other US features.

Disclosures

The authors whose names are listed certify that they have NO conflicts of interest with any organization or entity with any financial or non-financial interest in the subject matter or materials discussed in this manuscript.

References

- Ahuja A, Ying M. An overview of neck node sonography. Invest Radiol 2002;37 (6):333-42.
- [2] Sorin D, Manuela L, Carolina B, Dan V, Magdalena D. Ultrasonography of superficial lymph nodes: benign vs. malignant. Med Ultrason 2012;14 (4):294–306.
- [3] Rafael R, André G, Renata P, Viviane R. Axillary ultrasound and fine-needle aspiration in preoperative staging of axillary lymph nodes in patients with invasive breast cancer. Radiol Bras 2015;48(6):345–52.
- [4] Bohle W, Meier C, Zoller WG. Validity of endoscopic ultrasonography-guided fine needle aspiration of mediastinal and abdominal lymph nodes in daily clinical practice. Dtsch Med Wochenschr 2013;138(9):412–7.
- [5] Chaoqun H, Rong L, Qin Z, Jun L, Zhen D, Xiaohua H. Role of endoscopic ultrasound-guided fine needle aspiration in the diagnosis of mass lesions. Exp Ther Med 2016;12(2):1085–92.
- [6] Christoph D, Christian J, Paolo A, et al. Endoscopic ultrasound: elastographic lymph nodeevaluation. Endosc Ultrasound 2015;4:3.
- [7] Gennisson JL, Deffieux T, Fink M, Tanter M. Ultrasound elastography: principles and techniques. Diagn Interventional Imaging 2013;94:487–95.
- [8] Julio G, Björn L, Jose L, Enrique D. Endoscopic ultrasound elastography. Endosc Ultrasound 2012;1(1):8–16.
- [9] Hussein O, Mona M, Khaled A, et al. Role of high resolution ultrasound/ endosonography andelastography in predicting lymph node malignancy. Endosc Ultrasound 2014;1(3):58–62.
- [10] Hocke M, Ignee A, Topalidis T, et al. Back to the roots Should gastroenterologists perform their own cytology? Z Gastroenterol 2013;51:191–5.
- [11] Dietrich CF. Real-time tissue elastography. Multiple clinical applications. Multiple clinical solutions. Endo Heute 2011;8:48–67.
- [12] Dietrich CF, Jenssen C. Endoscopic ultrasound-guided sampling in gastroenterology: European society of gastrointestinal endoscopy technical guidelines. Endosc Ultrasound 2013;2:117–22.
- [13] Dietrich CF, Hocke M, Jenssen C. Ultrasound for abdominal lymphadenopathy. Dtsch Med Wochenschr 2013;138:1001–18.
- [14] Young C, Jeong L, Jung B. Ultrasound elastography for evaluation of cervical lymph nodes. Ultrasonography 2015;34(3):157–64.
- [15] Ahuja A, Ying M. Sonographic evaluation of cervical lymph nodes. AJR 2005;184:1689–91.
- [16] Khanna R, Sharma AD, Khanna S, Kumar M, Shukla RC. Usefulness of ultrasonography for the evaluation of cervical lymphadenopathy. World J Surg Oncol 2011;9:29.
- [17] Sohn YM, Kwak JY, Kim EK, Moon HJ, Kim SJ, Kim MJ. Diagnostic approach for evaluation of lymph node metastasis from thyroid cancer using ultrasound and fine-needle aspiration biopsy. AJR Am J Roentgenol 2010;194:38–43.
- [18] Dietrich CF, Jenssen C, Arcidiacono PG, et al. Endoscopic ultrasound: elastographic lymph node evaluation. Endosc Ultrasound 2015;4(3):176–90.
- [19] Zhi H, Xiao XY, Yang JY, et al. Ultrasonic elastography in breast cancer diagnosis: strain ratio versus 5-point scale. Acad Radiol 2010;17:1227–33.

- [20] Coe A, Conway J, Evans J, et al. The yield of EUS-FNA in undiagnosed upper abdominal adenopathy is very high. J Clin Ultrasound 2013;41(4):210–3.
- [21] Mayerle J, Beyer G, Simon P, et al. Prospective cohort study comparing transient EUS guided elastography to EUS-FNA for the diagnosis of solid pancreatic mass lesions. Pancreatology 2016;16(1):110–4.
- [22] Redondo E, Martínez JG, Esquivias J, et al. Endoscopic ultrasonography-fine needle aspiration versus PET-CT in undiagnosed mediastinal and upper abdominal lymphadenopathy: a comparative clinical study. Eur J Gastroenterol Hepatol 2015;27(4):455–9.
- [23] Jae C, Bong K, Sung K, et al. Role of sonographic elastography in the differential diagnosis of axillary lymph nodes in breast cancer. J Ultrasound Med 2011;30:429–36.
- [24] 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. AJR Am J Roentgenol 2008;191:604–10.
- [25] Dana S, Bogdan T, Marius C, Elena B, Izabela P, Mihaela C. Qualitative strain elastography, strain ratio evaluation an important tool in breast cancer diagnostic. Med Ultrason 2016;18(2):195–200.
- [26] Xu W, Shi J, Zeng X, et al. EUS elastography for the differentiation of benign and malignant lymph nodes: a meta-analysis. Gastrointestinal Endosc 2011;74:1001–9.
- [27] Paterson S, Duthie F, Stanley AJ. Endoscopic ultrasound-guided elastography in the nodal staging of oesophageal cancer. World J Gastroenterol 2012;18:889–95.

- [28] Larsen MH, Fristrup C, Hansen TP, et al. Endoscopic ultrasound, endoscopic sonoelastography, and strain ratio evaluation of lymph nodes with histology as gold standard. Endoscopy 2012;44:759–66.
- [29] Knabe M, Gunter E, Ell C, et al. Can EUS elastography improve lymph node staging in esophageal cancer? Surg Endosc 2013;27:1196–202.
- [30] Fumihide I, Takao I, Atsushi S, et al. EUS elastography combined with the strain ratio of tissue elasticity for diagnosis of solid pancreatic masses. J Gastroenterol 2011;46:843–53.
- [31] Larsen MH, Fristrup C, Hansen TP, et al. Endoscopic ultrasound, endoscopic sonoelastography, and strain ratio evaluation of lymph nodes with histology as gold standard. Endoscopy 2012;44:759–66.
- [32] Waki K, Murayama N, Matsumura T, et al. Investigation of strain ratio using ultrasound elastography technique. Proc ISICE 2007;2007:449–52.
- [33] Yerli H, Yilmaz T, Kaskati T, Gulay H. Qualitative and semiquantitative evaluations of solid breast lesions by sonoelastography. J Ultrasound Med 2011;30(2):179–86.
- [34] Jamil LH, Kashani A, Scimeca D, et al. Can endoscopic ultrasound distinguish between mediastinal benign lymph nodes and those involved by sarcoidosis, lymphoma, or metastasis? Dig Dis Sci 2014;59(9):2191–8.
- [35] Catalano MF, Alcocer E, Chak A, et al. Evaluation of metastatic celiac axis lymph nodes in patients with esophageal carcinoma: accuracy of EUS. Gastrointest Endosc 1999;50:352–6.
- [36] Hussain T, Salamat A, Farooq MA, et al. Indications for endoscopic ultrasound and diagnosis on fine-needle aspiration and cytology. J Coll Physicians Surg Pak 2009;19(4):223–7.