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Original article

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

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ABSTRACT

Background and study aims: Endoscopic ultrasound elastography (EUS-elastography), or sono-elastography, 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.

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

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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, PENTAX 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: ≥80% of the cross-sectional area was red or green (i.e., soft).

Pattern 2: ≥50% and <80% of the cross-sectional area was red or green.

Pattern 3: ≥50% and <80% of the cross-sectional area was blue.

Pattern 4: ≥80% of the cross-sectional area was blue (i.e., hard).

- The SR was calculated as R_2/R_1; where R_2 represented the elastography of a selected soft (red) reference area outside the target LNs, preferably the gut wall, perinodal tissue or subcutaneous tissue, 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.

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