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Is ultrasound elastography adding value in diagnosis of focal hepatic lesions? Our experience in a single-center study

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Abstract

Background: The aim of this study was to assess the use of ultrasound elastography in differentiating hepatic lesions in order to increase the sensitivity and specificity of grey-scale ultrasound.

Methods: This study included 104 patients who were referred to the radiology department at Alexandria Main University Hospital for focal hepatic lesions detected by grey-scale ultrasound and were recommended to undergo further evaluation by ultrasound elastography. All studied patients were subjected to the following: (1) grey-scale ultrasound and ultrasound elastography using semiquantitative technique and (2) triphasic MDCT of the liver. MRI was done in 11 patients with malignant lesions; further confirmation with histopathological assessment was conducted.

Results: Benign lesions showed a low strain ratio, while malignant lesions showed a high strain ratio. The mean ratio in the benign lesions was 1.08 ± 0.40, while the mean ratio in the malignant lesions was 4.14 ± 1.25. The cut-off value used to diagnose the malignant lesions and differentiate these lesions from the benign lesions was 1.7, which had a sensitivity of 100%, specificity of 93.10%, PPV of 97.40% and NPV of 100%.

Conclusion: Ultrasound elastography is a promising non-invasive, non-contrast technique that can be added to routine grey-scale sonographic examinations of the liver to characterize hepatic lesions.

Keywords: Ultrasound, Elastography, Focal hepatic lesions, Stiffness, Strain ratio

Background

In our practice, focal hepatic lesions constitute a daily challenge; thus, our aim is to use the least invasive imaging techniques to characterize and diagnose these lesions [1].

A differential diagnosis of focal hepatic lesions using different imaging modalities depends on the surrounding liver parenchyma, mainly the presence of cirrhosis, the clinical data of the patient and the diagnostic imaging findings of the mass [2].

Currently, different imaging techniques are used to examine the liver, and ultrasonography is the main modality used to detect additional hepatic lesions [3].

Ultrasound is typically used as the basic imaging study to detect focal hepatic lesions because it is a widely available, non-invasive, safe, low-cost technique. However, the main disadvantage of ultrasound is the inability to characterize and differentiate hepatic masses. Thus, unfortunately, ultrasound has a low sensitivity and specificity of less than 70% in characterizing hepatic lesions [4, 5].

Recently, non-invasive novel stiffness-based imaging techniques, such as MRI and ultrasound elastography, have been introduced to assess the degree of stiffness in hepatic lesions; these techniques can be used in the liver and other organs, such as the breast and thyroid. Different ultrasound elastography techniques exist, including shear wave elastography and acoustic radiation force impulse (ARFI) elastography [6].

The most commonly used ultrasound elastography techniques include strain elastography (SE) and shear wave elastography (SWE). Both techniques assess the degree of stiffness but use different methods [7].

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Table 1 Distribution of the studied cases according to demographic data (n = 104)

	No. (%)
Sex	
Male	45 (43.3%)
Female	59 (56.7%)
Age (years)	47.55 ± 14.71
≤ 50	49 (47.1%)
> 50	55 (52.9%)

Table 2 Comparison between benign and malignant lesions according to the strain ratio

Strain ratio	Benign (n = 29)	Malignant (n = 75)	p
Min.–Max.	0.60–2.0	1.80–7.0	< 0.001*
Mean ± SD	1.08 ± 0.40	4.14 ± 1.25	
Median	1.0	3.90	

p value for Mann-Whitney test
*Statistically significant at $p \leq 0.05$

The use of ultrasound elastography was approved by the Food and Drug Administration. Currently, ultrasound elastography is a popular technique that is widely used in many clinical applications, including in the differentiation of hepatic lesions [7].

Ultrasound elastography is a non-invasive, non-contrast, rapid easily applicable technique that is easy to perform as a continuation of routine ultrasound examinations of the liver. Ultrasound elastography increases the sensitivity and specificity of ultrasound in the differentiation of focal hepatic masses [8, 9].

Using ultrasound elastography, the lesion stiffness can be qualitatively expressed via a colour-coded map or semi-quantitatively via the strain ratio [5].

One of the ultrasound elastography techniques expresses the stiffness of the lesion in the form of a strain ratio, which is the ratio of the tension (stress) needed to produce a relative change in length (strain). Different agents can affect tissue elasticity, including ageing, inflammation and malignancies. Malignant lesions are commonly hard, less compressible and are less strained than softer tissues under the same pressure [5].

Aim of the study

The aim of this study was to assess the ability of ultrasound elastography, which is a type of stiffness-based imaging, to differentiate focal hepatic lesions to increase the sensitivity and specificity of grey-scale ultrasound.

Methods

This prospective study included 104 patients, who were referred to the radiology department at Alexandria Main University Hospital for focal hepatic lesions detected by grey-scale ultrasound and were recommended to undergo further evaluation by ultrasound elastography. This study was performed between December 2015 and June 2016.

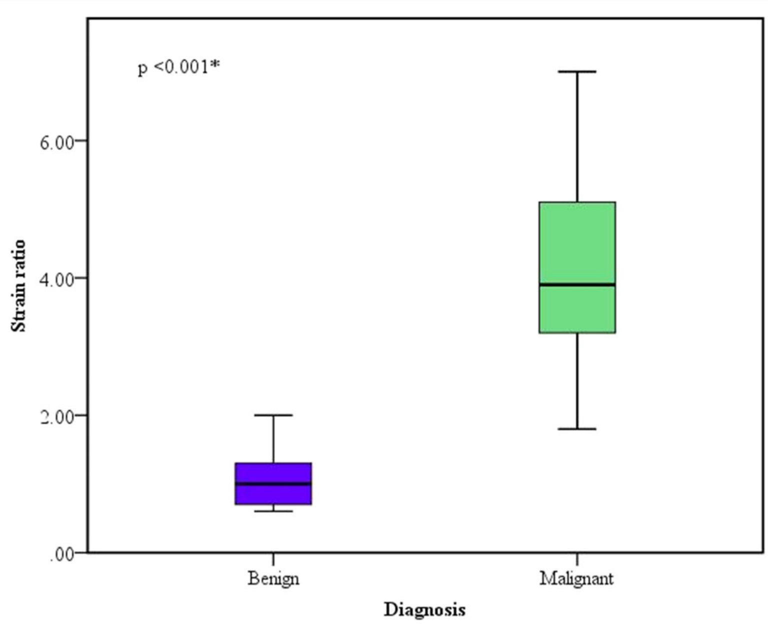

Fig. 1 Comparison of benign and malignant lesions according to the strain ratio

The study protocol was approved by the Research Review Committee of the Alexandria Faculty of Medicine, and informed consent was obtained from each subject included in the study.

All studied patients were subjected to the following:

1. Grey-scale ultrasound;
2. Ultrasound elastography using a semi-quantitative technique to compare the stiffness of the lesion to that of the surrounding liver parenchyma. A green signal on the right side of the image was an indicator of adequate compression;
3. Triphasic MDCT of the liver to further characterize the hepatic lesions. In 11 patients (9 patients with focal nodular hyperplasia (FNH) and 2 patients with adenoma), further assessment using triphasic MRI was conducted; and
4. In malignant lesions, histopathological assessment was conducted for further confirmation.

Statistical analysis

The data was collected and entered into the personal computer. Statistical analysis was done using Statistical Package for Social Sciences (SPSS/version 20) software.

Arthematic mean, standard deviation and Mann-Whitney test were used.

Results

This study included 104 patients, including 45 males and 59 females with a mean age of 47.55 ± 14.71 years (Table 1).

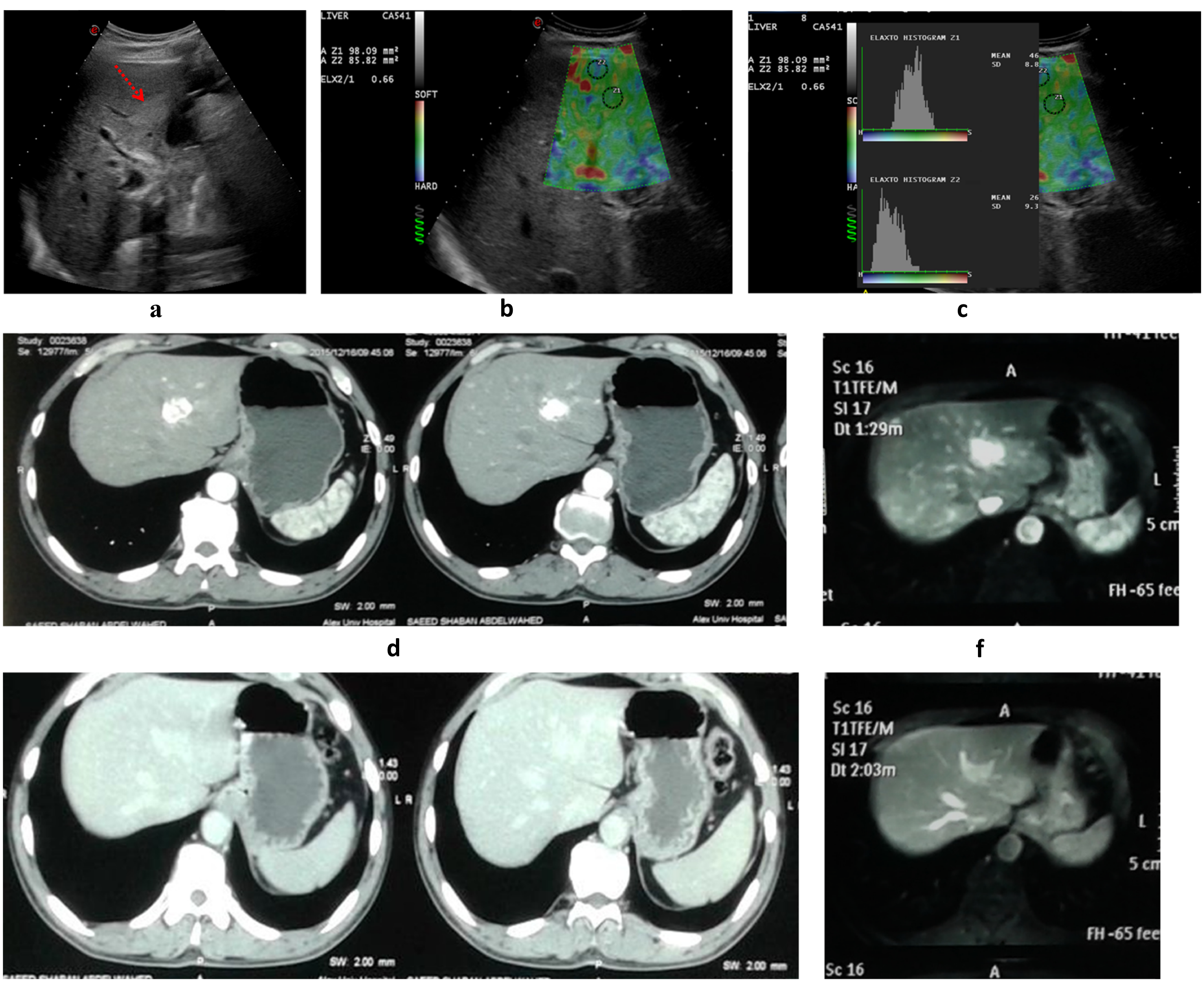

Fig. 2 A 38-year-old female patient with a well-defined hyperechoic lesion as determined by US. Arrow shown in **a** indicates a strain ratio of 0.66 by elastography (**b**) and a histogram of the lesion (**c**), HAP CT and MRI (**d**, **f**), PVP CT and MRI (**e**, **g**) showing homogenous enhancement of the lesion. This lesion was diagnosed as hepatic haemangioma

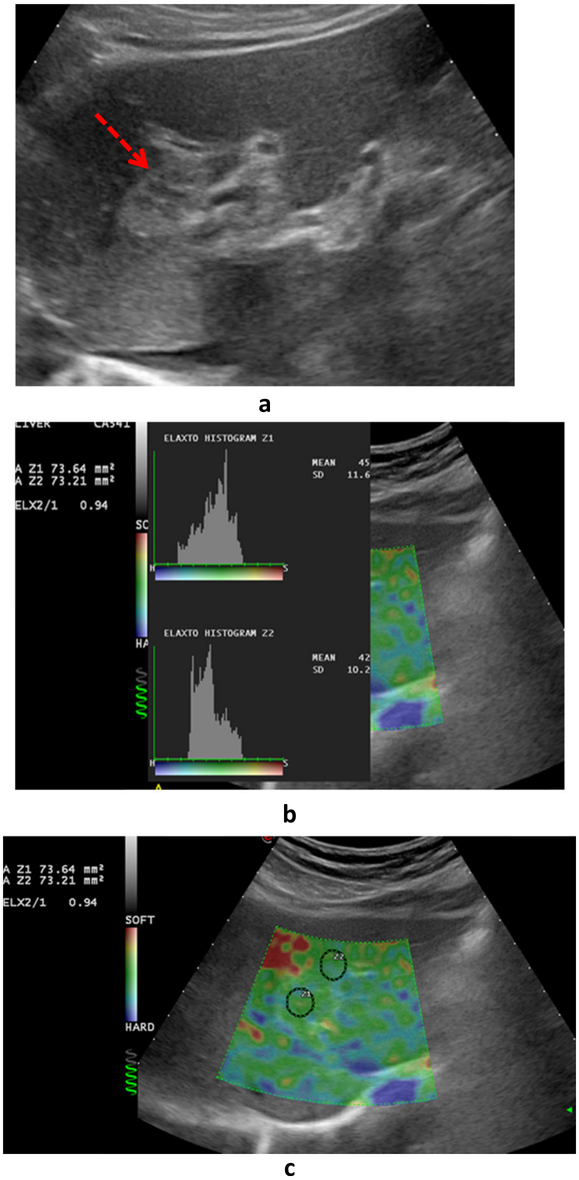

Fig. 3 A 32-year-old female patient with a well-defined foal lesion as determined by grey-scale US. Arrow shown in **a** indicates the lesion had the same colour as the normal liver in the colour map (**b**) and a strain ratio of 0.94 (**c**). This case was diagnosed as hepatic adenoma by MRI

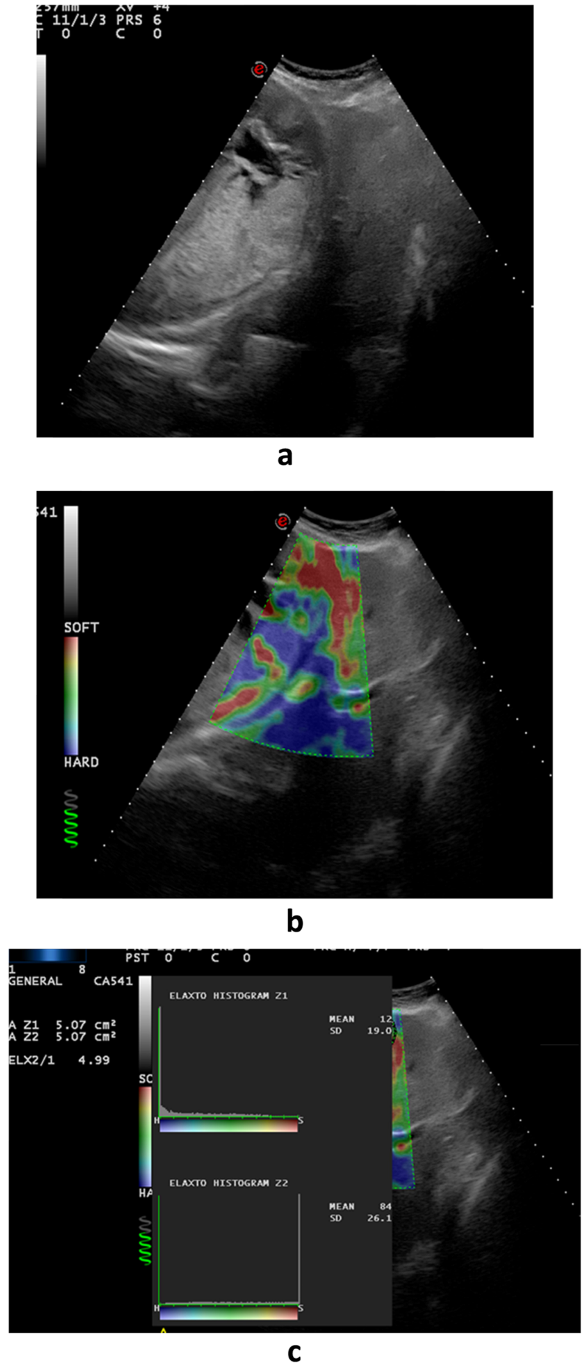

Fig. 4 A 48-year-old male patient with a well-defined FHL as determined by ultrasound (**a**) with a strain ratio of 4.9 as shown by ultrasound elastography (**b**), the histogram of the lesion (**c**) and the pathological finding of cholangiocarcinoma

Strain ratio in the studied lesions

The benign lesions showed a low strain ratio, while the malignant lesions showed a high strain ratio. The mean ratio in the benign lesions was 1.08 ± 0.40, while the mean ratio in the malignant lesions was 4.14 ± 1.25, and the difference in the strain ratios between the benign and malignant lesions was statistically significant ($p \le 0.05$) (Table 2 and Fig. 1).

Strain ratio in the benign lesions

In the benign lesions (29 cases), the lowest ratio was found in cases with haemangiomas (18 cases), which had a mean ratio of 0.82 ± 0.20 (Fig. 2), followed by

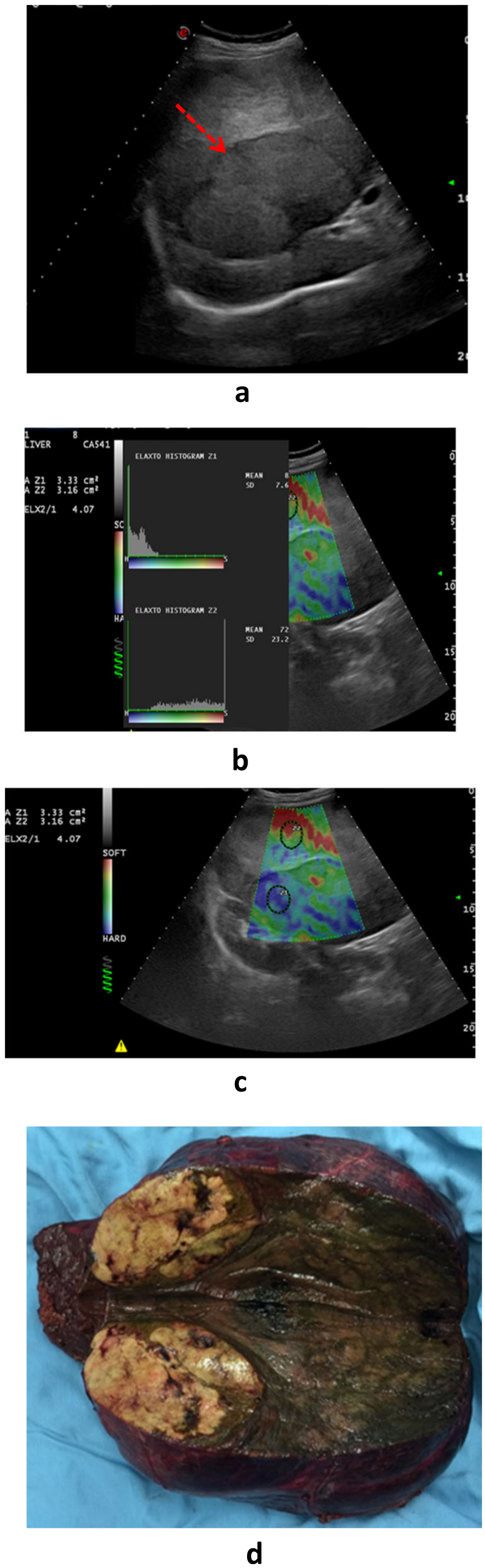

Fig. 5 A 12-year-old female patient with a rather well-defined focal hepatic lesion as determined by grey-scale US that was (**a**) variable in stiffness but mainly hard with a strain ratio of 4.07 (**b**), histogram of the mass lesion (**c**). This lesion was surgically removed and diagnosed as hepatoblastoma (**d**)

adenomas (2 cases), which had a mean ratio of 1.30 ± 0.14 (Fig. 3) and, finally, FNH (9 cases), which had a mean ratio of 1.54 ± 0.27(.

Strain ratio in the malignant lesions

In the malignant lesions (75 cases), the highest strain ratio was found in cases with cholangiocarcinoma (10 cases), which had a mean ratio of 6.25 ± 0.44 (Fig. 4), followed by hepatoblastoma (4 cases), which had a mean ratio of 4.05 ± 0.29 (Fig. 5), hepatocellular carcinoma (HCC) (40 cases), which had a mean ratio of 3.85 ± 1.14 (Fig. 6) and, finally, metastasis (21 cases), which had a mean ratio of 3.72 ± 0.72 (Fig. 7).

The mean strain ratios in each lesion are summarized in Table 3 and Fig. 8.

The cut-off value used to diagnose the malignant lesions and differentiate these lesions from the benign lesions was 1.7, which had a sensitivity of 100%, specificity of 93.10%, PPV of 97.40% and NPV of 100% (Table 4 and Fig. 9). The management of our cases was performed as follows: patients with benign lesions, including adenomas, FNH and haemangiomas, were scheduled to undergo non-surgical regimens with routine follow-up. In contrast, in the malignant cases, the management was tailored to each case. For patients with HCC, 25 cases were managed by TACE, 10 cases were managed with surgical resection and 5 cases with malignant portal vein thrombosis were candidates for chemotherapy. All cases with hepatoblastoma were managed surgically.

The 21 cases with hepatic metastases were managed as follows: 4 cases with solitary lesions were managed with surgical resection, while the other 17 cases with multiple lesions were scheduled to undergo chemotherapy.

Discussion

As radiologists, our aim is to diagnose the hepatic lesion and differentiate the benign masses from malignant masses using a non-invasive imaging technique with a high accuracy to avoid invasive procedures, such as liver biopsies [10].

Although ultrasound elastography has been used in different studies to assess the degree of hepatic fibrosis, few studies have used ultrasound elastography to differentiate focal hepatic masses according to their stiffness [4].

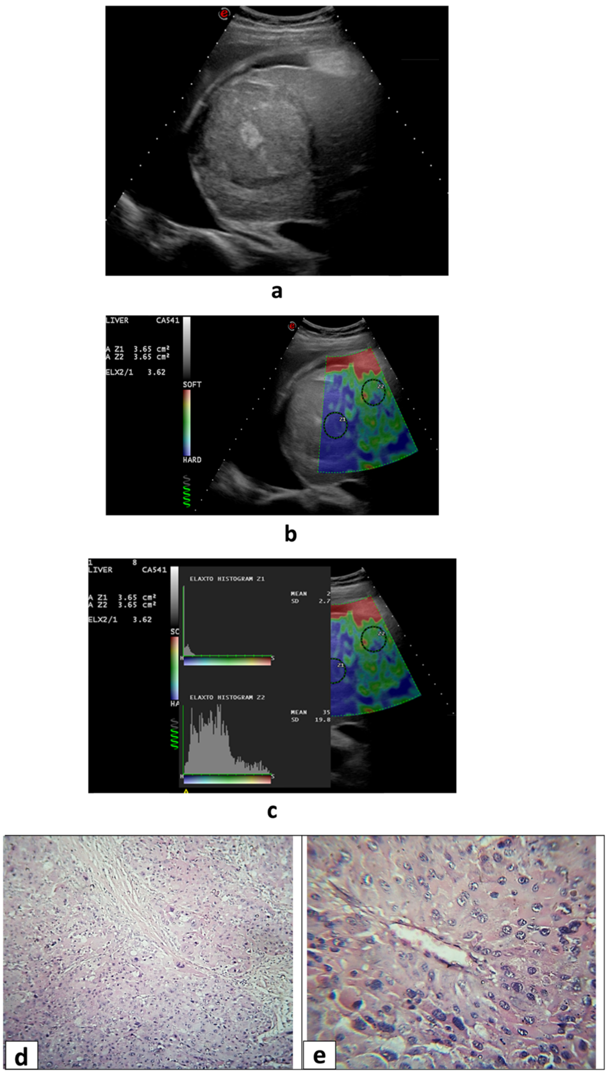

Fig. 6 A 52-year-old male patient with a cirrhotic liver and a well-defined FHL as determined by ultrasound (**a**) the strain ratio of the lesion was 3.6 as measured using ultrasound elastography, **b** the histogram of the lesion, **c** this lesion was shown to be HCC. **d** A case of moderately differentiated hepatocellular carcinoma showing thick cords and trabeculae of pleomorphic cells. (H&E × 100). **e** A higher power view showing cords of anaplastic tumour cells with bizarre nuclei surrounding a central vein (H&E × 400)

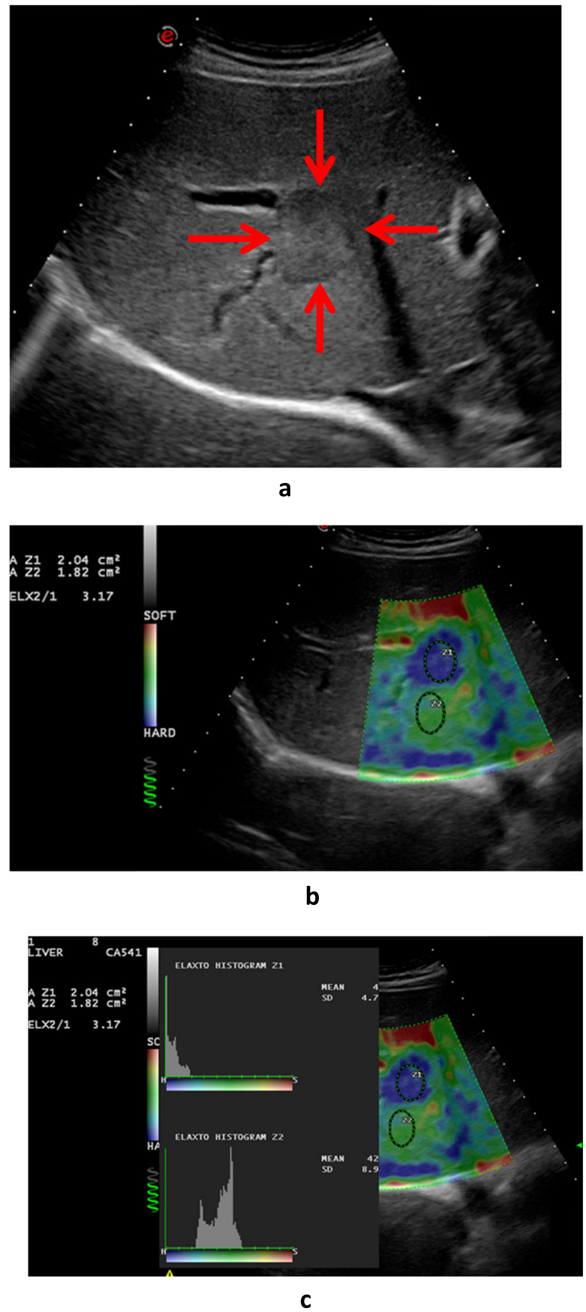

Fig. 7 A male patient with colon cancer and a solitary hepatic lesion as detected by US. Arrows shown in **a** indicate the stiffness by elastography, blue in the colour map (**b**) with a strain ratio of 3.17 (**c**). The pathology confirmed the lesion to be metastatic

Different ultrasound elastography techniques are available; however, in the current study, we used a semi-quantitative method using a strain index to express the elasticity of the lesion in relation to the surrounding normal liver parenchyma. This method is consistent with the semi-quantitative method used by Mehmet et al. [5] in 2013. In contrast, Hana et al. [2]. used ARFI to differentiate hepatic masses. Aymeric et al. used shear wave elastography [4].

In our study, the highest strain index was detected in cholangiocarcinoma (mean strain index = 6.25 ± 0.44), followed by hepatoblastoma, HCC and hepatic metastases. Metastatic lesions from colon cancer had a higher strain index than other metastases or cystic metastases due to fibrosis, which increased the stiffness of the lesion. Using semi-quantitative strain ratio or shear wave

Table 3 Relation between diagnoses with strain ratio

Diagnosis	*N*	Strain ratio
Cholangiocarcinoma	10	6.25 ± 0.44
Hepatoblastoma[a]	4	4.05 ± 0.29
HCC[a]	40	3.85 ± 1.14
Mets[a]	21	3.72 ± 0.72
Hemangioma[ab]	18	0.82 ± 0.20
FNH[ab]	9	1.54 ± 0.27
Adenoma[ab]	2	1.30 ± 0.14

Table 4 Agreement (sensitivity, specificity) for the strain ratio to diagnose malignant lesions

	Cutoff	Sensitivity	Specificity	PPV	NPV
Strain ratio	*> 1.7*	100.0	93.10	97.40	100.0

elastography, Aymeric et al. [4], Mehmet et al. [5] and Ji et al. [6] concluded that cholangiocarcinoma and colon cancer metastases had the highest stiffness.

The strain index of the cholangiocarcinoma lesions in our study was 6.25 ± 0.44, which was the highest value among the studied cases. Consistent with Mehmet et al. [5], we found the highest strain index in malignant lesions, particularly in cases with cholangiocarcinoma.

Aymeric et al. [4], Mehmet et al. [5] and Ji et al. [6] detected a higher degree of stiffness in hepatic metastases from colon cancer than that in metastases from other primary tumours due to the presence of fibrous tissue. In addition, we found a high strain index in hepatic metastases from colon cancer reaching up to 5, and this index was third highest in stiffness following hepatoblastoma and HCC.

We found a high strain index in HCC, which is a malignant lesion that is hard in consistency, reaching a value of 3.85 ± 1.14. Mehmet et al. [5] confirmed the stiffness of HCC with a high strain ratio of 3.24 ± 0.48.

Benign lesions, such as hepatic haemangiomas, adenomas and FNH, had a lesser degree of stiffness with a mean strain index of 0.82 ± 0.20, 1.30 ± 0.14 and 1.54 ± 0.27, respectively. This finding was consistent with reports by Mehmet et al. [5] who concluded that these benign lesions had a low strain index of 0.92 ± 0.14 in haemangioma and 1.75 ± 0.16 in FNH.

Mehmet et al. [5] found that the sensitivity and specificity of conventional ultrasound in differentiating benign and malignant hepatic lesions ranged from 28.1 to 58.8% and 34.6 to 50.7%, respectively. In their study, the authors attained a higher sensitivity and specificity using semi-quantitative strain elastography than those attained using conventional sonography. In addition, we attained a higher sensitivity and specificity reaching 100% and 93%, respectively, in differentiating benign from malignant hepatic lesions using strain elastography.

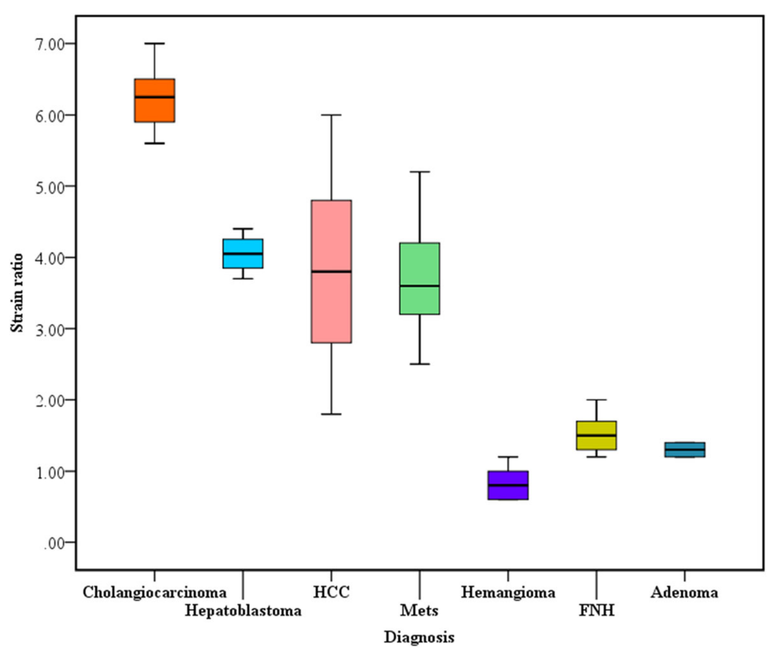

Fig. 8 Relationship between diagnoses and strain ratios

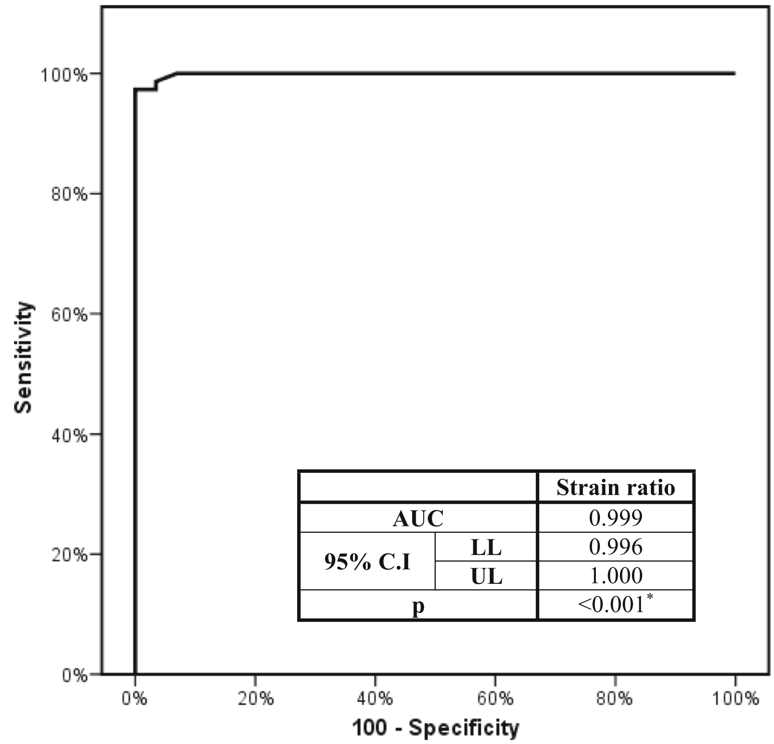

Fig. 9 ROC curve of the strain ratio used to diagnose malignant lesions

Conclusions

Ultrasound elastography is a promising, non-invasive, non-contrast technique that can be added to routine grey-scale sonographic examinations of the liver to characterize hepatic lesions. However, the heterogeneity of the lesions, i.e. malignant lesions with necrosis or benign lesions with fibrosis, should be considered because these characteristics can change the stiffness of the lesion as measured by elastography and can lead to false positive or false negative results.

Abbreviations

ARFI: Acoustic radiation force impulse; FNH: Focal nodular hyperplasia; HCC: Hepatocellular carcinoma; MDCT: Multidetector computed tomography; MRI: Magnetic resonance imaging; SE: Strain elastography; SWE: Shear wave elastography

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Authors' contributions

DE and ME drafted the manuscript and edited the images. AE reviewed the clinical part of the work. AY revised the pathology of the cases. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

Approval for this cross-sectional prospective study was obtained from the Research Ethics Committee of Alexandria Faculty of Medicine (Ethics committee's reference number: 0302521, IRB No: 00007555- FWA No: 00015712). All study procedures were carried out in accordance with the Declaration of Helsinki regarding research involving human subjects. Written informed consent was obtained from the patients.

Consent for publication

Written informed consent for publication of this data was given by the patients.

Competing interests

The authors declare that they have no competing interests.

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