

Endoscopic ultrasound (EUS) elastography and strain ratio, could it help in differentiating malignant from benign pancreatic lesions?

Hussein Hassan Okasha, MD^a, Reem Ezzat Mahdy, MD^b, Shaimaa Elkholy, MD^a, Mohamed Sayed Hassan, MD^a, Ahmed Nabil El-Mazny, MD^a, Kareem Essam Eldin Hadad, MD^{a,*}, Moustafa Saeed, MD^a, Mohamed El-Nady, MD^a, Osama Soliman Elbalky, MD^c, Asem Ashraf, MD^e, Amr Abo El-Magd, MD^d, Abeer Awad, MD^a

Abstract

Evaluating the role of endoscopic ultrasound (EUS) elastography and strain ratio in differentiation between malignant and benign pancreatic lesions.

Three hundred twenty-five patients with solid pancreatic lesions were enrolled in this prospective study from 2014 to 2017. EUS real-time elastography scoring and strain ratio were done to all patients and compared to the final diagnosis to assess its sensitivity, specificity, positive and negative predictive values (PPV and NPV) in differentiating malignant from benign lesions.

A cut-off value of 4.2 we had sensitivity of 95%, specificity of 63%, PPV of 89%, NPV of 81%, and accuracy of 87%. Another cut-off value of 10.9 showed a sensitivity of 75%, specificity of 88%, PPV of 95%, NPV of 54%, and accuracy of 79%. Adding the elastography to the better cut-off value gave a sensitivity of 97%, specificity of 63%, PPV of 89%, NPV of 88%, and accuracy of 89%.

Real-time elastography and strain ration are valuable in differentiating malignant from pancreatic lesions.

Abbreviations: EUS = endoscopic ultrasound, FNA = fine needle aspiration, NPV = negative predictive value, PPV = positive predictive value, SPL = solid pancreatic lesions.

Keywords: elastography, EUS, pancreatic lesions, strain ratio

1. Introduction

Solid pancreatic lesions (SPL) have less than 5% 5-year survival rate,^[1] so they need to be investigated thoroughly to reach the proper diagnosis. In advanced cases, surgery will not be a solution in spite being the best treatment at earlier stages.^[2]

In a previous study,^[3] we evaluated real-time EUS elastography and strain ratio as predictive tools to reach the correct diagnosis for SPL. It had a sensitivity of 98% and specificity of 77% and a diagnostic accuracy of 92%.^[3]

In this prospective study, we decided to increase the sample size of the studied group (325 patients) for more accurate diagnosis and to see if this would change the cut-off values of the strain ratio reached in the previous work for differentiating benign from malignant lesions.

2. Patients and methods

2.1. Patients

Patients with solid pancreatic lesions (SPL) identified by endoscopic ultrasound (EUS) in Cairo University hospital starting from January 2014 to June 2017 were enrolled in this prospective study. The inclusion criteria were solid pancreatic lesion from prior radiological imaging and patients with extrahepatic biliary radicle obstruction with inconclusive CT or MRI findings between 18 and 80-year-old. The exclusion criteria were patients that refused to participate, patients with contraindication to the procedure, and pregnant or breast-feeding patients. Informed consent was obtained from all patients before the procedure.

2.2. Methods

After approval from the ethical committee, patients who agreed to participate in the study were appointed to the endoscopy room on the day of the procedure for EUS examination. EUS examination was performed using a linear Echoendoscope Pentax EG3870UTK (HOYA Corporation, PENTAX Life Care Division, Showanomori Technology Center, Tokyo, Japan) connected to an ultrasound unit Hitachi AVIUS machine (Hitachi Medical Systems, Tokyo, Japan). All examinations were performed by 1 endosonographer. For EUS-fine needle aspiration (FNA), we used the Cook needle 22G (Echotip; Wilson-Cook,

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

^b Internal Medicine Department, Faculty of Medicine, Assiut University, Assiut,

^c General Surgery Department, Damanhur Teaching Hospital, Al Buhayrah,

^d Internal Medicine Department, Armed forces college of medicine, Cairo,

^e Gastroenterology Department, Military Medical Academy, Egypt.

* Correspondence: Kareem Essam Eldin Hadad, Zahraa Almaadi, Cairo, Egypt (e-mail: kareemessam8100@yahoo.com).

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Winston Salem, NC). Elastography was applied to evaluate the SPL.

2.2.1. Qualitative score. We used the “Elastic score” reported by Giovannini et al,^[4] that is, Score 1 (soft, green), corresponding to the normal pancreas; Score 2 corresponding to chronic pancreatitis as shown in Fig. 1. Elastographic images that were largely blue with minimal heterogeneity, corresponding to small adenocarcinomas, were given Score 3 as shown in Fig. 2. Score 4 represented a hypoechoic region in the center, with a green appearance within a small area surrounded by blue, or harder tissue, corresponding to neuroendocrine tumors.

2.2.2. Quantitative score. The semiquantitative score of elastography was represented by the strain ratio method. Two areas were selected, area (A) representing the region of interest and area (B) representing the normal area. Area (B) is then divided by area (A). Means of strain ratios were calculated and used as final results for each patient as shown in Figs. 3 and 4. The best cut-off value of strain ratio was also combined with results of elastography for calculation of diagnostic value.

2.2.3. Data analysis. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy were calculated by comparing diagnoses made by elastography, strain ratio, and final diagnoses.

Final diagnosis of the SPL was obtained by cytopathological examination of aspirate taken by EUS-FNA, excisional biopsy of surgically removed tumors, presence of metastases or follow up of benign lesions for at least 6 months.

3. Results

The study was done on 325 patients, 222 females with mean age of 55.6 and 103 males with mean age of 54.8.

The lesions were diagnosed to be benign in 78 patients and malignant in 247 patients, with the different diagnoses mentioned in Table 1.

Most of the lesions were located in the head of the pancreas reaching 220 cases, to be followed by lesions in the body of the pancreas reaching 38 and those involving the whole pancreas where 29 cases as mentioned in Table 2.

Elastography Scores 1 and 2 were considered benign while 3 and 4 were considered malignant. The calculated statistical parameters of elasticity score, cut-off strain ratio at 4.2 and 10.9 and combined elasticity score and strain ratio of 4.2 are shown in Table 3.

4. Discussion

As EUS has a limited ability to differentiate between benign and malignant solid pancreatic lesions, EUS guided tissue sampling is needed to improve its accuracy.^[5–9] Still, EUS-guided tissue sampling may face some limitations as the false-negative results,^[10] the difficult puncture in some lesions due to interposing vascular structure^[11] and the very small but present morbidity.^[12] This urged the need for a noninvasive method to be used with the EUS to differentiate between the malignant and benign lesions.

We previously investigated 172 patients identified to have SPL by the previously mentioned noninvasive modalities beside the EUS-FNA to predict the nature of the lesion.^[3] At the cut-off level

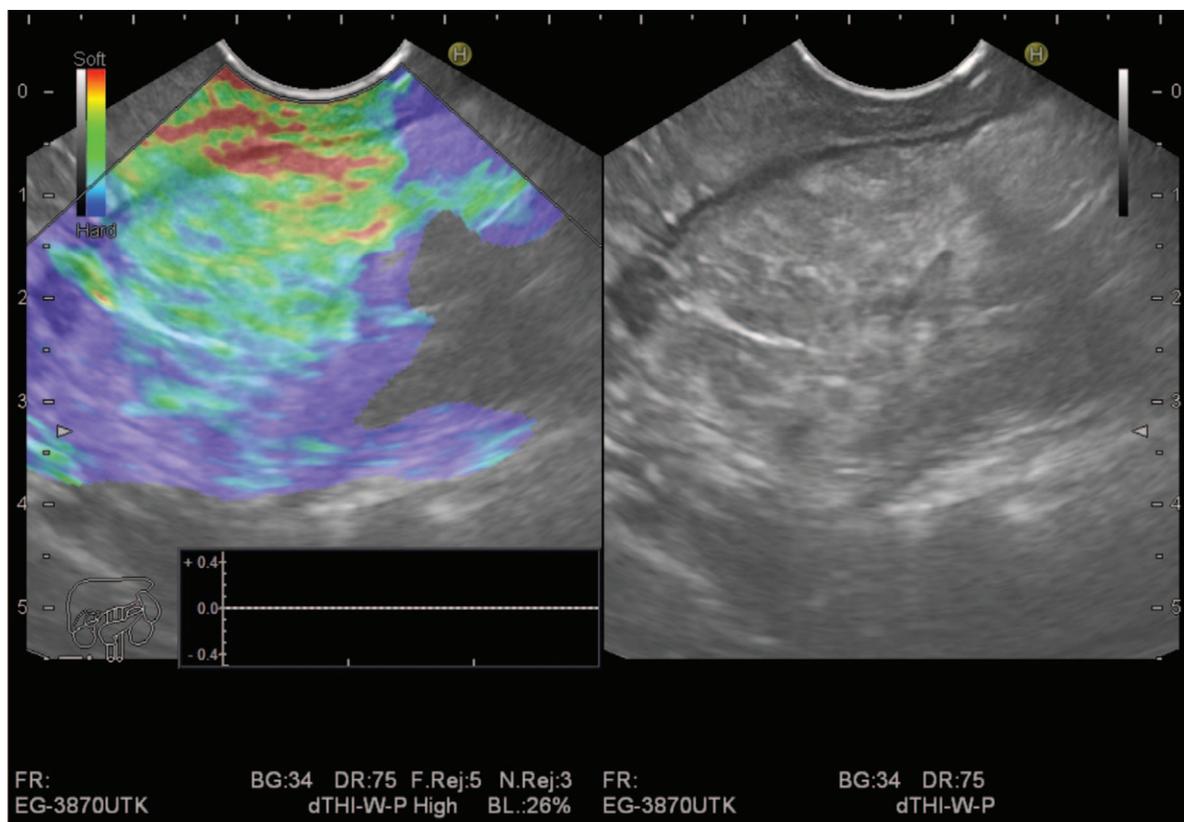


Figure 1. Chronic pancreatitis with elasticity score 2.

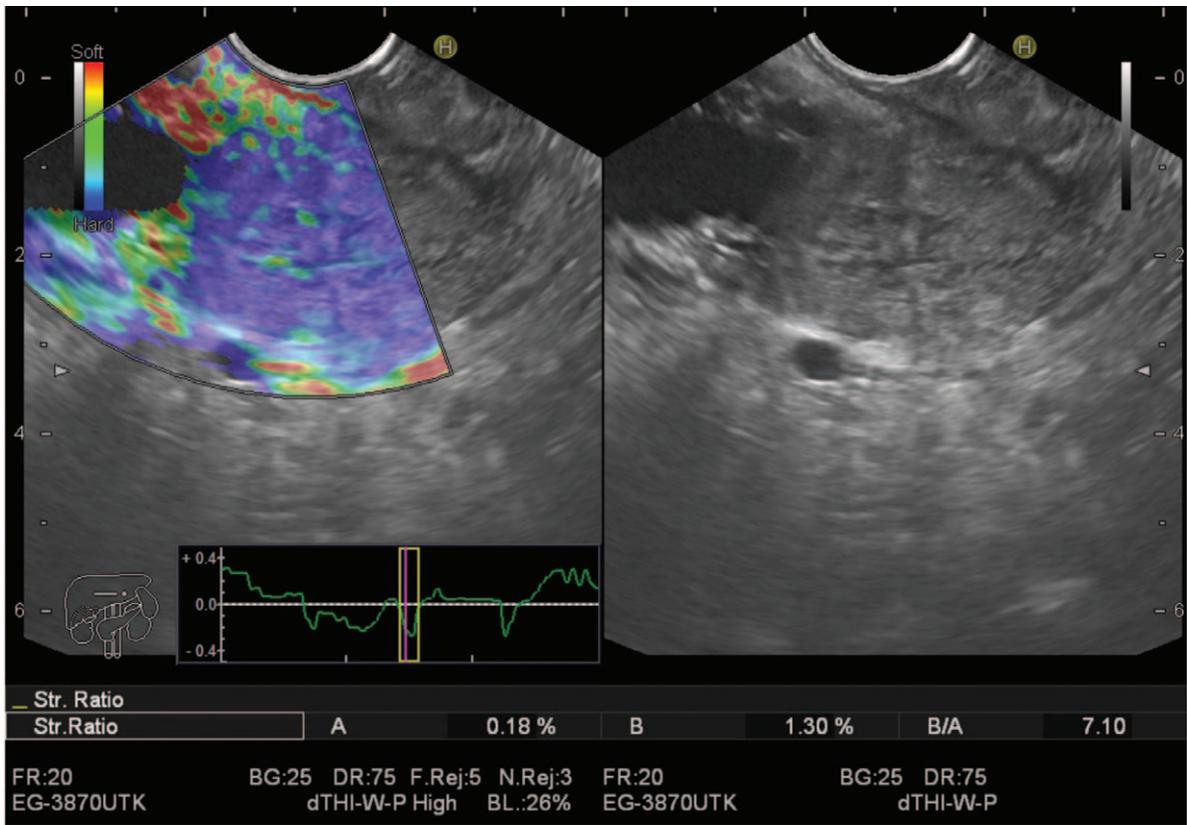


Figure 2. Pancreatic adenocarcinoma with elasticity score 3.

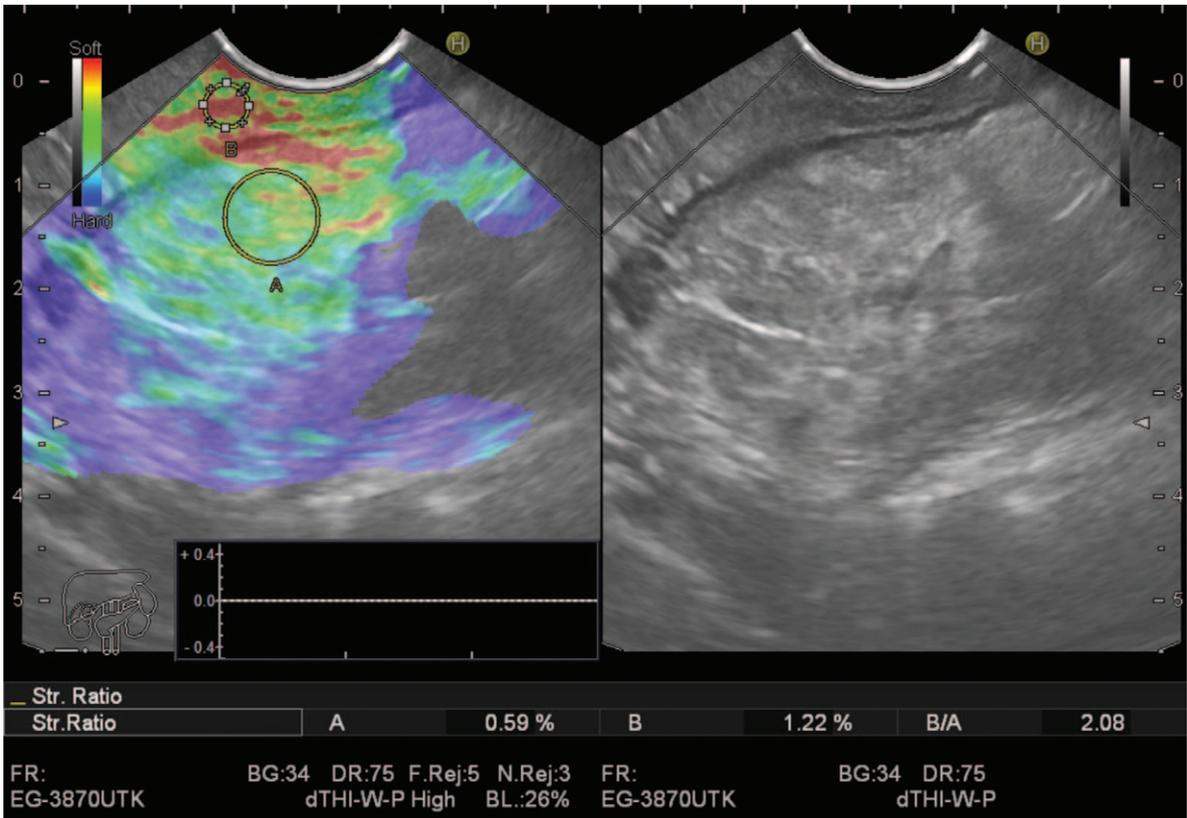


Figure 3. Chronic pancreatitis showing low strain ratio.

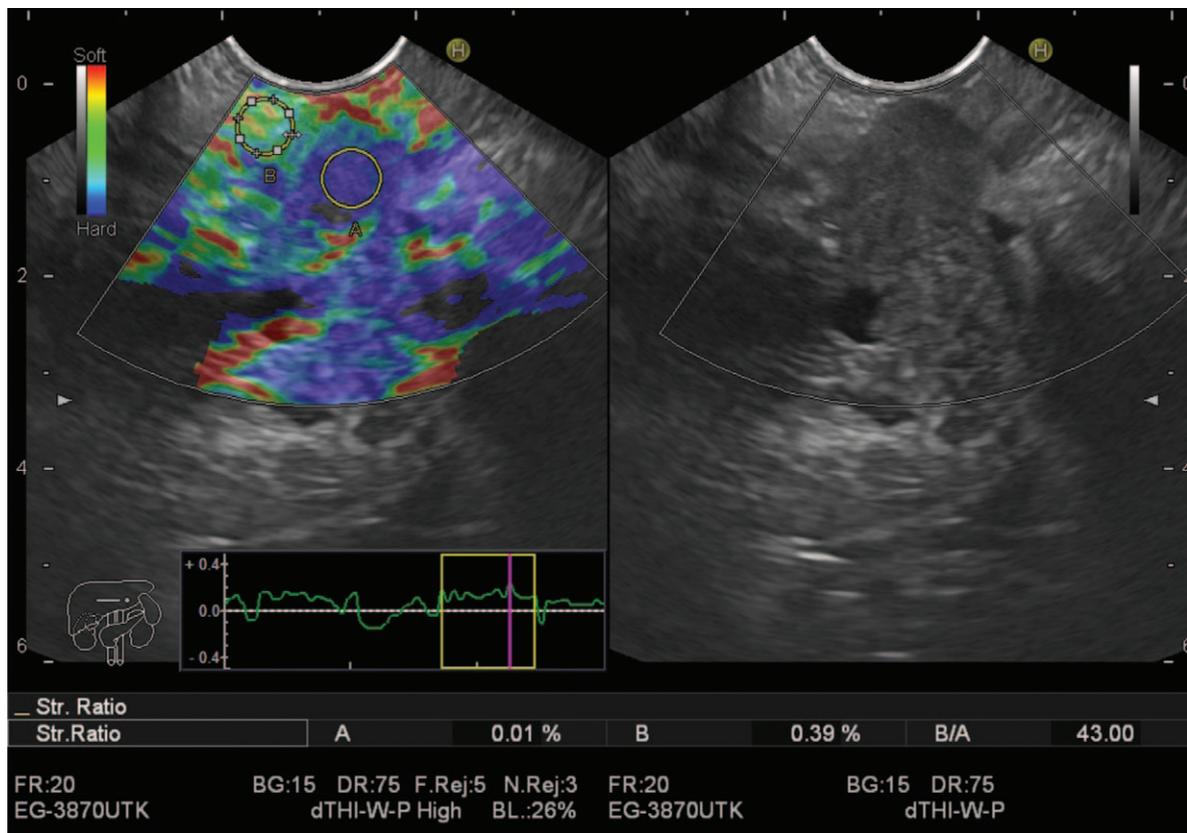


Figure 4. Pancreatic adenocarcinoma with high strain ratio.

of 3.8, we had sensitivity, specificity, PPV, NPV, and accuracy of 99%, 53%, 84%, 86%, and 96%, respectively. Then we calculated the best cut-off value to have 7.8 to differentiate between benign and malignant SPL. We had sensitivity of 92%, specificity of 77%, accuracy of 88%, PPV of 91%, and NPV of 80%. To increase the efficacy of diagnosing SPL, we combined elastography to the strain ratio level of 7.8 to have sensitivity of 98%, specificity of 77%, accuracy of 92%, PPV of 91%, and

Table 1
Nature of the diagnosed lesions.

Nature	No. of cases
Benign—78 (24%)	
Chronic pancreatitis	67
Autoimmune pancreatitis	10
Adenoma	1
Malignant—247 (76%)	
Ductal adenocarcinoma	193
Mucinous adenocarcinoma	28
Neuroendocrine tumor	4
Severe metaplasia	5
Metastasis	3
Solid pseudopapillary tumor	6
Pan intraductal neoplasm	2
Lymphoma	1
Cholangiocarcinoma	2
Papillary adenocarcinoma	2
Undifferentiated carcinoma	1

Table 2
Location of the lesions and their numbers.

Location	Number
Head	220
Body	38
Tail	7
Diffuse	29
Uncinate process	12
Papilla	3
Body and tail	1
Distal cholangiocarcinoma	2
Head and body	2
Neck	10

Table 3
Elastography and strain ratio.

	Elastography	Strain ratio 4.2	Strain ratio 10.9	Elastography with strain ratio 4.2
Sensitivity	96	95	75	97
Specificity	63	63	88	63
PPV	88	89	95	89
NPV	85	81	54	88
Accuracy	88	87	79	89

NPV = negative predictive value, PPV = positive predictive value.

NPV of 95% raising the accuracy than if every tool was used alone.

At this paper, we decided to find out the effect of increasing the sample size on the cut-off values for strain ratio by investigating 325 patients.

On a cut-off value of 4.2 we had sensitivity of 95%, specificity of 63%, PPV of 89%, NPV of 81%, and accuracy of 87%. Another cut-off value of 10.9 had a sensitivity of 75%, specificity of 88%, PPV of 95%, NPV of 54%, and accuracy of 79%.

This decrease in the better reached cut-off value with better sensitivity and higher accuracy may be attributed to the increased sample size which gives results of better diagnostic value and may postulate that small values for strain ratio can include malignant lesions. The work carried by Dalibor et al^[13] recorded a cut-off value of 1.153 with sensitivity of 98%, specificity of 50%, and accuracy of 69%.

Iglesias-Garcia et al reported their results on the strain ratio on 86 patients. This methodology even increased the accuracy of qualitative elastography, yielding an overall diagnostic accuracy for malignancy of 97.7% when presenting strain ratio level >6.04. In addition, EUS-guided elastography could differentiate pancreatic cancers from inflammatory masses (100% sensitivity and 96% specificity) and pancreatic cancers from neuroendocrine tumors (100% sensitivity and 88% specificity).^[14] Several studies reported different cut-off values from 3.7 to 24, with diagnostic sensitivities ranging from 67% to 98% and specificities between 45% and 71%.^[15-21] This issue highlights that standardization of the techniques is needed.

Another study by Iglesias-Garcia et al^[22] reported that a strain ratio >10 is the optimal cut-off values for the classification of lesions as malignant with an overall accuracy of 98%. Several meta-analyses have been performed to determine the role of EUS-guided elastography in the differential diagnosis of solid pancreatic masses. Two meta-analyses evaluated the role on the differentiation of malignant pancreatic tumors from inflammatory pancreatic masses, showing a sensitivity of 95% and a specificity ranging from 67% to 69%.^[23,24] The third meta-analysis included 7 studies and 752 patients, with a global sensitivity of 97% and a specificity of 76%. This meta-analysis highlighted the difficulties of differentiating adenocarcinoma and neuroendocrine tumors, due to the similar hardness of both tumors.^[25] The fourth meta-analysis found that the use of a color pattern for elastographic interpretation was associated with a sensitivity of 99% and a specificity between 69% and 76%.^[26]

Adding the elastography to the better cut-off value gave a sensitivity of 97%, specificity of 63%, PPV of 89%, NPV of 88%, and accuracy of 89%. This was near to the values obtained by elastography alone. This also was different from the previous work where adding the strain ratio to elastography increased accuracy to 92% with sensitivity of 98%. This finding suggests that elastography, although being a subjective method, in good experienced hands and with large sample size can be very objective.

Using elastography and strain ratio as guide to accurately target FNA tissue sampling will improve its accuracy, moreover, in highly suspicious lesions based on elastography and strain ratio with negative FNA, another trial of FNA will be justified.

Many previous publications showed similar results, however the large sample size of this study will consolidate the elastography and strain ratio role in the future as an important complementary tool to EUS and FNA.

Still, the value of the strain ratio as a numerical non subjective method cannot be dismissed. The large sample size beside the

nature of the study being a prospective one, gave us confidence in our results, whether the subjective or the numerical ones.

5. Conclusion

EUS-guided elastography with strain ratio provides very useful and valuable information on the malignant potential of lesions. Although tissue confirmation is frequently needed for the final diagnosis and is included in the diagnostic algorithm, elastography should be included in the diagnostic work up of solid pancreatic lesions.

Author contributions

Conceptualization: Hussein Hassan Okasha.

Data curation: Mohamed El-Nady.

Formal analysis: Asem Ashraf.

Funding acquisition: Moustafa Saeed.

Investigation: Amr Abo El-Magd.

Project administration: Shaimaa Elkholy.

Resources: Reem Ezzat Mahdy, Abeer Awad.

Software: Ahmed Nabil El-Mazny.

Visualization: Osama Soliman Elbalky.

Writing—original draft: Mohamed Sayed Hassan.

Writing—review & editing: Kareem Essam Eldin Hadad.

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