



## **Role of Endoscopic Ultrasound in the Diagnosis of Solid Pancreatic Lesions: A Prospective Study**

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### **Authors' contributions**

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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### **ABSTRACT**

**Background:** Endoscopic ultrasonography (EUS) provides high-resolution images of the pancreas, and it is considered one of the most accurate methods for the diagnosis and staging of solid pancreatic lesions (SPL), EUS guided fine-needle aspiration (EUS-FNA) can obtain cytological samples of pancreatic lesions, making a pathologic diagnosis possible, however, it is associated with small, but not insignificant, morbidity. The aim of this work is to determine in a prospective study, the role of EUS in the diagnosis of SPL in comparison with different radiological studies and to determine the diagnostic value of EUS guided FNA and elastography in differentiation between benign and malignant pancreatic lesions.

**Patients and methods:** A total of 50 patients with SPL identified by EUS after imaging studies were enrolled in the study. The qualitative elastography score was done, also the semi quantitative score of elastography was represented by the strain ratio (SR) method where two areas were selected, area (A) representing the region of interest and area (B) representing the normal area. Area (B) was then divided by area (A). Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy were calculated by comparing diagnosis made by elastography, SR with the final diagnosis (by EUS-FNA, surgery, and/or follow up for 6 months).

**Results:** SPL were found to be malignant in 38 patients and benign in 12 patients. SPL was diagnosed by different imaging modalities in 39 patients with a percentage of (78%), while it was

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diagnosed by EUS in all 50 patients with a percentage of (100%). Elastography score alone had a sensitivity of 89.4%, a specificity of 75%, a PPV of 91.8% and an NPV of 69.2% and an accuracy of 86%. The best cut-off level of SR to obtain the maximal area under the curve was 8.42 with a sensitivity of 92.1%, specificity of 83.3%, PPV of 94.6%, NPV of 76.9% and an accuracy of 93.1%. Adding both elastography score to SR resulted in a sensitivity of 94.7%, specificity of 83.3%, PPV of 94.7%, NPV of 83.3% and accuracy of 94.3% for the diagnosis of SPL.

**Conclusion:** EUS has a role in diagnosis of SPL which may be superior to different radiological studies; also, EUS-elastography and SR can be a valuable complementary supplement for EUS-FNA.

*Keywords: Endoscopic ultrasound; solid pancreatic lesions; fine-needle aspiration; elastography.*

## 1. INTRODUCTION

Solid pancreatic lesions (SPL) can result from a variety of causes, including malignant or benign pancreatic tumors, chronic pancreatitis, or autoimmune pancreatitis (AIP). Despite numerous imaging techniques, differential diagnosis of focal pancreatic masses is still a diagnostic problem in a significant number of patients and the prognosis of pancreatic cancer is extremely poor as a result of the difficulty in early detection of small pancreatic cancer [1].

Computed tomography (CT) is generally used for initial screening for pancreatic masses, but the imaging sensitivities are generally insufficient to detect small masses. Recent studies indicated that EUS and magnetic resonance imaging (MRI) showed high sensitivity for the detection of pancreatic tumors. However, these imaging were limited in their ability to identify benign and malignant pancreatic masses [2].

EUS-FNA has been established as a sensitive, specific, and safe tool for acquiring a histological diagnosis in pancreatic tumors. However, it is an invasive procedure and associated with a low but not negligible risk for complications. Furthermore, seeding of malignant cells along the FNA needle tract has been reported in EUS-FNA of pancreatic lesions [3].

Elasticity measurements have been reported to be useful for the diagnosis of many tumors, which are usually stiffer than normal soft tissues [4].

Giovannini *et al.* first described elastography for EUS in 2006. Qualitative EUS elastography was defined as elastographic color pattern according to the predominant color and the homogeneity or heterogeneity of color distribution, quantitative EUS elastography including strain ratio (SR) was considered as the measure of the elastographic

evaluation by the elasticity quotient between the pancreatic masses and surrounding tissue [5].

The aim of this study is to evaluate the role of endosonography in the diagnosis of SPL in comparison with the various radiological studies (CT and MRI), and to determine the diagnostic value of EUS-FNA and elastography in the differentiation between benign and malignant pancreatic lesions.

## 2. PATIENTS AND METHODS

This prospective study was conducted in the endoscopy unit, Kasr Al Aini Hospitals, Cairo University in the period between March 2017 to March 2018. The study included 50 patients with SPL.

Inclusion criteria were patients  $\geq 18$  years old, patients with identified SPL from prior radiological imaging (CT or MRI), patients with extrahepatic biliary obstruction and suspected to have pancreatic lesion with negative imaging results and referred for EUS.

Exclusion criteria were patients with cystic pancreatic lesions identified by radiological imaging or EUS, patients with contraindication to the procedure, patients who declined to participate to the study and patients whose final diagnosis couldn't be reached.

Patients were divided into 2 groups: Malignant pancreatic mass group including 38 patients and Benign pancreatic mass group including 12 patients.

All patients were subjected to the following: Careful history taking, clinical examination, laboratory investigations, pelviabdominal ultrasonography. Other imaging modalities were used with attention to visualization of pancreas, its size, the number of focal lesions, biliary tree

and intra-abdominal lymphadenopathy CT scan of abdomen and pelvis and/or; MRI of abdomen and pelvis and/or; MRCP &/or; ERCP.

## 2.1 EUS Examination

Using a Pentax linear array EUS machine type EG-3870-UTK (HOYA Corporation, PENTAX Life care Division, Showanomori Technology Center, Tokyo, Japan) connected to a Hitachi EUB-7000 HV ultrasound unit (Hitachi Medical Systems, Tokyo, Japan). All examinations were performed by one endosonographer.

The patients underwent the examination under sedation with intravenous propofol injection.

For EUS-FNA biopsies, we used the Cook needle 22G (Echotip®; Wilson-Cook, Winston Salem, NC, United States). The final diagnosis was obtained by cytopathological examination of the specimens and the pathological evaluation was done by a single pathologist.

## 2.2 Elastography

Elastography is the sound wave technique to measure tissue deformation in response to compression. Theoretically, malignant lesions are harder than inflammatory ones. The hardness of the lesion is reflected by the degree of deformation represented by a color map (red-green-blue colors represent soft to hard tissue, respectively). Qualitative scores and strain ratios were determined during the procedure.

The probe was attached to the wall just exerting the pressure needed for an optimal and stable B-mode image at 7.5 MHz. The region of interest for the elastographic evaluation was selected manually to include the whole targeted lesion when possible as well as surrounding tissues. Maximal sensitivity for elastographic registration was used consistently in the study. Because elastographic images tend to show rapidly changing colors, a stable image for at least 5 seconds was required for quantitative analysis and final pattern definition. Two different areas (A and B) from the region of interest were selected for quantitative elastographic analysis. Area A is a representative area of the mass and included the biggest possible area of the tumor. Area B refers to a soft (red) peripancreatic reference area outside the tumor. The quotient B/A (strain ratio) is considered as the measure of the elastographic evaluation and it was repeated 3 times and the mean of 3 measures was

calculated for each patient. Because selection of area B can to some extent be biased, the elasticity of area A also independently was considered for analysis as another measure of the elastographic evaluation.

### 2.2.1 Qualitative score

Elastic score” reported by Giovannini et al, [5] was used. A score of 1 was defined as homogeneous soft tissue (green) and interpreted as normal tissue. A score of 2 was given to heterogeneous soft tissue (green, yellow, and red), and interpreted as fibrosis or inflammation. A score of 3 represented mixed hard and soft tissues (mixed colors) or a honeycombed elastography pattern, interpreted as indeterminate for malignancy. A score of 4 was given for hard (blue) lesions with a soft (green) central area, interpreted as malignant, hypervascularized lesions. Finally, a score of 5 represents predominantly hard (blue) lesions with dispersed heterogenic soft (green, red) areas, interpreted as advanced malignant lesions with necrotic areas.

### 2.2.2 Strain ratio

This is the semi-quantitative form of elastography. The means of strain ratios were calculated and used as final results for each patient.

Final diagnosis of malignant or benign tumor was defined according to the following:

- (1) Histology of surgical specimens in cases undergoing surgery;
- (2) A definitely positive cytology by EUS-FNA for malignancy together with compatible EUS and CT scan findings for final diagnosis of malignant disease in unresectable tumors; and
- (3) EUS and CT scan findings at entry, clinical presentation, and a minimum follow-up period of 6 months including EUS ± FNA and CT scan, for final diagnosis of benign disease in cases of benign cytology.

### 2.2.3 Follow up

Follow up was done to cases whome imaging prior to EUS showed evidence of solid focal lesion while the EUS examination pattern suggested chronic pancreatitis (stones, lobularity, hyperechoic foci). FNA is repeated after six months if any focal lesion appeared.

## 2.3 Statistical Analysis of the Data

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0.

(Armonk, NY: IBM Corp). Qualitative data were described using number and percent and compared by Chi-square test, Fisher's Exact or Monte Carlo correction when appropriate. Quantitative data were described using range (minimum and maximum), mean and standard deviation and were compared by unpaired Student t-test. Significance of the obtained results was judged at the 5% level. The area under the ROC curve denotes the diagnostic performance of the test. The ROC curve allows also a comparison of performance between two tests.

### 3. RESULTS

Table 1 shows a statistically significant difference among both studied groups as regard sex and special habits, as most of patients with malignant disease group were males (76.3%) and smokers (65.8%). There was also statistically significant difference between the 2 studied groups as regard age. The patients of malignant disease group were older (mean age is  $59.3 \pm 8.15$  years). As regard co morbidities we found diabetes mellitus among 40% of studied patients, while hypertension and chronic liver disease among 24% for each of them. There was no significant difference between the 2 studied groups as regard co morbidities.

The commonest presenting symptom among studied patients was epigastric pain with a percentage of 76%. There was a statistical significant difference among both studied groups as regard presenting symptoms, as 86.8% of malignant pancreatic mass group presented with epigastric pain, 68.4% presented with jaundice and 28.9% of them presented with abdominal mass versus (41.7%, 16.7% and 0.0% respectively) of benign pancreatic mass group. There was no significant difference between the 2 studied groups as regard weight loss Table 1.

Table 2 shows a statistically significant difference among both studied groups in imaging and EUS assessment of biliary pancreatic system as liver deposit(s) detection was higher by EUS (24% vs 10%), CBD diameter was higher by EUS ( $7.74 \pm 3.29$  vs  $6.10 \pm 2.30$ ), and also detection of SPL was significantly higher by EUS than imaging (100% vs 78%).

There was no significant difference between both studied groups in imaging and EUS assessment of biliary pancreatic system for detection of CBD dilatation, IHBR dilatation, pancreatic duct dilatation, and lymph node enlargement.

Show a statistically significant difference among both malignant and benign pancreatic mass groups as regard site of the lesions detected by EUS, as 63.2% of patients with malignant lesions presented in the head of pancreas versus 33.3% of the benign group, while 50% of benign lesions presented diffusely in the whole organ versus 0.0% of malignant lesions.

Table 3 shows statistically significant difference in the size of SPL between the two studied groups as the mean  $\pm$  SD in benign pancreatic mass group was  $1.49 \pm 0.33$  (cm) while it was  $3.03 \pm 1.21$  (cm) in malignant pancreatic mass group.

Table 3 also shows a statistically significant difference in the size of SPL between the two studied groups as most benign pancreatic lesions (91.7%) had size  $< 2$  cm, while most malignant pancreatic lesions (71.1%) had size  $\geq 2$  cm.

Table 3 shows a statistically significant difference among both studied groups as regard area A, which represents the lesion. It significantly had lower elasticity in malignant pancreatic group ( $0.02 \pm 0.02$ ).

Table 3 also shows statistically significant difference among both studied groups as regard SR levels that was higher in malignant pancreatic mass group ( $39.20 \pm 43.30$ ). There was no significant difference between the two studied groups as regard area B, which represents the normal tissue surrounding lesion.

Table 4 shows a statistically significant difference among both studied groups as regard elastography scores as most of malignant pancreatic mass group patients (42.1%) have elastography score five versus 8.3% of benign pancreatic mass group, while most of benign pancreatic mass group patients (58.3%) have elastography score two versus 10.5% of malignant pancreatic mass group.

The commonest benign lesion found among studied patients was chronic pancreatitis among 18% of them, followed by autoimmune pancreatitis (6%). while the commonest malignant lesion found to be ductal adenocarcinoma among 58% of studied patients, followed by mucinous adenocarcinoma (12%), then lymphoma, NETs, and metastasis 2% for each of them.

**Table 1. Comparison between the two studied groups as regard demographic data and clinical data**

	Total (n = 50)		Malignant pancreatic mass group (n = 38)		Benign pancreatic mass group (n = 12)		P -value
	No.	%	No.	%	No.	%	
Sex							
Male	33	66.0	29	76.3	4	33.3	FEp=0.012*
Female	17	34.0	9	23.7	8	66.7	
Age (years)							
Min. – Max.	22.0 – 70.0		39.0 – 70.0		22.0 – 66.0		0.038*
Mean ± SD.	57.70 ± 9.87		59.32 ± 8.15		52.58 ± 13.15		
Special habit							
No	19	38.0	11	28.9	8	66.7	MCp=0.034*
Smoking	28	56.0	25	65.8	3	25.0	
Alcoholism	3	6.0	2	5.3	1	8.3	
Comorbidity							
Diabetes mellitus	20	40.0	14	36.8	6	50.0	FEp=0.506
Hypertension	12	24.0	10	26.3	2	16.7	FEp=0.705
Chronic liver disease	12	24.0	9	23.7	3	25.0	FEp=1.000
Comorbidity							
Epigastric pain	38	76.0	33	86.8	5	41.7	FEp=0.004*
Wt loss	17	34.0	12	31.6	5	41.7	FEp=0.728
Jaundice	28	56.0	26	68.4	2	16.7	0.002*
Abdominal mass	11	22.0	11	28.9	0	0.0	FEp=0.046*

$\chi^2$ : Chi square test, MC: Monte Carlo, FE: Fisher Exact, t: Student t-test, p: p value for comparing between the studied groups, \*: Statistically significant at  $p \leq 0.05$

**Table 2. Comparison between imaging and EUS examination as regard different parameters**

	Imaging (n = 50)		EUS (n = 50)		P –value
	No.	%	No.	%	
Liver deposit(s)					
No	45	90.0	38	76.0	0.039*
Yes	5	10.0	12	24.0	
CBD dilation					
Normal	38	76.0	31	62.0	0.130
Dilated	12	24.0	19	38.0	
CBD diameter (mm)					
Min. – Max.	3.0 –12.0		4.0 –16.0		<0.001*
Mean ± SD.	6.10 ±2.30		7.74± 3.29		
IHBR					
Normal	36	72.0	29	58.0	0.142
Dilated	14	28.0	21	42.0	
Pancreatic duct					
Normal	38	76.0	29	58.0	0.056
Dilated	12	24.0	21	42.0	
SPL					
No	11	22.0	0	0.0	0.001*
Yes	39	78.0	50	100.0	
Lymph node enlargement					
No	18	36.0	14	28.0	0.388
Peri pancreatic	23	46.0	24	48.0	
Celiac	6	12.0	11	22.0	0.063
Portahepatis	17	34.0	12	24.0	
					0.267

Z: Wilcoxon signed ranks test; p: p value for comparing between imaging and EUS; \*: Statistically significant at  $p \leq 0.05$ ; CBD: Common bile duct; IHBR: Intrahepatic biliary radicles; SPL: Solid pancreatic lesion.

**Table 3. Comparison between the two studied groups as regard site and size of SPL and EUS strain ratio detected by EUS**

	Total (n = 50)		Malignant pancreatic mass group (n = 38)		Benign pancreatic mass group (n = 12)		P –value
	No.	%	No.	%	No.	%	
Site							
Head of pancreas	28	56.0	24	63.2	4	33.3	0.001*
Body of pancreas	10	20.0	8	21.1	2	16.7	
Diffuse	6	12.0	0	0.0	6	50.0	
Tail of pancreas	3	6.0	3	7.9	0	0.0	
Uncinate process	3	6.0	3	7.9	0	0.0	
Size (cm)							
<2	22	44.0	11	28.9	11	91.7	<0.001*
≥2	28	56.0	27	71.1	1	8.3	
Min. – Max.	0.90 – 4.50		0.90 – 4.50		1.0 – 2.0		0.002*
Mean ± SD.	2.66 ± 1.26		3.03 ± 1.21		1.49 ± 0.33		
EUS strain ratio							
Area A							
Min. – Max.	0.01 – 0.56		0.01 – 0.09		0.01 – 0.56		<0.001*
Mean ± SD.	0.05 ± 0.11		0.02 ± 0.02		0.15 ± 0.18		
Area B							
Min. – Max.	0.05 – 2.04		0.09 – 2.04		0.05 – 0.50		0.086
Mean ± SD.	0.42 ± 0.36		0.47 ± 0.40		0.26 ± 0.13		
SR (B/A)							
Min. – Max.	0.77 – 223.3		5.27 – 223.30		0.77 – 22.77		<0.001*
Mean ± SD.	31.16 ± 40.42		39.20 ± 43.30		5.70 ± 6.38		

$\chi^2$ : Chi square test; MC: Monte Carlo, U: Mann Whitney test p: p value for comparing between the studied groups \*: Statistically significant at  $p \leq 0.05$

**Table 4. Comparison between the two studied groups as regard elastography score**

Elastography score	Total (n = 50)		Malignant pancreatic mass group (n = 38)		Benign pancreatic mass group (n = 12)		P –value
	No.	%	No.	%	No.	%	
1	2	4.0	0	0.0	2	16.7	MCp <0.001*
2	11	22.0	4	10.5	7	58.3	
3	6	12.0	5	13.2	1	8.3	
4	14	28.0	13	34.2	1	8.3	
5	17	34.0	16	42.1	1	8.3	
Min. – Max.	1.0 – 5.0		2.0 – 5.0		1.0 – 5.0		<0.001*
Mean ± SD.	3.66 ± 1.27		4.08 ± 1.0		2.33 ± 1.15		

$\chi^2$ : Chi square test; MC: Monte Carlo; U: Mann Whitney test; p: p value for comparing between the studied groups; \*: Statistically significant at  $p \leq 0.05$



Figs 1-3 show a statistically significant assessment of malignant pancreatic lesions using SR at cut-off level of 8.4, showing sensitivity of 92.1%, specificity of 83.3%, PPV of 94.6%, NPV of 76.9% and accuracy of 93.1%.

lesions was 75% of all true benigns detected, with accuracy 86% of the diagnostic tool.

Fig. 4 show a statistically significant assessment of malignant pancreatic lesions using elastography score  $\geq 3$ , showing high sensitivity of 89.4%, but ability of test to exclude benign

Figure show a statistically significant assessment of malignant pancreatic lesions using elastography score  $\geq 3$  and SR of 8.4, showing high sensitivity of 94.7%, and ability of test to exclude benign lesions was 83.3% of all true benign lesions detected, with accuracy 94.3% of the diagnostic tool.

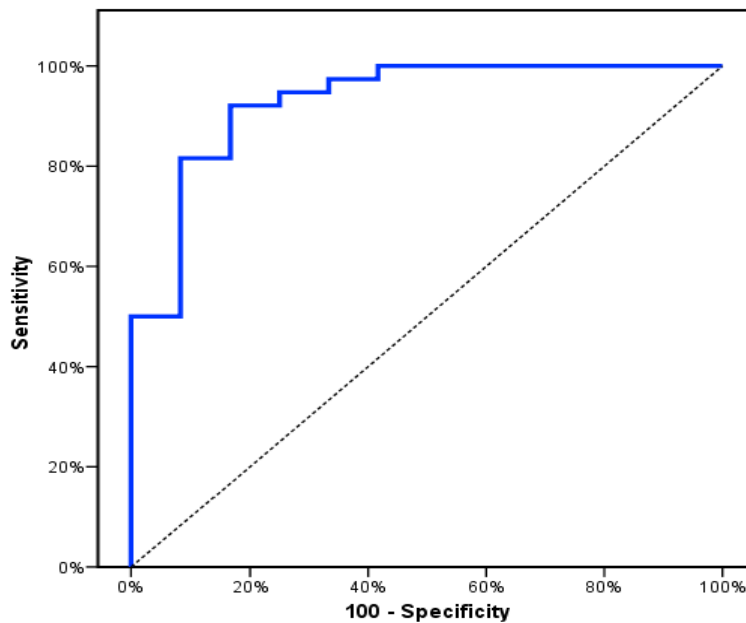


Fig. 1. ROC curve for SR as predictor of malignant pancreatic lesion

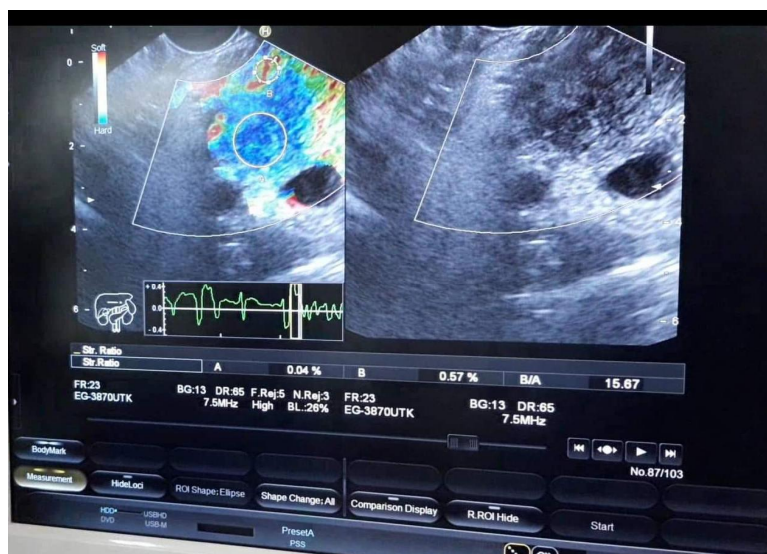


Fig. 2. EUS of pancreatic adenocarcinoma with high strain ratio

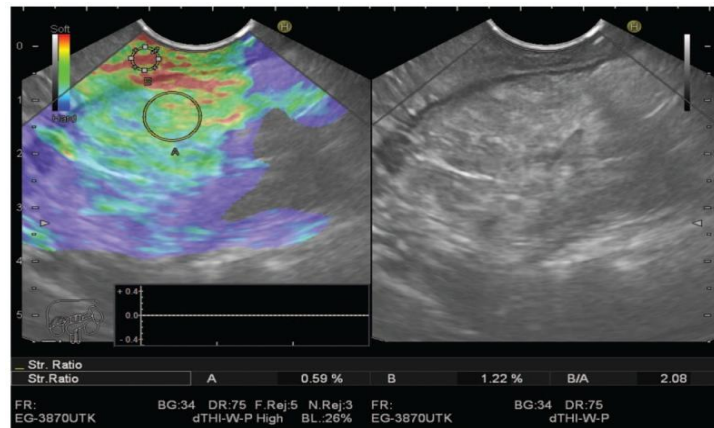


Fig. 3. EUS of chronic pancreatitis with low strain ratio

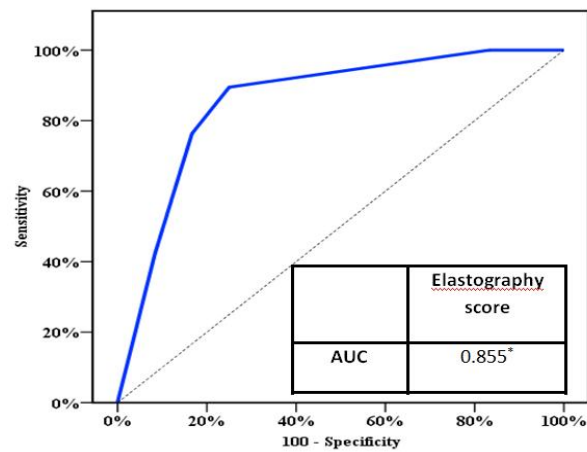


Fig. 4. ROC curve for Elastography score as predictor of malignant pancreatic lesion

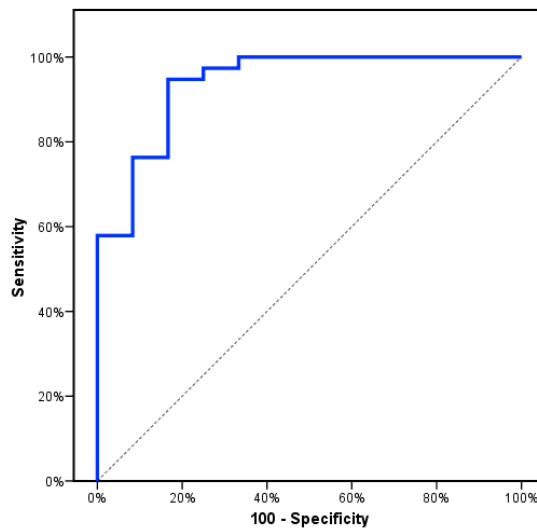


Fig. 5. ROC curve for SR + Elastography score as predictor of malignant pancreatic lesion

#### 4. DISCUSSION

It is always a great challenge to differentiate SPL; nevertheless, figuring out its final diagnosis is of critical importance, as it will have significant influence on the clinical decision makings [6].

Imaging methods play an important role in the diagnostic process of solid pancreatic tumors from the moment of detection and help evaluate the disease severity and plan the treatment. There is no perfect, widely accepted method that would meet the challenge of the assessment of pancreatic malignancy and the possible surgical approach to it [7].

Currently, endosonography is used for diagnosing and staging several pancreatic diseases. EUS-guided biopsies and fine needle aspirations are used to improve diagnostic performance of cases where a definitive diagnosis cannot be obtained through conventional EUS. However, it has several drawbacks, including learning curve, number of cases per year to maintaining efficacy, multiple needle passages to obtain adequate tissue, and iatrogenic complications [8].

In this prospective study conducted on 50 patients diagnosed by EUS to have SPL, we investigated the efficacy of endosonographic elastography and strain ratio for the differentiation of benign from malignant lesions.

In our study 38 patients were found to have malignant SPL with a percentage of (76 %) while 12 patients were found to have benign SPL with a percentage of (24 %), 29 cases of malignant lesions were diagnosed as ductal adenocarcinoma with a percentage of (76.3 %) being the most common malignant SPL.

On the other hand, 9 cases of benign lesions were diagnosed as chronic pancreatitis with a percentage of (75 %) being the most common benign SPL.

These results are compatible with what was reported by Giovannini et al., [9], Iglesias-Garcia et al., [10], Kongkam et al., [11], Okasha et al., [12], that reported in their study malignant SPL as (75.2%, 68.6%, 76.3%, 76%,) respectively, and benign SPL as (24.8%, 31.4%, 23.7%, 24%,) respectively, ductal adenocarcinoma was the most common malignant SPL (80%, 83%, 79.3%, 78.1,) respectively.

The results of our study and the above four mentioned studies confirming that most SPL are

malignant, and most common malignant is pancreatic ductal adenocarcinoma.

Analysis of demographic data of our study groups revealed that malignant SPL is much more common in males (76.3% versus 23.7%) while benign SPL is much more common in females (66.7% versus 33.3%), this is also compatible with the results obtained by Okasha et al., [13] with (78.9% males versus 21.1% females) in malignant SPL, while (53.1% females versus 46.9 % males) in benign SPL.

Not surprisingly, these results are in accordance with the fact that male gender is a non-modifiable risk factor for pancreatic carcinoma [14].

On further sub analysis, Patients of malignant SPL group in our study are of older age than benign SPL (mean age 59.3 years versus 52.5 years), this is compatible with the results obtained by, Iglesias-Garcia et al., [10], Kongkam et al., [11] and Dyrla et al., [15].

Regarding analysis of special habit in both groups, smoking is much more common in malignant SPL group (65.8% versus 25 %), in concordance with our study, Bartell et al., [16] also found similar results.

Wolfgang et al., [14] reported that pancreatic adenocarcinoma occur more in smoker males of older age between 60-80 years.

Analysis of results of clinical examination of our study groups revealed that, the most common presenting symptoms in our studied patients were epigastric pain, jaundice and weight loss with a percentage of (76%, 56% and 34% respectively), this was similar to Kongkam et al., [11] who found that these three presenting symptoms are the most common in his studied groups.

Regarding imaging (CT, MRI) assessment of our studied patients, it was done for the entire 50 patients and SPL was diagnosed in 39 patients with a percentage of (78%), but it failed to reach a diagnosis in 11 patients (22%), those patients showed small (< 2cm) SPL by EUS evaluation. This is not in concordance with Deerenberg et al., [17] who found that imaging failed to establish a diagnosis in their study in only (11%) of patients suspected to have pancreatic masses, this may be explained by variability of radiologists and radiology centers in which imaging was done in our study, and also difference in number of patients included in his study.

Analysis of results of EUS examination revealed that, SPL was detected in all 50 patients (100%) compared to (78%) of SPL detected by imaging studies, Al-Haddad et al., [18] stated that EUS is especially useful for identification of small tumors ( $\leq 2$  cm in diameter) that have been undetected by other imaging studies.

On further sub analysis of EUS results, EUS detected liver deposits in 12 patients out of the 38 patients with malignant SPL with a percentage of (31.6%) while imaging could detect only 5 cases out of them (13.2%), DeWitt et al., [19] stated that EUS may diagnose and sample metastatic liver deposits, ascites, or distant lymph nodes missed by other imaging modalities and therefore meticulous search for these lesions should be always done as it may change the whole management of patients with malignant SPL.

As regard the location of SPL, they located in the head, body, diffusely involving the pancreas, tail and the uncinate process with a percentage of (56%, 20%, 12%, 6% and 6%) respectively and this was similar to the study conducted by Kongkam et al., [11] who found the distribution of SPL in the head, body, tail and the uncinate process of the pancreas with a percentage of (60.5 %, 21%, 13.1% and 5.3%) respectively.

Also, Iglesias-Garcia et al., [10], Opacic et al., [20] Dyrła et al., [15], and Bartell et al., [16], showed similar results to our study as regard location of SPL confirming that head of pancreas is the most common site of SPL.

Comparison between the two studied groups as regard size of SPL, there was significant difference between both groups as the mean  $\pm$  SD was (3.03  $\pm$  1.21 cm) and (1.49  $\pm$  0.33 cm) for malignant and benign SPL respectively, similar results were also found by Kongkam et al., [11] who found the mean  $\pm$  SD of malignant and benign SPL to be (3.6  $\pm$  1.52 cm) and (2.79  $\pm$  1.36 cm) respectively, and also by Dyrła et al., [15] where mean  $\pm$  SD of malignant and benign SPL found to be (3.91  $\pm$  1.15 cm) and (3.53  $\pm$  1.05 cm) respectively.

Analysis of results of qualitative elastography score in our study groups showed a sensitivity, specificity, PPV, NPV, and accuracy of (89.4%, 75%, 91.8%, 69.2%, and 86%) respectively, many studies showed results that were in concordance with our results as Iglesias-Garcia et al., [10], Ying et al., [21], Lu et al., [6], and Okasha et al., [12].

Interestingly, in contrast to our study and the above mentioned four studies, Dawwas et al., [22] reported a sensitivity of 100% for EUS elastography in diagnosis of SPL but with a very low specificity of 16.7%.

This discrepancy between our results and Dawwas et al., [22] clarify that there is still a problem when using the elastic score due to its subjectivity.

On further sub analysis of elastography score, 25% (3/12) of patients with benign SPL had scores from 3 to 5 which is supposed to indicate malignancy. This could be explained by the presence of calcifications and fibrous strands, which increase the score.

Also, 16.7% (2/12) with benign SPL scored 1 although this score is supposed to reflect normal pancreatic tissue.

On the other hand, 10.5% (4/38) of patients with malignant SPL had score of 2, although this score is supposed to reflect benign SPL. In a study done by Giovannini et al., [9]. 16.1% of the lesions that had scores of 1 or 2 were malignant. This renders elastography scoreless specific although it has high sensitivity; in our study sensitivity was 89.4% despite low specificity (75%).

As an elastography score is a very subjective technique and depends on the endosonographer in most of the cases, <sup>(204)</sup> another technique was added to increase its specificity to reach a better diagnosis. The strain ratio with different cut off levels was mentioned in many studies by, Giovannini et al., [9], Iglesias-Garcia et al., [10], and Dawwas et al., [22].

Analysis of results of SR in our study revealed that, the best cut off value to differentiate benign from malignant SPL was 8.4, it has a sensitivity of 92.1%, specificity of 83.3%, PPV of 94.6%, NPV of 76.9% and accuracy of 93.1%.

Review of relevant publications revealed that, other studies have analyzed the usefulness of SR. Iglesias-Garcia et al., [10] published the SR results of 86 consecutive patients with SPL, at a cut off value of 6.04, sensitivity, specificity, PPV, NPV, and accuracy were (100%, 92.9%, 96.7%, 100%, and 97.7%) respectively, also, Ying et al., [21], showed that SR had a sensitivity, specificity, PPV, and NPP of (96%, 76%, 78%, and 95%) respectively.

By contrast, Hirche et al., [23], showed a low sensitivity and specificity of SR (41% and 53%) respectively, and gave an explanation of his results that the size of evaluated tumors appeared as a significant limitation of the method. In case of a tumor > 3.5 cm, the method failed to include the whole tumor and to select a sufficiently large area of healthy tissue surrounding the lesion, which is used as a reference.

On further sub analysis of SR results, our study showed that there was a statistical significant difference between both studied groups as regard SR levels, the mean  $\pm$  SD of SR in malignant SPL group was  $39.20 \pm 43.30$  while it was  $5.70 \pm 6.38$  in benign SPL group (P value <0.001), these results were in concordance with the results of Dyrila et al [15] where mean  $\pm$  SD of SR in malignant SPL group was  $41.05 \pm 17.97$  while it was  $5.51 \pm 1.45$  in benign SPL group, similar results were also reported by Iglesias-Garcia et al., [10], Itokawa et al., [24], and Okasha et al., [12].

To increase the efficacy and accuracy of the diagnosis of SPL, we combined elastography score with the SR level of 8.4 to have a sensitivity of 94%, a specificity of 83%, a PPV of 94% and a NPV of 83% and an accuracy of 94.3%. In concordance with our results, Okasha et al., [12] also found that combination of elastography score with SR increased the efficacy and accuracy of diagnosis.

## 5. CONCLUSIONS

EUS elastography is a sensitive noninvasive method for evaluation of SPL. EUS elastography with strain ratio provides very useful and valuable information on the differentiation of benign from malignant pancreatic 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 SPL.

## CONSENT AND ETHICAL APPROVAL

Written informed consent for participation in the study was obtained from all patients and approval of the Ethical Committee.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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