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Original article

Accuracy of Endoscopic Ultrasound Elastography for Evaluation of Pancreatic Masses

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Abstract

Background: Endoscopic ultrasound elastography (EUS) is an imaging modality that has recently been proposed for the visualization and evaluation of tissue elasticity. This study aimed to assess the role of EUS elastography in the diagnosis of pancreatic mass lesions in comparison to EUS fine needle aspiration (FNA) biopsy and to differentiate between benign and malignant lesions. Methods: This was a cross-sectional study that was conducted on 53 patients are coming to hospital suspected to have pancreatic mass clinically (jaundice, cachexia epigastric pain) or radiological (ultrasound, Computed tomography (CT) and/or Magnetic resonance imaging (MRI) of the abdomen). EUS was done and strain ratio was calculated and fine needle aspiration was done for histopathological examination. Results: Regarding the Pancreatic FL on EUS elastography was hard in 42 (79.25%) patients and soft in 11 (20.75%) patients. Strain ratio of hard Pancreatic FL was significantly higher than soft Pancreatic FL. The type of lesion by histopathological examination, 37(69.81%) patients had adenocarcinoma, 11(20.75%) patients had chronic pancreatitis and 5(9.4%) had neuroendocrinal tumors. EUS- strain ratio can significantly predict the type of Pancreatic FL (malignant or benign) with AUC =0.909, with 100 % sensitivity, 100%specificity, 98%PPV and 93.7%NPV, P value <0.05. There is high concordance between Endoscopic Ultrasound Elastography and biopsy outcomes, as indicated by a Concordance Correlation Coefficient (0.95). Conclusion: FNA biopsy can be replaced by EUS elastography in diagnosis of pancreatic masse and distinction of benign and malignancy.

Keywords: Abdominal imaging; Endoscopic Ultrasound Elastography; Pancreatic Masses.

Introduction

Endoscopic ultrasound (EUS) was used firstly in 1980s as a diagnostic imaging technique for pancreatic lesions (1). It has the ability to detect the histological layers of the gastrointestinal (GI) tract wall as well as the periluminal structures (2). EUS has been used to perform fine needle aspiration (FNA) from lesions that are difficult to access by conventional methods (3).

EUS has the advantage of using both ultrasound and endoscopy to give the exact diagnostic features of the GI tract. EUS role has grown dramatically to include both diagnostic and therapeutic advantage in **GI**, pancreatic and hepatobiliary tree diseases (4).

The use of EUS was not limited to visualization only, but also in obtaining tissue biopsy for diagnostic purpose through EUS guided **FNA**, and it has played a major role in revolutionizing the diagnosis of focal hepatic lesions as it is a minimally invasive procedure (5).

Abdominal imaging [computed tomography(CT), magnetic resonance imaging (MRI), and transabdominal ultrasonography (USG)] are the diagnostic tests of choice to detect pancreatic lesions suspicious of metastasis (6).

Unfortunately, Differential diagnosis between benign and malignant lymph nodes and focal pancreatic masses based on the EUS appearance is difficult and frequently requires EUS-guided fine needle aspiration (EUS-FNA) for confirmation of malignancy (7).

EUS elastography is an imaging modality that has recently been proposed for the visualization and evaluation of tissue elasticity. This method enables areas with varying elasticities to be differentiated within a target organ. The principle of elastography is based on the assumption that compression of a target tissue by an echo-endoscopic probe creates a strain (i.e. displacement of one tissue structure by another) that differs according to the hardness and softness of the tissue. Thus, by calculating the elasticity of tissue, it is possible to differentiate benign (soft) tissue from malignant (hard) tissue (8).

The purpose of this study was to assess the role of **EUS** elastography in the diagnosis of pancreatic mass lesions in comparison to **EUS-FNA** biopsy and to differentiate between benign and malignant lesions.

Patients and methods

This was a cross-sectional study designed to assess the role of **EUS** elastography in the diagnosis of pancreatic mass lesions in comparison to **EUS-FNA** biopsy and to differentiate between benign and malignant lesions.

This cross-sectional study that was conducted on 53 patients attending in

Kobry El Kobba Hospital and EL Maadi hospital on duration from January 2020 to December 2021. All patients are coming to hospital suspected to have pancreatic mass clinically (jaundice, cachexia epigastric pain) or radiological (ultrasound, Computed tomography (CT) and/or Magnetic resonance imaging (MRI) of the abdomen). The patients were consecutive selected and an informed written consent was obtained from the patients. Every patient received an explanation of the purpose of the study and had a secret code number. The study was done after being approved by the Research Ethics Committee, Faculty of Medicine, Benha University.

All patients where were contraindicating **EUS** guided fine-needle aspiration were excluded from this work (platelets less than 50,000, prothrombin time more than 16 second or INR more than 2)

Approval Code :-MS.35.2.2022

Methodology:

All patients were subjected to the following: **Patient History:** a detailed patient history, which included age, gender, clinical history straining on (yellowish discoloration of skin and mucous membrane, abdominal pain or enlargement, weight loss), comorbidity (diabetes mellitus, hypertension, hepatitis B and/or C virus infection). **Clinical general examination**: straining on (vital sign, jaundice, pallor, and cachexia). **Clinical local abdominal examination**: straining on (organomegaly, abdominal pain, and ascites). Laboratory investigations: Complete blood count (CBC), prothrombin time (PT) and International normalized ratio (INR), serum creatinine and blood urea, serum albumin, alanine aminotransferase (ALT), aspartate transaminase (AST), serum amylase and serum lipase, tumor markers: (Carbohydrate antigen (CA) 19-9, Carcinoembryonic Antigen (CEA) and alpha-fetoproteins (AFP)).

Abdominal Ultrasound, Triphasic CT and MRI: for evaluation of pancreatic lesions: site, size, echogenicity (Hypoechoic, Hyperechoic, Isoechoic) and doppler signal, liver, spleen, kidney: (Site, size, echogenicity (Hypoechoic, Hyperechoic, Isoechoic) and doppler signal, metastasis (Site, size, echogenicity (Hypoechoic, Hyperechoic, Isoechoic) and doppler signal, lymphadenopathy (site, size, Hypoechoic, Hyperechoic, Isoechoic) and ascites.

Endoscopic Ultrasound:

It was ideally performed following an overnight, patients should avoid solid foods for 6 hours and liquids (except sips of water to ingest medications) for 4 hours before the procedure. The patient lied on the left lateral position. Heavier sedation may be required for EUS than for routine endoscopic procedures because of the often-longer examination time and the need to minimize movement of the patient. All patients were examined by, Hitachi Avius (EZU-

MT29-S1), US machine. The shaft of the endoscope pass throw the esophagus then to the stomach and examine the pancreas, then the scope pass to the duodenum and examine the rest of pancreas (9).

During EUS examination the pancreas was examined thoroughly to detect pancreatic focal lesions (FL).

Endoscopic Ultrasound elastography: The pancreatic FLs by calculating the elasticity of tissue, we could differentiate benign (soft) tissue from malignant (hard) tissue. By using the strain ratio in differentiating benign from malignant pancreatic masses (quantitative analysis of tissue elasticity).

Fine aspiration needles: Several needles were used for performing **EUS-FNA** biopsy, and each needle uses a catheter assembly with an attached handle mechanism that secures to the biopsy channel's lock adapter on the echoendoscope. Needles range in size from 19 to 25 gauge with a depth of penetration of up to 10 cm. Selecting a specific needle size depends on the target lesion type, lesion location, and endoscopist preference. Smaller needles was more easily directed and inserted into target lesions than larger needles.

Histpatholgical examination: All specimens were examined in hospital histopathological laboratory to determine the type of lesions.

Statistical analysis

Statistical analysis was done by SPSS v25 (IBM©, Chicago, IL, USA). Descriptive statistics included mean and standard deviation (± SD) for numerical data and frequency/percentage for non-numerical data. The unpaired student t-test used to compare two groups in quantitative data, Chi-square (x^2) used for comparison between two groups as regards qualitative data. Mann Whitney-test used to analyze quantitative non-parametric data were presented as the median and interquartile range (IQR). p-value considered significant if <0.05.

Results

The current study was carried out on 53 patients suspected to have pancreatic mass clinically (jaundice, cachexia epigastric pain) or radiological (ultrasound, Computed tomography (CT) and/or MRI of the abdomen). Their mean age was 60.4 ± 9.34 years. There were 7 (13.21%) females and 46 (86.79%) males. Regarding residence, 14 (26.42%) lived in urban areas and 39 (73.58%) lived in rural areas. 31 (58.49%) were smokers. The most common presentation was patients with abdominal pain 45 (84.91%) followed by weight loss, 40 (75.47%), then patients with jaundice, 33 (62.26%), then patients presented with abdominal enlargement 13 (24.53%). The past history of the studied patients, diabetes mellitus was the higher incidence in patients. Table 1

Regarding the EUS data, pancreatic FL were presented in all patients. The size of the primary lesion ranged from 2-30.55 mm^2 with a mean of 16.265 mm^2.

The primary lesion was located at the body in 3 (5.66%) patients, at the body and tail in 2 (3.77%) patients, at the head in 43 (81.13%) patients, at the pancreatic tail in 2 (3.77%) patients and at the tail in 2 (3.77%) patients. Table 3

Regarding the Echopattern of primary lesion, it was hyperechoic in 8 (15.09%) patients and hypoechoic in 45 (84.91%) patients. EUS lymphadenopathy was presented in 27 (50.94%) patients. Table 2

The pancreatic FL on EUS elastography was hard in 42 (79.25%) patients and soft in 11 (20.75%) patients. Strain ratio of hard Pancreatic FL was significantly higher than soft Pancreatic FL. Table 5 figure 2&3

Regarding the type of lesion, 37(69.81%) patients had adenocarcinoma, 11 (20.75%) patients had Chronic pancreatitis and 5 (9.4%) had neuroendocrinal tumors. Table 4

EUS- strain ratio can significantly predict the type of Pancreatic FL (malignant or benign) with AUC =0.909 and P value <0.001, with 100 % sensitivity, 100%specificity, 98%PPV and 93.7%NPV. p-value considered significant if <0.05. Table 6 - Figure 1

Table 1: Demographic data, Clinical Presentation, Past history, Clinical signs, Local examination of the studied patients

N = 53		
Age (years)	**Mean ± SD**	60.4 ± 9.34
	Range	39 – 86
Gender	**Female**	7 (13.21%)
	Male	46 (86.79%)
Residence	**Urban**	14 (26.42%)
	Rural	39 (73.58%)
Smoking		31 (58.49%)
Abdominal pain		45 (84.91%)
Weight loss		40 (75.47%)
Yellowish discoloration of sclera		33 (62.26%)
Abdominal enlargement		13 (24.53%)
Hypertension		**27 (50.94%)**
Diabetes mellitus		**29 (54.72%)**
Hepatitis C virus infection		**12 (22.64%)**
Hepatitis B virus infection		**4 (7.55%)**
Operations		**17 (32.08%)**

Table 2: Laboratory investigation of the studied patients

		N=53
Hb (g/dL)	**Mean ± SD**	11.7 ± 2.28
	Range	6.8 - 15.4
PLT (*10^3cells/ml)	**Mean ± SD**	227.9 ± 108.63
	Range	8.3 – 570
TLC (*10^3cells/ml)	**Mean ± SD**	16.1 ± 48.24
	Range	3.2 – 351
PT (s)	**Mean ± SD**	17.3 ± 23.06
	Range	11.1 – 174
	Median (IQR)	13.2 (11.8 - 13.6)
INR	**Mean ± SD**	1.2 ± 0.28
	Range	0.7 - 2.2
ALT (U/L)	**Mean ± SD**	77.4 ± 85.52
	Range	11 – 521
	Median (IQR)	50 (34 – 94)
AST (U/L)	**Mean ± SD**	69.7 ± 46.24
	Range	17 – 220
	Median (IQR)	53 (34 – 92)
Serum Albumin (g/dL)	**Mean ± SD**	3.7 ± 0.77
	Range	2.1 – 5
Serum Creatinine (mg/dL)	**Mean ± SD**	1.1 ± 0.67
	Range	0.5 – 4
Total Bilirubin (µmol/L)	**Mean ± SD**	7.9 ± 6.67
	Range	0.5 – 21
	Median (IQR)	6.3 (1.2-13.3)
Direct Bilirubin (µmol/L)	**Mean ± SD**	5.8 ± 5.03
	Range	0.1 – 18
	Median (IQR)	4.6 (0.9-10.2)
Serum Amylase (U/L)	**Mean ± SD**	447.3 ± 695.84
	Range	0.7 – 3434
	Median (IQR)	95 (50-423)
Serum Lipase (U/L)	**Mean ± SD**	455.2 ± 543.84
	Range	23 – 2132
	Median (IQR)	232 (93 – 532)
Blood urea (mmol/L)	**Mean ± SD**	55.1 ± 44.39
	Range	16 – 245
	Median (IQR)	44 (27 – 64)
CA 19-9 (U/mL)	**Mean ± SD**	691.6 ± 822.28
	Range	0 – 3914
	Median (IQR)	374 (43 – 974)
CEA (ng/mL)	**Mean ± SD**	35.2 ± 21.9
	Range	0 – 89
	Median (IQR)	33 (23 – 43)
AFP (ng/mL)	**Mean ± SD**	37.3 ± 101.91
	Range	0 – 579
	Median (IQR)	4 (2.9 – 11)

Hb: haemoglobin, PLT: platelets, TLC: total leukocyte count, PT: Prothrombin Time, INR: international normalized ratio, ALT: alanine transaminase, AST: aspartate transferase, CA: Carbohydrate antigen, CEA: Carcinoembryonic Antigen. AFP: Alpha Fetoprotein. SD: standard deviation. IQR: interquartile range.

Table 3: Pancreatic FL EUS data of the studied patients

N = 53		
Pancreatic FL		53 (100%)
Size of the primary lesion (mm)	**Mean ± SD**	16.265
	Range	4.96-30.55
Site of the primary lesion	**Body**	3 (5.66%)
	Body and tail	3 (3.77%)
	Head	43 (81.13%)
	Pancreatic tail	2 (3.77%)
	Tail	2 (3.77%)
Echopattern of primary lesion	**Hyperechoic**	8 (15.09%)
	Hypoechoic	45 (84.91%)
EUS lymphadenopathy		27 (50.94%)

FL: focal lesion

Table 4: Results of Pancreatic FL on EUS elastography of the studied patients

N=53		**P value**
Pancreatic FL on EUS elastography		
Hard	**Soft**	
42 (79.25%)	11 (20.75%)	
Strain ratio	**Strain ratio**	
68-93	12-32	<0.001
81.54 ± 7.87	23.14±6.83	

Table 5: Diagnostic accuracy of EUS -strain ratio for prediction of the type of Pancreatic FL (malignant or benign)

	Cut of value	**AUC**	**P value**	**Sensitivity**	**Specificity**	**PPV**	**NPV**
EUS- strain ratio	≥12	0.909	**<0.001**	100%	100%	98%	93.7%

EUS: Endoscopic Ultrasound Elastography, FL: focal lesion, AUC: area under the curve, PPB: positive predictive value, NPV: negative predictive value, *: statistically significant as P value <0.05

Table 6: Concordance of EUS elastography with the result of biopsy

Concordance correlation coefficient	0.95
95% Confidence interval	0.8094 - 0.9321
Pearson ρ (precision)	0.8853
Bias correction factor Cb (accuracy)	1.0000

EUS: Endoscopic Ultrasound Elastography

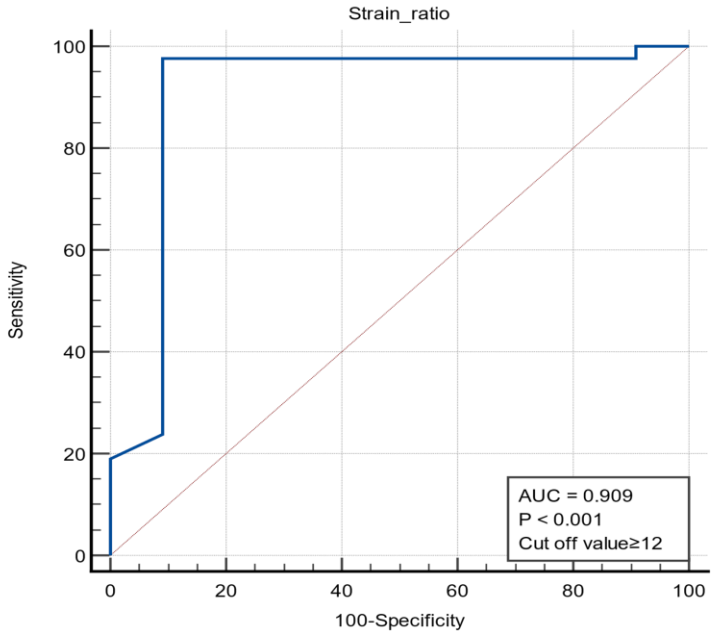

Figure 1: ROC curve analysis of EUS- strain ratio for prediction of the type of Pancreatic FL (malignant or benign)

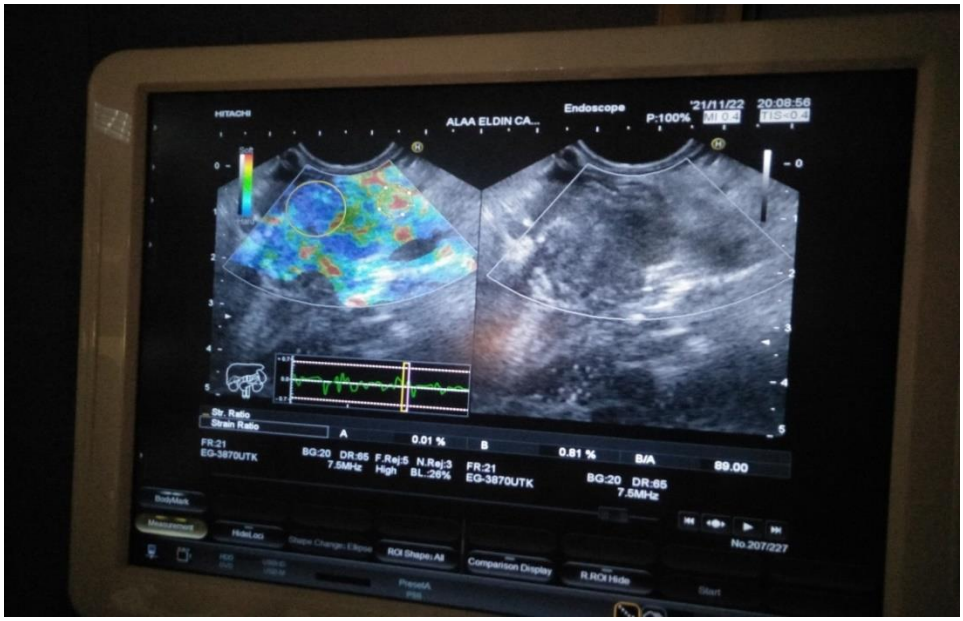

Figure: 2 EUS strain elastography show bluish discoloration on hard pancreatic lesion (strain ratio: 89)

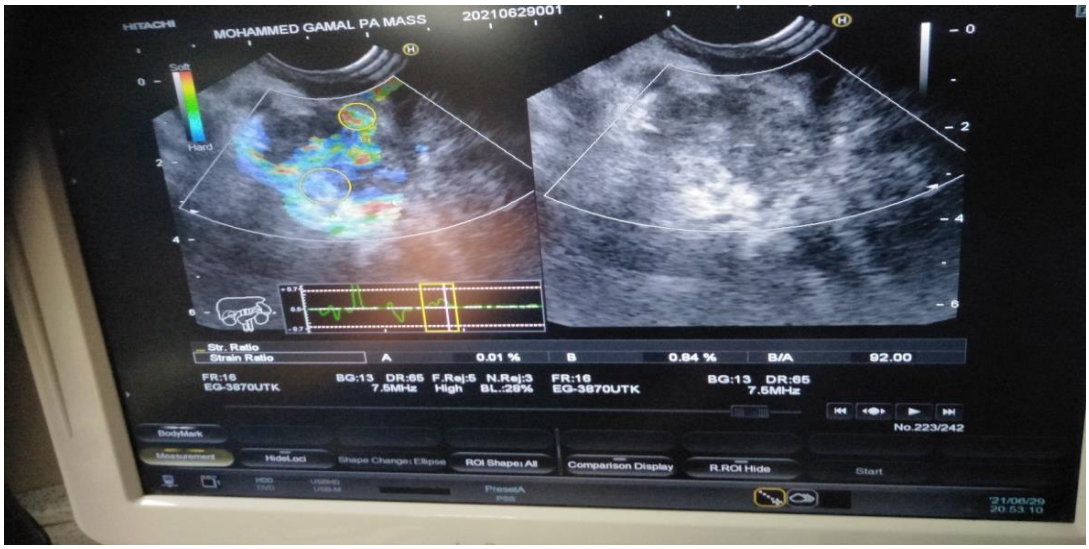

Figure: 3 EUS strain elastography show bluish discoloration on hard pancreatic lesion (strain ratio: 92)

Discussion

By EUS examination, the pancreatic FL was presented in all patients. The size of the primary lesion ranged from 2-30.55 mm with a mean of 16.265 mm., and the site of the lesion, The primary lesion was located at the head in 43 (81.13%) patients, at the body in 6 (11.3%) patients, at the pancreatic tail in 4 (7.5%).

A group of researchers found that the mass lesion diameter was 31.7 mm; SD = 13.2 mm. FLs were most frequently located in the head of the pancreas (51.5%), less frequently in the body (39.5%), whereas only 9% of them were located in the pancreatic tail (10).

The pancreatic FL on EUS elastography was hard in 42 (79.25%) patients and soft in 11 (20.75%) patients and this result when it compared with the result of biopsy, the hard lesions were malignant, and the soft lesions were benign. So EUS can significantly predict the incidence of pancreatic FL with AUC 0.943 and P value <0.001, with 98 % sensitivity, 91% specificity, 96% accuracy, 98% PPV and 91% NPV significant as P value <0. 05. There was a strong concordance between EUS elastography and the result of biopsy in the diagnosis of pancreatic FL.

Researchers found that the sensitivity and specificity of EUS elastography to differentiate benign from malignant pancreatic lesions are 92.3% and 80.0%, respectively, compared to 92.3% and 68.9%, respectively, for the conventional B-mode images. The sensitivity and specificity of EUS elastography to differentiate benign from malignant lymph nodes was 91.8% and 82.5%, respectively, compared to 78.6% and 50.0%, respectively, for the B-mode images (11).

Regarding the results of biopsy, malignancy was presented in 42 (79.25%) mostly pancreatic adenocarcinomas patients where 11 (20.75%) had no malignancy.

In agreement with our results Pishvaian show that the most common type of cancer pancreas was adenocarcinoma, accounts for about 90% of cases, and the term "pancreatic cancer" is sometimes used to refer only to that type (12).

Endoscopic ultrasound elastography must be done in all patients examined by endoscopic ultrasound have pancreatic mass especially if fine needle aspiration was risky (7).

In scientific research, it was shown that in patients with small solid pancreatic lesions, EUS elastography can rule out malignancy with a high level of certainty if the lesion appears soft. (12)

Endoscopic ultrasound elastogaphy in diagnosis of pancreatic mass and differentiate between benign or malignancy has high sensitivity and specificity, and it has been proved to be a safe and useful method, in comparison of endoscopic ultrasound fine needle aspiration biopsy.

There is high concordance between Endoscopic Ultrasound Elastography and biopsy outcomes, as indicated by a Concordance Correlation Coefficient (0.95).

EUS-elastography had a sensitivity of 86–96% and a specificity of 43–66%, whereas EUS-FNA had a sensitivity of 82–90% and a specificity of 100%. However, the combination of EUS-elastography and EUS-FNA showed a high negative predictive value to exclude malignant pancreatic lesions (13).

We can replace fine needle aspiration biopsy by endoscopic ultrasound elastography in diagnosis of pancreatic mass and distinction of benign and malignancy especially if it is not necessary or if there is risk for its procedure.

Moreover, a study in patients with pancreatic masses and negative cytopathology on EUS-FNA found that the combination of CH-EUS and EUS-elastography had a sensitivity of 88.9% and a specificity of 100%. Thus, EUS-elastography may complement EUS-FNA as a diagnostic tool. (14)

Conclusion

In conclusion, our study demonstrates that **FNA** biopsy can be replaced by **EUS** elastography in diagnosis of pancreatic masse and distinction of benign and malignancy especially if it not necessary or if there is risk for its procedure.

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