Role of Endoscopic Ultrasound Elastography Strain Histograms in the Evaluation of Patients with Pancreatic Masses

Hussein Hassan Okasha[1], *Hussein El-Amin*[2], *Zain El-Abdeen Sayed*[2], *Ahmed Abd ElFadeel Maghraby*[2]

[1]Hepatogastroenterology Unit, Department of Internal Medicine, Kasr Al-Ainy School of Medicine, Cairo University, Cairo, Egypt
[2]Hepatogastroenterology Unit, Department of Internal Medicine, Assiut University Hospital, Egypt

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ABSTRACT

Background: *The Endoscopic Ultrasound (EUS) quantitative elastography strain ratio (SR) and strain histogram (SH) methods for non-invasive pancreatic masses differentiation have been recently developed. The aim of this research was to investigate the accuracy of the diagnostic differentiation methods for patients with pancreatic masses, based on the EUS SR and SH.*

Methods: *This is a prospective study involving 100 cases with pancreatic masses. Patients were classified into 2 groups: group that was diagnosed with pancreatic malignancy with positive histopathology by biopsy obtained by fine-needle aspiration or postoperative pathology (72 patients) and the group diagnosed with pancreatitis with negative pathology and follow-up for at least 1 year (28 patients).*

Results: *Based on the ROC curve, the cut-off point for Mode 1 was set at 97. Values under it showed the presence of malignant pancreatic masses. Mode 1 achieved a sensitivity of 89% and a specificity of 43% with an overall accuracy of 76%. The predictive positive value was 70%, and the predictive negative value was 60%. The cut-off point for SR was set at 3.04, and the values were equal or above the suggested pancreatic malignancy. The SR achieved a sensitivity of 95.83%, a specificity of 61%, with an overall accuracy of 86%. The predictive positive and negative values were 86.2% and 85%, respectively.*

Conclusion: *Mode 1 SH showed good sensitivity in the identification of pancreatic malignant tumors but were disappointingly of low specificity. Higher sensitivity, specificity, and overall accuracy were obtained by using the SR.*

Keywords: *Strain histogram, strain ratio, solid pancreatic lesions*

INTRODUCTION

Early and proper diagnosis of solid pancreatic lesions is mandatory as most cases are diagnosed at a late stage with no operable solutions.

Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) is approved as one of the gold standard tests in the diagnosis of solid pancreatic masses[1] with a sensitivity, specificity, and negative predictive value (NPV) of 91%, 94%, and 85%, respectively, and so negative results cannot exclude malignancy.[2]

Elastography is used to assist in diagnosis by evaluating tissue elastic properties without being an invasive measure. It is considered a qualitative measure to distinguish between malignant and benign lesions. Giovannini and colleagues developed a 5-point scoring system, but it is still very subjective.[3]

Strain elastography is a quantitative method that is used to evaluate tissue stiffness by the degree of its distortion under manual compression.[4,5] Strain ratio (SR) is the comparison between an area of interest and a reference control area in a greyscale image.

The other quantitative method is strain histogram (SH). Many of the new generation ultrasound systems have incorporated strain (hue) histogram calculation software, which automatically calculates the graph in real time. Within this research, we analyzed the accuracy of the strain ratio (SR) and strain histogram (SH) based on EUS methods to identify and differentiate patients with pancreatic masses.

PATIENTS AND METHODS

Patients

This prospective research was carried on from March 2017 to January 2019, after obtaining the approval of our

Corresponding author: ***Ahmed Abd ElFadeel Maghraby****, e-mail:* ***dr_magraby@yahoo.com***
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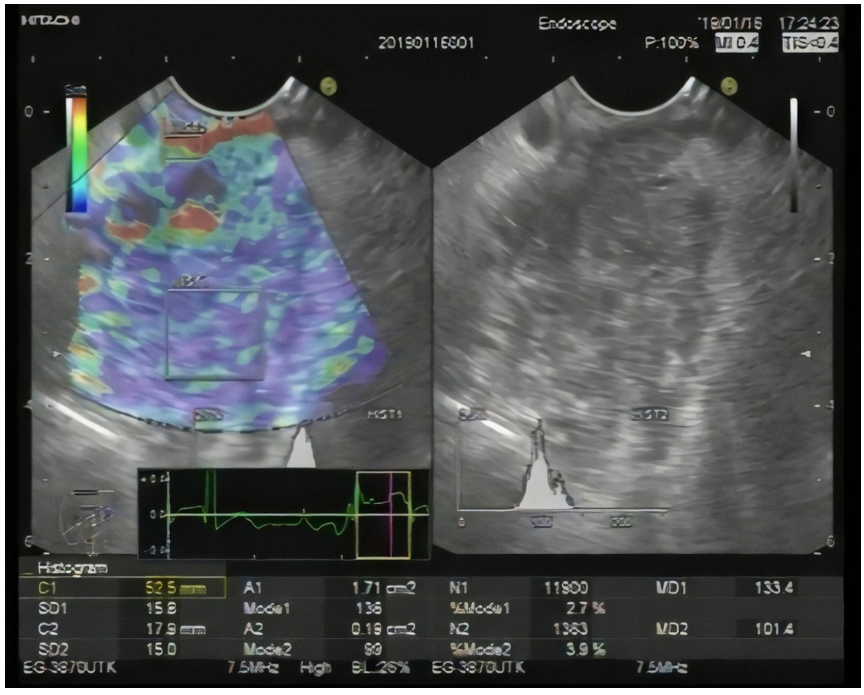

Figure 1. Strain histogram of a pancreatic head mass.

ethics committee. Prior to study registration, all patients participating in the study gave written consent.

Inclusion criteria were patients above 18 years old, with solid pancreatic lesions diagnosed with imaging modalities, and acceptance to participate in the study.

Exclusion criteria were cystic-component tumors, patients with procedure contraindications, and those who refused to participate.

Main Points

- *Strain histogram is a promising new semi-quantitative technique to evaluate tissue stiffness of pancreatic lesions.*
- *This technique is used for diagnostic differentiation between benign and malignant pancreatic masses.*
- *In our study, strain histogram showed good sensitivity in identifying pancreatic malignant tumors but were disappointingly of low specificity. Higher sensitivity, specificity, and overall accuracy were obtained by using the strain ratio.*
- *Till now, it is not a replacement of tissue acquisition and more prospective studies are needed to standardize the cut-off value for accurate differentiation between benign and malignant pancreatic lesions.*

Methods

On the day of the EUS examination, patients who decided to take part in the research were assigned to the endoscopy room after approval by the ethics committee.

Our analysis included 100 patients. Both endosonographic measurements were performed by 2 qualified EUS examiners. Pentax linear probes FG-38 UX and EG-3870 UTK EUS with Hitachi Avius ultrasound devices were used to capture elastography images.

The Cook needle 22 G (Echotip, Wilson-Cook, Winston Salem, NC) was used for EUS FNA. This type and size of needles is especially suitable for sampling the uncinate process masses with an angulated echoendoscope in the deep second part of the duodenum. Pancreatic lesions have been evaluated with elastography.

SH (Figure 1) was automatically determined by software in areas of interest selected by the examiner and presented as the average values (Mode 1 over the lesion and Mode 2 over a homogenous portion of the pancreas adjacent to the area of interest). SR (Figure 2) was later determined by dividing the B2 value by the B1 value for every patient.

SH is measured by obtaining different strain patterns, and then statistical analysis is done to reach quantitative

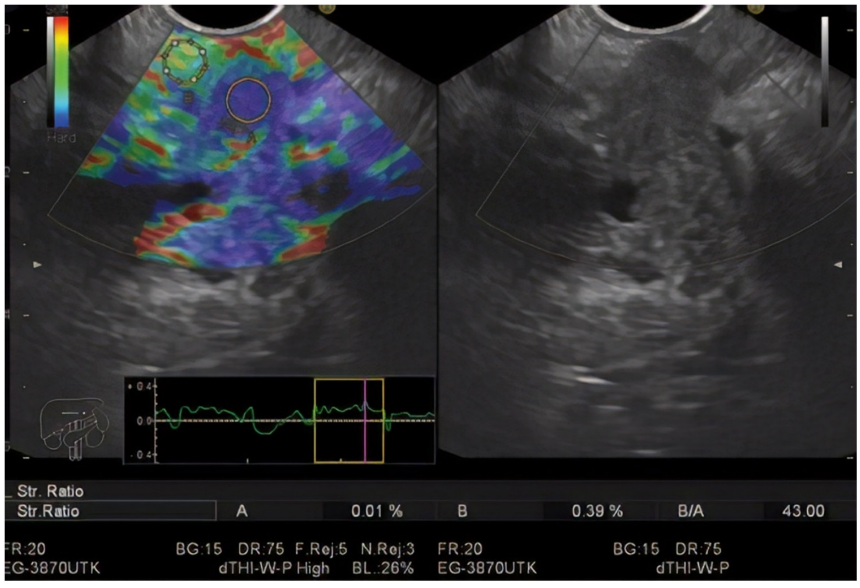

Figure 2. Strain ratio of a pancreatic head mass.

evaluation.[6] This measurement represents elasticity measured qualitatively from 0 (hardest) until 255 (softest) along the *X*-axis,[7] with the important parameters being mean strain, the standard deviation of the mean, the percentage of the blue area, and the complexity of the blue area.

Sequential images were taken during strain elastography in each patient and then the average value was taken.

FNA was performed in all patients following elastography measurements. In patients with negative cytology, monthly follow-up of serum CA-19-9 and computed tomography after at least 8 months was done with no increase in the size of the pancreatic masses or development of metastasis.

In the end, after a follow-up period of 8 months with histopathology and clinical course, patients with pancreatic lesions were classified into 2 classes, namely one class of patients diagnosed with pancreatic cancer and the other class of patients diagnosed with pancreatitis.

Statistical Analyses

All statistical analyses were conducted in SPSS 16 (Statistical Package for the Social Science, version 20, IBM, and Armonk, New York).

The diagnostic validity analysis included receiver operating characteristics (ROC) curve analysis, with specific values for the area under the curve, the significance of the area, and confidence intervals. Sensitivity (SS), specificity (SP), positive predictive value (PPV), and NPV, and positive and negative likelihood ratios are also expressed in the analysis.

The calculation of the overall accuracy (ACC) of the prediction was based on previous parameters. The cut-off point for measurement of the calculation based on the coordinates of the ROC curve is also presented in the analysis.

RESULTS

The studied group was divided into 67 males and 33 females with age ranging from 24 to 89 with mean ± SD of 59.89 ± 13.30. In this study, 66% of the patients didn't have any comorbidity, but 23% were diabetics, 11% were hypertensive, and 4% of the patients had ischemic heart diseases. Complaints in the patients varied between jaundice (40%), abdominal pains, and weight loss (20%). Fever was detected in 6% of patients, and lastly, diarrhea was recorded in only 5% of the patients in the studied group (Table 1).

In this study, 72% of cases were malignant, 69% of which were adenocarcinoma, and the remaining 3% were neuroendocrine tumors. The remaining 28 cases were diagnosed as benign lesions with pancreatitis taking the upper hand in diagnosis by reaching 23 cases and the last 5 patients had papillary adenoma (Table 2).

Table 1. Baseline Clinical Data of the Study Population

	N = 100
Sex	
Male	67 (67%)
Female	33 (33%)
Age (years)	
Range	24-89
Mean ± SD	59.89 ± 13.30
Age groups	
<40	8 (18%)
40-60	52 (52%)
>60	40 (40%)
Comorbidities	
Nothing	66 (66%)
Diabetes mellitus	23 (23%)
Hypertension	11 (11%)
Ischemic heart disease	4 (4%)
Chronic kidney disease	2 (2%)
Smoking	33 (33%)
Residence	
Rural	52 (52%)
Urban	48 (48%)
Abdominal pain	20 (20%)
Jaundice	40 (40%)
Weight loss	20 (20%)
Diarrhea	5 (5%)
Fever	6 (6%)

The lesions were found mainly in the pancreatic head (including the uncinate process) in both malignant and benign ones, being 50 and 20, respectively. There were 9 cases of malignant uncinate process masses included in the 50 cases of pancreatic head masses. But the site of the lesions did not show any statistically significant difference. The size was ≥2 cm in 88% of malignant lesions and 57% of benign ones, while 22% of malignant masses and 43% of benign masses were <2 cm. Heterogeneity was mainly reported in malignant lesions to be in 91% of cases. Vascular invasion was reported in 20 cases, all of them diagnosed to be malignant. On the other hand, calcifications were detected both in benign and malignant masses to be 10 cases in the first and 7 in the second diagnosis (Table 3).

Table 2. Final Diagnosis of the Study Population

	N = 100
Malignant lesion	72 (72%)
Adenocarcinoma	69 (69%)
Neuroendocrine tumor	3 (3%)
Benign lesions	28 (28%)
Pancreatitis	23 (23%)
Papillary adenoma	5 (5%)

Table 3. EUS Characteristics of Pancreatic Lesions in the Study Population

	Malignant Lesions,(*n* = 72)	Benign Lesions,(*n* = 28)	*P*
Site			.09
Head	41 (56.9%)	20 (71.4%)	
Uncinate process	9 (12.5%)	0 (0%)	
Body	18 (25%)	4 (14.3%)	
Tail	4 (5.6%)	4 (14.4%)	
Size			**<.001**
<2 cm	8 (11.1%)	12 (42.9%)	
≥2 cm	64 (88.9%)	16 (57.1%)	
Consistency			**<.001**
Homogenous	7 (9.7%)	28 (100%)	
Heterogeneous	65 (91.3%)	0	
Number of lesions			
Single	15 (20.8%)	17 (60.7%)	
Multiple	57 (79.2%)	11 (39.3%)	**<.001**
Calcification	7 (9.7%)	10 (35.7%)	
Vascular invasion	20 (27.8%)	0	
Lymph nodes	40 (55.6%)	5 (17.8%)	

At a cut-off point <97 according to the ROC curve coordinators, M1 demonstrated 89% sensitivity, 43% specificity, 70% PPV, 60% NPV, 76% accuracy, and *P* value <.001 in detecting malignant pancreatic lesions (Figure 3). At a cut-off point of >3.04 according to the ROC curve coordinators, SR demonstrated 95.83% sensitivity, 61% specificity, 86.2% PPV, 85% NPV, 86% accuracy, and *P* value <.001 (Figure 4) (Table 4).

DISCUSSION

EUS-FNA is the most commonly used method for the diagnosis of solid pancreatic lesions; however, it has many drawbacks. The NPV may reach up to 40%, so a negative biopsy cannot entirely exclude malignancy. Multiple needle passes are required for adequate sampling, and

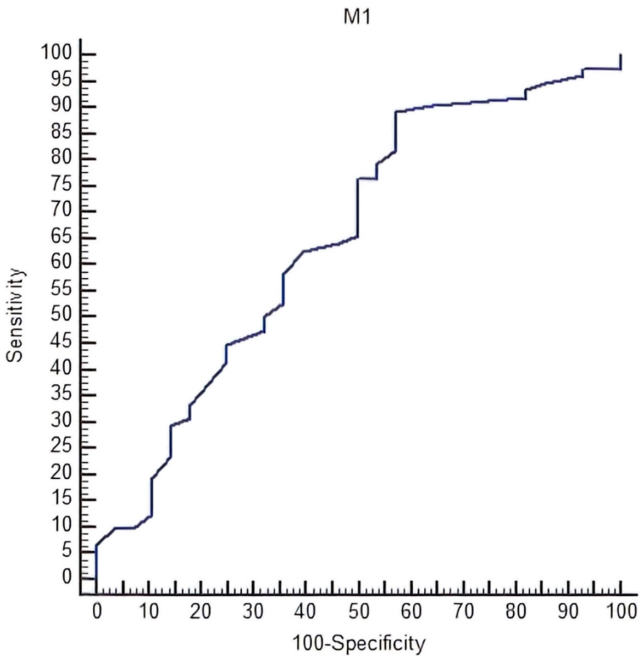

Figure 3. ROC curve for strain histogram.

difficult puncture may occur in some lesions due to the interposing vascular structures.[8] Iatrogenic complications are not few, and experience is required to obtain better efficacy.[9] This suggested the need for less invasive methods to help in distinguishing between benign and

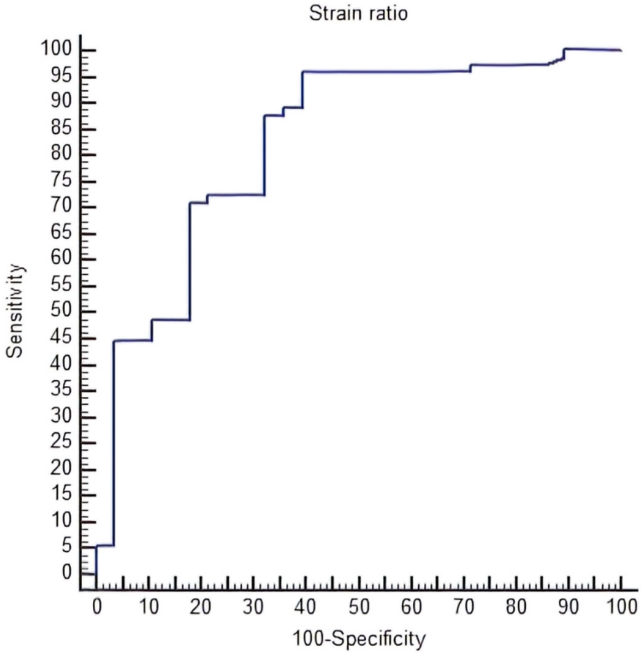

Figure 4. ROC curve for strain ratio.

Table 4. Validity of M1* and SR** in Diagnosing Malignant Pancreatic Lesions

	Value	
Indices	M1	SR
Sensitivity	89%	95.83%
Specificity	43%	61%
Positive predictive value	70%	86.2%
Accuracy	76%	86%
Cut-off point	<97	>3.04
Negative predictive value	60%	85%
Area under curve	0.65	0.82
P	<.0801	<.001

*Strain histogram; **Strain ratio.

malignant pancreatic lesions . SR and SH were the investigated methods in this study.

In our study, the benign lesions represented 28% of the examined cases which was similar to Okasha et al.'s[10] study. It was also very close to Kongkam et al.'s study,[11] which reached 23% of its examined group and is nearly identical to another meta-analysis which had a close figure of 26.5%.[12]

Ten patients with benign lesions had associated calcifications which definitely will affect elastography if it was the only diagnostic tool as it is very subjective and operator dependent. More tools are required to increase the yielding and specificity of the procedure.[13,14,15] We used SR with a cut-off value of >3.04 according to the ROC curve coordinators and it was 95.83% sensitivity, 61% specificity, 86.2% PPV, 85%NPV, 86% the accuracy, and *P* value <.00. Okasha et al.[10] reported a nearby cut-off value of 3.8 and a sensitivity value reaching 99%, a specificity of 53%, but better accuracy of 96%. Kongkam et al.[11] with a cut-off value of 3.17 gave a good specificity of 66.7%, but decreased values in sensitivity, NPV, and accuracy of 86.2%, 60%, and 81.6%, respectively.

EUS elastography quantitative methods were investigated in many studies. Iglesias-Garcia et al.[16] mentioned that according to a study that included 86 patients with solid pancreatic masses, the SR was significantly higher for patients with malignant pancreatic tumors than those with inflammatory lesions. The normal pancreatic tissue had an average SR of 1.68 in his study, and once an inflammatory mass was diagnosed, the SR reached an average of 3.28. On the other hand, Dalibor et al.[17] reported a cut-off

value of 1.153 with a sensitivity of 98%, a specificity of 50%, and an accuracy of 69%, suggesting that a lower SR can detect more malignant lesions.

At a cut-off point <97 according to the ROC curve coordinators, M1 (SH) demonstrated 89% sensitivity, 43.0% specificity, 70% PPV, 60% NPV, 76.0% accuracy, and a *P* value <1.001 in detecting malignant pancreatic lesions. In 3 previously published studies, with a cut-off value for the SH of 175 (much higher than our result), sensitivity was 91.4%, 84.8%, and 93.4%, and the specificity reached 87.9%, 76.2%, and 66.0%, with overall accuracy of 89.7%, 81.5%, and 85.4%.[18,19,20] In another study that was conducted by Dalibor et al.,[17] with a cut-off value of 86, sensitivity was 100%, and specificity was 45% with an ACC of 66%. The predictive positive and negative values were recorded as 54% and 100%, respectively.[17]

Tissue elastography was the strain that was used in this study, which has a negative correlation with tissue stiffness and shear wave speed, which has a positive correlation with tissue stiffness.[21] This newly introduced shear wave technique is very promising and we recommend comparing its diagnostic ability for solid pancreatic lesions with the SRs and SH.

CONCLUSION

Mode 1 SH showed high sensitivity (89%) in the detection of pancreatic malignant tumors but disappointingly had low specificity (43%) at a cut-off level of <97. Higher sensitivity (95, 83%), specificity (61%), and accuracy (86%) were obtained using the SR at a level cut-off >3.04.

Ethics Committee Approval: The study was approved by the committee for ethics of medical experiment on human subjects, Assiut University Faculty of Medicine.

Informed Consent: Written informed consent was obtained.

Peer Review: Externally peer- reviewed.

Author Contributions: Conception-H.O;Design-Z.A;Supervision-H.O;findings-H.O;Materials-A.A.M;Data collection and processing-A.A.M;Analysis and interpretation-H.A;Literature review-H.O;writing-A.A.M;Critical review-H.O.

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The manuscript has been read and approved by all the authors, the requirements for authorship have been met, and each author believes that the manuscript represents honest work.

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