ORIGINAL ARTICLE

Role of Endoscopic Ultrasound in Predicting Solid Pancreatic Lesions Using Strain Ratio and Elastography

Kiran Bajaj[1], Taha Yaseen[2], Abbas Ali Tasneem[3], Syed Mudassir Laeeq[4], Ali Khalid[5], Nasir Hasan Luck[6], Nasir Mehmood[7], Sandeep Kumar[8], Muhammad Qaiser Panezai[9], Danish Kumar[10], Nadir Sattar[11], Nida Rasool[12], Reeaa Kumari[13]

Received on: 20 November 2022; *Accepted on*: 21 December 2022; *Published on*: 03 August 2023

Abstract

Background: Despite advancement in imaging techniques, the diagnosis of solid pancreatic lesions (SPLs) remains challenging. The latest advancement in elastography permits the quantitative measurements of the average elasticity of a lesion. Therefore, our main aim of this study was to determine the utility of endoscopic ultrasound-guided elastography (EUS-EG) and strain ratio (EUS-SR) in predicting SPLs.

Materials and methods: This cross-sectional study was performed at the Department of Hepatogastroenterology, Sindh Institute of Urology and Transplantation. All patients with radiological diagnosis of SPLs underwent EUS-EG, followed by strain ratio (SR) measurement and targeted pancreatic fine needle lesion biopsy (FNB). Area under the receiver operating curve (AUROC) was obtained for SR and combined elastography and SR and at an optimal cutoff, diagnostic accuracy was obtained in predicting the nature of SPLs.

Results: A total of 52 patients were included in this study. Out of them, 32 (61.5%) patients were males while 20 (38.5%) were females. The mean age was 50.8 ± 12.5 years. Twenty-four (46.2%) patients had malignant pancreatic lesions. Among malignant lesions, the most common etiology was pancreatic adenocarcinoma seen in 18 (34.6%) patients. Out of 28 (53.8%) patients with benign lesions, 14 (26.9%) patients had inflammatory disease. Area under the receiver operating curve was obtained for both SR alone and SR combined with elastography score in differentiating benign from malignant SPLs which was 0.832 (p-value < 0.001) for SR alone and a slightly higher for combined SR with elastography (AUROC-0.839)(p-value < 0.001). At an optimal cutoff of SR of >17, the sensitivity was 94.8% and the diagnostic accuracy was 74% in predicting SPLs. While, when SR and elastography were combined together, the sensitivity increased to 96% with a diagnostic accuracy of 75%.

Conclusion: Combined EUS-EG and SR were accurate in diagnosing malignant pancreatic lesions with a diagnostic accuracy of 75% providing additional diagnostics information before biopsy. However, multicentric studies with larger sample sizes are required for the validation of our results to determine the utility and diagnostic accuracy of EUS-SR in defining the characteristic of pancreatic lesions.

Keywords: Elastography, Endoscopic ultrasound, Solid pancreatic lesions, Strain ratio.

Euroasian Journal of Hepato-Gastroenterology (2023): 10.5005/jp-journals-10018-1386

Introduction

Solid pancreatic lesions are characterized by a diverse group of lesions that can be generally categorized as either benign or malignant. Malignant lesions widely range from severe metaplasia to adenocarcinoma of the pancreas, neuroendocrine tumor of the pancreas, cholangiocarcinoma, solid pseudopapillary tumor of the pancreas, pancreatic lymphoma, secondary metastases, and rare various cancers. Benign SPLs range from chronic pancreatitis, and autoimmune pancreatitis to congenital anomalies.[1] It is still difficult to diagnose and characterize SPLs preoperatively despite recent advancements in the field of radiology. SPLs are associated with a 5-year survival of less than 5% and an average survival of approximately 3–6 months.[2] Hence, there is an emergent need to investigate them thoroughly to reach the proper diagnosis.[3]

In the current era of advancement in endoscopic techniques, endoscopic ultrasonography (EUS) has emerged as an indispensable therapeutic tool in gastroenterology with the advantage of being a minimally invasive tool and at the same time, it is a well-tolerated procedure.[4] However, without tissue sampling, the ability of EUS to characterize, differentiate, and predict different solid lesions is limited and requires tissue sampling to improve its diagnostic yield, but despite this, there are certain limitations attributed to it such as the tissue sampling can be falsely negative,[5] the challenging puncture of certain SPLs due to intervening vessels, and finally, the little risk of complications.[6] Thus, there was a requirement for a noninvasive method to be utilized with EUS to distinguish between benign and malignant SPLs. Okasha H et al.[7] determined the diagnostic utility of real-time endoscopic ultrasound-guided elastography (EUS-EG) and strain ratio (SR) in predicting the nature of SPLs with an excellent sensitivity of 98% and diagnostic accuracy of 92% when both EUS-EG and SR were combined together.[7] It is already known that malignancy alters tissue hardness. The determination of elasticity of the tissue aids the endosonologist with additional information regarding the nature of the lesion. Recently, EUS-guided elasticity measurement has emerged as a technique that not only reveals the physical properties and

[1–13]Department of Hepatogastroenterology, Sindh Institute of Urology and Transplantation, Karachi, Sindh, Pakistan

Corresponding Author: Taha Yaseen, Department of Hepatogastroenterology, Sindh Institute of Urology and Transplantation, Karachi, Sindh, Pakistan, Phone: +00923312812391, e-mail: raja_taha101488@hotmail.com

How to cite this article: Bajaj K, Yaseen T, Tasneem AA, *et al*. Role of Endoscopic Ultrasound in Predicting Solid Pancreatic Lesions Using Strain Ratio and Elastography. Euroasian J Hepato-Gastroenterol 2023;13(1):1–4.

Source of support: Nil

Conflict of interest: None

characteristics of the tissue but also identifies the variations in the tissue hardness caused by certain diseases.[8]

Tissue elasticity was utilized to aid in the analysis of the lesion by the comparison of color images in the B mode before and after compression. The elasticity of the tissue can be obtained from the strain and the stress of the observed lesions which was then utilized in EUS to estimate the elastography of the masses without the utility of additional interventions.[8] Giovannini et al.[5] proposed a model to differentiate benign and malignant lesions which were very subjective and operator-dependent. Later on, SR was introduced which is obtained by dividing the area of interest into the normal tissue to increase the diagnostic yield of the lesion.[5]

To the best of our knowledge, no study has been performed in Pakistan on EUS for determining the utility of yield of elastography and SR in diagnosing SPLs and very few studies have been done in other countries. Hence, the main objective of our research was the validation of the results obtained from previous studies on our patients. This study will help us in improving the diagnostic yield of SPLs by using the EUS-EG and SR.

Objective: To determine the utility of EUS-EG and strain ratio of SPLs in distinguishing benign from malignant pancreatic lesions.

Materials and Methods

This cross-sectional study was conducted on outpatients in the Department of Hepatogastroenterology, Sindh Institute of Urology and Transplantation, Karachi from June 2019 to December 2021. After the ethical committee's approval was obtained, all the patients aged between 19 and 90 years and diagnosed with SPL from prior radiological imaging (either ultrasound or cross-sectional imaging) were enrolled in the study. While excluded patients were those who refused to participate or patients having comorbidities, such as heart failure, asthmatic attack, or history of recent myocardial infarction (MI) assessed by taking history and using medical records and clinical methods, and lastly, the pregnant or breast-feeding females.

The EUS was then performed in all the patients enrolled in the study using a linear Echoendoscope Pentax EG3870UTK. All the procedures were carried out by a single expert endoscopist with expertise in EUS-guided procedures. EUS-fine needle aspiration (FNA) was carried out using the 22G Cook needle. Elastography and strain ratio were calculated for the SPLs. The definitive diagnosis of the SPL was made based on histopathological analysis of the EUS-FNA of the lesion, histopathological biopsies of surgically removed tumors, and lastly based on local and distant metastasis on cross-sectional imaging. All tests done were free of cost as per institutional policy.

EUS Elastography[5]

Elastography is used as a qualitative assessment tool in predicting SPLs. It is relatively a new ultrasound technique providing information regarding tissue stiffness. The elastic feature of the pancreatic tissue was utilized to aid in the diagnosis by the comparison of color images in the B mode before and after compression. The distribution of elasticity within the tissue was measured from the strain and the stress of the SPLs.

Here, we have utilized the "Elastic score" proposed by Giovannini et al.[5] which is classified as follows:

Score 1: Soft, green, consistent with the normal pancreas.

Score 2: Consistent with chronic pancreatitis.

Score 3: Blue color with minimal heterogeneity on the elastographic images, consistent with small adenocarcinomas.

Score 4: Refers to a central hypoechoic area, with a green appearance within a small area surrounded by a blue, or harder tissue, consistent with neuroendocrine tumors.

Strain Ratio[3]

It is a semi-quantitative score of elastography. It is done by selecting two areas:

One is Area (A) denoting the abnormal lesion or the lesion of interest.

The second one is Area (B) referring to the normal area.

SR is obtained by dividing Area (A) to Area (B)

Means of SR were obtained for each patient.

Data Analysis

SPSS version 22.0 was used for data entry and analysis. Expression of continuous variables was done in terms of mean + SD while frequencies and percentages were used to express categorical variables. Comparison of continuous variables was performed using the student's *t*-test while Chi-square test was used for the comparison of categorical variables.

The SPLs with elastography Scores of 1 and 2 were considered benign while those with Scores 3 and 4 were considered malignant. AUROC was obtained for SR and also for combined elastography and SR of SPLs. At an optimal cutoff, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy were obtained in differentiating benign from malignant SPLs.

Results

Fifty-two patients were included in this study. Out of them, most of them were males, that is, 32 (61.5%) patients. The mean age was 50.8 ± 12.5 years. Twenty-four (46.2%) patients had malignant while 28 (53.8%) patients had benign pancreatic lesions. Among malignant lesions, the most common etiology was pancreatic adenocarcinoma seen in 18 (34.6%) patients followed by lymphoma in 3 (5.8%), neuroendocrine tumor in 2 (3.8%) and squamous cell carcinoma in 1 (1.8%) patients, respectively. Out of 28 (53.8%) patients with benign lesions, 14 (26.9%) patients had inflammatory disease while 12 (22%) patients had granulomatous disease. A size of more than 20 mm was present in 18 (35%) patients. Mean SR was 70.4 + 90.2. The mean elastography score was 3 + 1. Thirty (57.7%) patients had an elastography score of 4 while 11 (21.2%) patients had an elastography score of 3 (Table 1). Advanced age, increased size of the pancreatic lesion, higher SR, elastography score, and combined SR with elastography score were significantly associated with malignant SPLs (Table 2).

AUROC was obtained for both SR alone and SR combined with elastography score in differentiating benign from malignant SPLs which was 0.832 (p-value < 0.001) for SR alone and slightly higher for combined SR with elastography (AUROC-0.839) (p-value < 0.001) (Fig. 1).

At an optimal cutoff of SR of >17, the sensitivity was 94.8%, specificity of 57.4%, PPV of 65.71%, NPV of 94.12%, and a diagnostic accuracy of 74% in predicting malignant SPLs.

Similarly, at an optimal cutoff of >17 for combined SR and elastography score, the sensitivity was 96%, specificity of 53.4%,

Table 1: Baseline characteristics of the studied population ($n = 52$)

Continuous variable		*Mean ± SD*
Age (years)		*50.8 ± 12.5*
Categorical variable		*Frequency (%)*
Sex	Male	32 (61.5)
	Female	21 (40.4)
Site	Head	47 (90.4)
	Body	3 (5.8)
	Tail	2 (3.8)
Histology	Benign	24 (46.2)
	Malignant	28 (53.8)
Lymphadenopathy	Yes	31 (59.6)
	No	21 (40.4)
Vascular involvement	Yes	4 (7.7)
	No	48 (92.3)
Metastasis	Yes	12 (23)
	No	40 (77)

Table 2: Comparison of variables in predicting malignant pancreatic lesions

Variable	*Malignant*	*Benign*	*p-value*
Age	55.8 + 10.2	46.7 + 12.8	0.006
Strain ratio(SR)	106 + 83.2	39.6 + 85	0.007
Elastography	4 + 0	2.7 + 0.94	<0.001
Combined elastography and SR	110 + 83	42.4 + 86	0.006

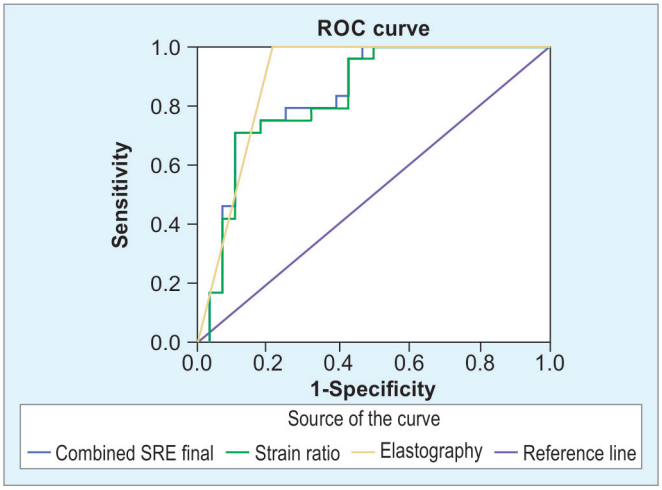

Fig. 1: AUROC for EUS-guided strain ratio (AUROC-0.832) (p-value < 0.001), elastography (AUROC-0.893) (p-value < 0.001) and combined SR and elastography (AUROC-0.839) (p-value < 0.001) in predicting SPLs

PPV of 63.8%, NPV of 93.75%, and a diagnostic accuracy of 74.6 % in predicting malignant SPLs (Table 3).

Discussion

The diagnostic yield and accuracy of EUS in distinguishing benign from malignant SPLs are augmented by the use of EUS-guided tissue sampling.[4,9–13] However, there are certain limitations associated with tissue sampling including lesions with a difficult window for puncture due to vasculature in the pathway, false-negative results, or increased risk of complications.[5,6,9] Therefore, there is a need for a noninvasive method that can be utilized in combination with EUS to differentiate benign from malignant SPLs.

Table 3: Diagnostic accuracy of strain ratio and elastography

	Strain ratio (SR) >17	*Elastography >2*	*Combined elastography and SR = 17*
Sensitivity	94.8%	90%	96%
Specificity	57.4%	39%	53.4%
Positive predictive value	65.71%	46%	63.8%
Negative predictive value	94.12%	58.14%	93.75%
Diagnostic accuracy	74%	67.31%	75%

A study by Okasha et al.[7] utilized the SR in characterizing the nature of SPL. At the cut-off level of 3.8, the SR showed an excellent sensitivity and a good diagnostic accuracy in predicting malignant SPLs but lacked specificity. The specificity was improved to 77% when the SR cutoff was increased to 7.8 along with diagnostic accuracy of 88%. The diagnostic yield of EUS-guided noninvasive techniques in predicting the nature of SPLs was improved when elastography was combined with SR had an excellent sensitivity of 92%, specificity of 77%, and a good diagnostic accuracy of 92% as compared with the accuracy when each of the modality was used alone. Another study by Okasha H et al.[3] with increased sample size of greater than 300 patients showed increased sensitivity and diagnostic accuracy of the SR in predicting malignant SPLs at a cutoff of 4.2. Another study done by Iglesias-Garcia et al.[14] used the SR cutoff >10 showing an excellent diagnostic accuracy of 98% in predicting malignant SPLs. In our study, we took a slightly higher SR cutoff of >17 which showed an excellent sensitivity of 95.8%, NPV of 94.12%, and a good diagnostic accuracy of 75% in predicting malignant SPLs. However, it lacked specificity.

Several studies have shown the utility of EUS-EG in characterizing SPLs and differentiating benign from malignant SPLs with varied sensitivity and diagnostic accuracy.[14–18] Our study also showed an excellent sensitivity of elastography in predicting malignant lesions. However, when used alone, elastography lacked specificity and diagnostic accuracy in diagnosing malignant SPLs. Okasha H et al.[3] revealed an excellent sensitivity of 97% and a good diagnostic accuracy of 89% when SR > 4.8 was combined with an elastography score for the prediction of malignant SPLs. These results explain the utility of elastography especially in combination with SR in the prediction of the nature of SPLs.

Our study showed also showed results similar to the previous studies when SR was combined with elastography as compared with SR alone with a sensitivity increased to 96% along with diagnostic accuracy of 75% when elastography combined with SR > 17 in predicting malignant SPLs. However, it lacked specificity. This can be attributed to the small sample size and fewer presentations of pancreatic lesions in our outpatient department.

The small sample size is the limitation of our study. The strength of the study is that it is a prospective study and secondly, it is the pioneer study on the utility of EUS-guided elastography and SR in the characterization of SPLs as EUS is relatively a new technique and no local data are currently available regarding the efficacy of EUS in diagnosis and characterization of SPLs.

Conclusion

In our study, the EUS-guided elastography combined with strain ratio has increased sensitivity and diagnostic accuracy in detecting malignant SPLs as compared with the use of SR alone. However, further studies comprising larger sample sizes are required to validate these results.

Orcid

Taha Yaseen https://orcid.org/0000-0002-5504-5084

References

1. Gavin Low, Anukul Panu, Noam Millo, et al. Multimodality imaging of neoplastic and nonneoplastic solid lesions of the pancreas. 2011;31(4):993–1015. DOI: 10.1148/rg.314105731.
2. Gong Z, Holly EA, Bracci PM. Survival in population-based pancreatic cancer patients: San Francisco Bay area, 1995–1999. Am J Epidemiol 2011;174(12):1373–1381. DOI: 10.1093/aje/kwr267.
3. Okasha HH, Mahdy RE, Elkholy S, et al. Endoscopic ultrasound (EUS) elastography and strain ratio, could it help in differentiating malignant from benign pancreatic lesions? Medicine (Baltimore). 2018; 97(36):e11689. DOI: 10.1097/MD.0000000000011689.
4. Hewitt MJ, McPhail MJ, Possamai L, et al. EUS-guided FNA for diagnosis of solid pancreatic neoplasms: a meta-analysis. Gastrointest Endosc 2012;75(12):319–331. DOI: 10.1016/j.gie.2011.08.049.
5. Giovannini M, Seitz JF, Monges G, et al. Fine-needle aspiration cytology guided by endoscopic ultrasonography: results in 141 patients. Endoscopy 1995;27(2):171–177. DOI: 10.1055/s-2007-1005657.
6. DeWitt J, McGreevy K, Sherman S, et al. Utility of a repeated EUS at a tertiary-referral center. Gastrointest Endosc 2008;67:610–619. DOI: 10.1016/j.gie.2007.09.037.
7. Okasha H, Elkoly S, El-Sayed R, et al. Real time endoscopic ultrasound elastography and strain ratio in the diagnosis of solid pancreatic lesions. World J Gastroenterol 2017;23:5962–5968. DOI: 10.3748/wjg.v23.i32.5962.
8. Frey H. [Realtime elastography. A new ultrasound procedure for the reconstruction of tissue elasticity]. Radiologe. 2003;43:850–855. DOI: 10.1007/s00117-003-0943-2.
9. Eloubeidi MA, Tamhane A, Varadarajulu S, et al. Frequency of major complications after EUS-guided FNA of solid pancreatic masses: a prospective evaluation. Gastrointest Endosc 2006;63:622–629. DOI: 10.1016/j.gie.2005.05.024.
10. Hartwig W, Schneider L, Diener MK, et al. Preoperative tissue diagnosis for tumours of the pancreas. Br J Surg 2009;96:5–20. DOI: 10.1002/bjs.6407.
11. Puli SR, Bechtold ML, Buxbaum JL, et al. How good is endoscopic ultrasound-guided fine-needle aspiration in diagnosing the correct etiology for a solid pancreatic mass? A meta-analysis and systematic review. Pancreas 2013;42:20–26. DOI: 10.1097/MPA.0b013e3182546e79.
12. Dumonceau JM, Polkowski M, Larghi A, et al. Indications, results, and clinical impact of endoscopic ultrasound (EUS)-guided sampling in gastroenterology: European Society of Gastrointestinal Endoscopy (ESGE) clinical guideline. Endoscopy 2011;43(10):897–912. DOI: 10.1055/s-0030-1256754.
13. Iglesias-Garcia J, Dominguez-Munoz JE, Abdulkader I, et al. Influence of on-site cytopathology evaluation on the diagnostic accuracy of endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) of solid pancreatic masses. Am J Gastroenterol 2011;106:1705–1710. DOI: 10.1038/ajg.2011.119.
14. Iglesias-Garcia J, Lindkvist B, Larino-Noia J, et al. Differential diagnosis of solid pancreatic masses: contrast-enhanced harmonic (CEH-EUS), quantitative-elastography (QE-EUS), or both? United European Gastroenterol J 2017;5(2):236–246. DOI: 10.1177/2050640616640635.
15. Pei Q, Zou X, Zhang X, et al. Diagnostic value of EUS elastography in differentiation of benign and malignant solid pancreatic masses: a meta-analysis. Pancreatology 2012;12(5):402–408. DOI: 10.1016/j.pan.2012.07.013.
16. Mei M, Ni J, Liu D, et al. EUS elastography for diagnosis of solid pancreatic masses: a meta-analysis. Gastrointest Endosc 2013; 77(4):578–589. DOI: 10.1016/j.gie.2012.09.035.
17. Xu W, Shi J, Li X, et al. Endoscopic ultrasound elastography for differentiation of benign and malignant pancreatic masses: a systemic review and meta-analysis. Eur J Gastroenterol Hepatol 2013; 25(2):218–224. DOI: 10.1097/MEG.0b013e32835a7f7c.
18. Li X, Xu W, Shi J, et al. Endoscopic ultrasound elastography for differentiating between pancreatic adenocarcinoma and inflammatory masses: a meta-analysis. World J Gastroenterol 2013;19(37):6284–6291. DOI: 10.3748/wjg.v19.i37.6284.