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Case Control Study

Endoscopic ultrasound elastography for malignant pancreatic masses and associated lymph nodes: Critical evaluation of strain ratio cutoff value

Miguel Puga-Tejada, Raquel Del Valle, Roberto Oleas, Maria Egas-Izquierdo, Martha Arevalo-Mora, Jorge Baquerizo-Burgos, Jesenia Ospina, Miguel Soria-Alcivar, Hannah Pitanga-Lukashok, Carlos Robles-Medranda

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Abstract

BACKGROUND

Endoscopic ultrasound (EUS) can detect small lesions throughout the digestive tract; however, it remains challenging to accurately identify malignancies with this approach. EUS elastography measures tissue hardness, by which malignant and nonmalignant pancreatic masses (PMs) and lymph nodes (LNs) can be differentiated. However, there is currently little information regarding the strain ratio (SR) cutoff in Hispanic populations.

AIM

To determine the diagnostic accuracy of EUS elastography for PMs and LNs with an SR cutoff value in Hispanics.

METHODS

A retrospective study of patients who underwent EUS elastography for PMs between December 2013 and December 2014. A qualitative (analysis of color maps) and quantitative (SR) analysis of PMs and their associated LNs was performed. The accuracy of EUS elastography in identifying malignant PMs and LNs and cutoff value for SR were analyzed. A PM and/or its associated LNs were considered malignant based on histopathological findings from fine-needle aspiration biopsy samples.

RESULTS

A sample of 121 patients was included, 45.4% of whom were female. 69 (57.0%) PMs were histologically malignant, with a median SR of 50.4 *vs* 33.0 for malignant *vs* nonmalignant masses ($P < 0.001$). EUS evaluation identified associated LNs in 43/121 patients (35.5%), in whom 22/43 (51.2%) patients had histologically confirmed malignant diagnosis, with a median SR of 30 *vs* 40 for malignant *vs* nonmalignant LNs ($P = 0.7182$). In detecting malignancy in PMs, an SR cutoff value of > 21.5 yielded a sensitivity of 94.2%, while a cutoff value of > 121 yielded a specificity of 96.2%. There were significant differences in the Giovannini scores, a previously established elastic score system, between the patients grouped by their final histology results ($P < 0.001$). For LNs, SR cutoff values of > 14.0 and > 155 yielded a sensitivity of 90.9% and a specificity of 95.2%, respectively, in detecting malignancy.

CONCLUSION

EUS elastography is a helpful technique for the diagnosis of solid PMs and their associated LNs. The proposed SR cutoff values have a high sensitivity and specificity for the detection of malignancy.

Key Words: Ultrasound; Elastography; Pancreas; Lymph nodes; Neoplasm

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Core Tip: This single-center retrospective study aimed to determine the diagnostic accuracy of endoscopic ultrasound (EUS) elastography in the diagnosis of pancreatic masses (PMs) and associated lymph nodes (LNs) with a defined strain ratio (SR) cutoff value in a Hispanic population. In determining if PMs were malignant, an SR cutoff value > 21.5 had a sensitivity of 94.2%, while a cutoff value > 121 had a specificity of 96.2%. For diagnosing LNs, an SR cutoff value > 14.0 had a sensitivity of 90.9%, while a cutoff value > 155 had a specificity of 95.2% for malignancy. The proposed SR cutoff values have high sensitivity and specificity for malignancy detection during EUS elastography.

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INTRODUCTION

Pancreatic masses (PMs) include neoplastic and nonneoplastic lesions (*i.e.*, anatomical variants, inflammatory lesions). One of the essential tasks during the assessment of PMs is identifying their benign or malignant nature. Along with the identification of malignant lesions, the presence of involved lymph nodes (LNs) is a prognostic factor of the disease. To date, one of the most sensitive methods for detecting PMs is endoscopic ultrasound (EUS), which allows for the visualization of small lesions throughout the digestive tract; however, EUS has a limited capacity in accurately determining the malignant or nonmalignant nature of a lesion. In addition, EUS-guided fine-needle aspiration (EUS-FNA) provides a histological diagnosis for lesions suspicious of malignancy; nevertheless, this invasive technique has a false-negative rate of 25%[1].

These shortcomings have been addressed with EUS elastography, an additional imaging technique used to determine tissue hardness. Malignant tissue is often more rigid than the normal surrounding tissue; thus, EUS elastography can differentiate between malignant and nonmalignant lesions. As a result, this technique has been applied in the diagnostic workup of PMs and their associated LNs[2-4]. EUS elastography is considered an accurate imaging technique for characterizing and detecting pancreatic lesions[2].

EUS elastography can be used to evaluate PMs and their associated LNs through qualitative and quantitative analyses; the former involves the analysis of color maps, while the latter is achieved by assessing the strain ratio (SR). However, previous studies, such as the one published by Altonbary *et al* [4], have reported differences in the SR cutoff value and the optimal internal sensitivity and specificity, suggesting a potential limitation of this technique[3,4]. The accuracy of this technique in differentiating malignant from nonmalignant lesions has only been assessed for masses consisting of solid tissue. The suitability of EUS elastography for solid-cystic lesions, which comprise an important percentage of

pancreatic tumoral lesions, has not been reported.

Based on the above, through this retrospective study, we aim to determine the diagnostic accuracy of EUS elastography for diagnosing malignant PMs and LNs in a Hispanic cohort and define the SR cutoff values in this population, comparing the results with those obtained through FNA biopsy.

MATERIALS AND METHODS

Study design

This was an observational, analytic, retrospective, case-control study performed at the Instituto Ecuatoriano de Enfermedades Digestivas (IECED, Guayaquil, Ecuador) from December 2013 to December 2014. Consecutive Hispanic patients (≥ 18 years old) were referred for the evaluation of suspected PMs using EUS following computed tomography (CT) or magnetic resonance imaging (MRI). Patients with incomplete clinical records were excluded. The patients were allocated into two groups (malignant or nonmalignant) according to the histological findings of biopsy samples and results from a 6-mo clinical follow-up (*i.e.*, laboratory tests, imaging, and surgical findings). All participants or their legal guardians gave written informed consent before the procedure. The Institutional Review Board approved the use and management of the corresponding data, and the study was conducted in accordance with the Declaration of Helsinki.

EUS elastography

All procedures were performed by two expert endoscopists (CRM and RV), who perform ≥ 300 EUS procedures *per year*. The patients were examined under general anesthesia using a 3.8 mm working-channel linear-array echoendoscope (EG3870UTK, Pentax Medical, Pentax, Hamburg, Germany) attached to a Hitachi AVIUS Ultrasound Console (Avius Hitachi, Tokyo, Japan).

First, PMs or any associated LNs were examined under conventional B-mode scanning. Then, EUS elastography of the region of interest was performed using the ultrasound console. Tissue hardness was measured qualitatively and quantitatively in all regions of interest *via* EUS color maps and the SR, respectively. Subsequently, EUS-guided FNA was performed using a 22-gauge needle (Expect[®], Boston Scientific, Marlborough, MA). A pathologist blinded to the EUS elastography results performed the histological analysis.

Scoring system

Two expert endoscopists (CRM and RV) performed the qualitative assessed by classifying the elastography images using the elastic score, as reported by Giovannini[3]. Giovannini elastic scores of 1 and 2 correspond to large green areas of soft and nonmalignant tissue; a score of 3 corresponds to a mainly blue area, considered a small adenocarcinoma; scores of 4 and 5 correspond to blue areas of hard and malignant tissue. For practical purposes, scores of 1 and 2 were considered nonmalignant lesions, whereas scores of 3, 4, and 5 were considered malignant lesions. Conventional EUS B-mode characteristics, such as size, shape, density, and ability to determine the border of suspicious lesions, were also recorded as part of the qualitative analysis. According to these factors, lesions with a size greater than 1 cm, irregular shape, anechoic density, or undefined borders were considered malignant[3-6].

The quantitative diagnosis was performed by calculating the *semiquantitative proportion* of tissue elasticity by measuring the SR of the region of interest. According to the method described by Iglesias-Garcia *et al*[6], at least three elasticity measurements for the mass lesion (A) and one for the surrounding area (B) were obtained. The corresponding SRs were then calculated by dividing B by each of the A values, and their mean was calculated[7]

Data collection

Baseline data were extracted from medical records. The location, size, diameter, and color pattern of PMs and their associated LNs on EUS elastography, SR, and histological diagnosis were thoroughly described. Malignancy in solid and solid-cystic PMs was defined following the Fukuoka Consensus Guidelines, as detailed in Table 1[5].

Statistical analysis

Technical considerations: All statistical analyses were performed by an institutional GI attending and biostatistician (MPT) with 8 years of experience, using R v4.0 (R Foundation for Statistical Computing; Vienna, Austria). A *P* value < 0.05 was considered statistically significant.

Sample size: The sample size was estimated considering a 100% specificity for an SR > 6.04 on EUS elastography in predicting malignancy in solid PMs, with a corresponding disease prevalence of 67.4% [5], $\delta = 10\%$, and α - and β -errors of 5% and 20%, respectively. Using these parameters, a sample size of twenty-four cases and eleven controls was estimated, with 80% statistical power. To respect the central limit theorem (in which thirty observations are necessary to reach a Gaussian distribution), we aimed to analyze no fewer than thirty patients with malignant PMs during the study period.

Table 1 Classification of pancreatic lesions

	Malignant	Nonmalignant
Solid	Adenocarcinoma	Acute pancreatitis
	Lymphoma	Chronic pancreatitis
	PNETs	Adenoma
	Pancreatoblastoma	Insulinoma
	Metastatic cancer	
Solid-Cystic	Mucinous cystadenoma ¹	Serous cystadenoma
	Serous cystadenocarcinoma	
	Mucinous cystadenocarcinoma	
	IPMN ¹	

¹Considered malignant if the Fukuoka criteria are met.

PNET: Pancreatic neuroendocrine tumor; IPMN: Intraductal papillary mucinous neoplasm.

Comparisons of baseline data, EUS, and EUS elastography diagnostic outcomes: Quantitative variables are described as the mean (standard deviation) or median (minimum-maximum range) according to their statistical distribution (Kolmogorov-Smirnov test). Qualitative variables are described as frequency (%). The potential differences in baseline data (*i.e.*, age, sex, PM location) and EUS elastography diagnostic outcomes between malignant and nonmalignant PMs and LNs were confirmed with statistical hypothesis testing and illustrated with a boxplot, when necessary. Associations of PM and LN SR with diameter were demonstrated through Spearman's rank correlation (ρ).

EUS and EUS elastography qualitative analysis: The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of a Giovannini elastic score of 3 to 5 (cyan and dark blue) in predicting malignancy in PMs and their associated LNs were estimated. In the case of PMs, the subgroup analysis considered only solid PMs (excluding solid-cystic PMs). In the case of associated LNs, the sensitivity, specificity, PPV, NPV, and accuracy of conventional B-mode EUS criteria in predicting malignancy were also determined.

EUS elastography quantitative analysis: The sensitivity, specificity, PPV, NPV, and accuracy of SR measurements in predicting malignancy in PMs and their associated LNs were estimated. Subgroup analysis was also performed for only solid PMs (excluding solid-cystic PMs). In each situation, two internally derived SR cutoff values, one yielding the optimal sensitivity (and accuracy) and the other the optimal specificity, were calculated from the study data. We also calculated the corresponding areas under the receiver operating characteristic curve (AUROCs), in which AUROCs of 0.5 suggested a prediction of malignancy equivalent to chance, with values of 0.7 to 0.8 considered acceptable, 0.8 to 0.9 considered excellent, and more than 0.9 considered outstanding discriminability[6]. The corresponding ROC curves were also generated and compared using the *roc.test* function of the *pROC* (v1.16.2; Robin X, 2020) package when necessary.

RESULTS

A sample of 121 patients with previous CT or MRI scans for PMs underwent EUS evaluation and were enrolled in the study. In this cohort, 55/121 (45.5%) were female, and the median age was 67 years (13–99). There was a histologically confirmed diagnosis of malignancy in 69/121 (57%) patients who were allocated to the malignant group; the remaining patients were placed in the nonmalignant group. Additionally, 43/121 (35.5%) patients had associated LNs surrounding the gastrointestinal tract. The baseline data and EUS elastography diagnostic outcomes of the cohort are summarized in [Table 2](#).

We compared both PM groups in terms of the variables obtained from the EUS elasticity qualitative and quantitative analyses. Regarding the qualitative outcomes, there were significant differences in the Giovannini scores between the patients grouped by their final histology results ($P < 0.001$). For the quantitative outcomes, there was a significant difference in the median SR between patients with malignant (50.4, range 7.8–22.5) and nonmalignant PMs (33.0, range 2.6–321.0) ($P < 0.001$). In the solid PM subgroup, the median SR values were 51.0 (7.8–225.0) and 21.9 (2.6–321.0), respectively ([Figure 1](#)). A proportionally significant association was demonstrated between a higher PM SR and a larger PM diameter ($\rho = 0.251$, 95%CI: 0–0.481; $P = 0.05$).

Table 2 Baseline data and endoscopic ultrasound elastography diagnostic outcomes of pancreatic masses

	Malignancy (n = 69)	Nonmalignancy (n = 52)	P value
Age (yr), median (range)	67 (13–93)	68 (20–99)	0.8907 ^a
Sex (female), n (%)	36 (52.2)	19 (36.5)	0.1271 ^b
PM location, n (%)			0.6891 ^b
Head	50 (72.5)	35 (67.3)	
Neck	3 (4.3)	4 (7.7)	
Body	13 (18.8)	12 (23.1)	
Tail	3 (4.3)	1 (1.9)	
PM diameter (mm), median (range)	37.0 (7.4–70.0)	30 (10.0–60.0)	0.0616 ^a
Giovannini elastic score, n (%)			< 0.001 ^b
Green (score 1 to 2)	-	11 (21.2)	
Cyan (score 3)	5 (7.2)	11 (21.2)	
Dark blue (score 4 to 5)	64 (92.8)	30 (57.7)	
Strain ratio, median (range)	50.4 (7.8–225.0)	33.0 (2.6–321.0)	< 0.001 ^a
Firmness/histopathology, n (%)			< 0.001 ^b
Solid-cystic masses (n = 36)	26/69	10/52	< 0.001 ^b
Serous cystadenoma	-	10 (19.2)	
Mucinous cystadenoma	5 (7.2)	-	
Mucinous cystadenocarcinoma	3 (4.3)	-	
IPMN	18 (26.1)	-	
Solid masses (n = 85)	43/69	42/52	< 0.001 ^b
Normal	-	4 (7.7)	
Acute pancreatitis	-	10 (19.2)	
Chronic pancreatitis	-	26 (50.0)	
Adenoma	-	1 (1.9)	
Insulinoma	-	1 (1.9)	
Adenocarcinoma	33 (47.8)	-	
Lymphoma	3 (4.3)	-	
PNETs	6 (8.7)	-	
Pancreatoblastoma	1 (1.4)	-	

^aMann-Whitney U test.^bPearson Chi-Quadrat Test.

IPMN: Intraductal papillary mucinous neoplasm; PNET: Pancreatic neuroendocrine tumor; PM: Pancreatic masses.

In detecting malignancies among all PMs, a Giovannini elastic score of 3 to 5 had a sensitivity, specificity, PPV, NPV, and accuracy of 100.0%, 21.2%, 62.7%, 100.0%, and 66.1%, respectively. For the subgroup of solid PMs, the corresponding sensitivity, specificity, PPV, NPV, and accuracy were 100%, 23.8%, 57.3%, 100%, and 62.4%, respectively (Table 3).

In the quantitative analysis, we found that optimal sensitivity and specificity values were obtained for SR cutoff values of 21.5 and 121.0, respectively, for both all PMs and solid PMs. The diagnostic accuracy parameters for both groups of PMs are shown in Table 3. Notably, in the overall PM analysis, the lower SR cutoff value (≥ 21.5) was associated with a higher sensitivity (94.2%) and NPV (84.0%), and the higher SR cutoff value (≥ 121.0) was associated with higher specificity (96.2%) and PPV (83.3%). A similar observation was made in the solid PM subgroup analysis; however, the SR cutoff value of ≥ 121.0 yielded higher accuracy in the subgroup analysis than in the overall PM analysis (54.1% vs 49.6%), while the SR cutoff of ≥ 21.5 yielded a lower accuracy (69.4% vs 71.1%). Additionally, the AUROC was slightly higher in the solid PM subgroup analysis (AUROC = 0.713) than in the overall PM analysis

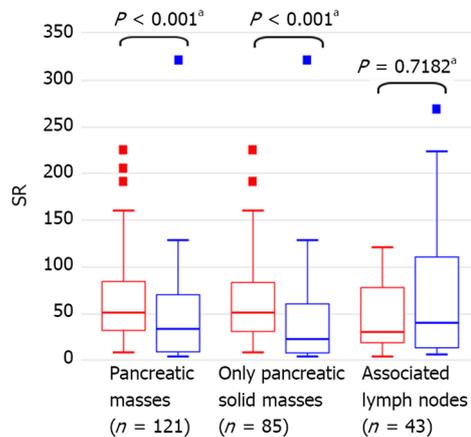
Table 3 Qualitative and quantitative diagnostic accuracy of endoscopic ultrasound elastography for detecting malignant pancreatic masses: All lesions ($n = 121$) and only solid pancreatic masses ($n = 85$)

	EUS-elastography qualitative analysis		EUS-elastography quantitative analysis			
	All masses	Only solid pancreatic masses	All PMs		Only solid PMs	
			SR $\geq 21.5^1$	SR $\geq 121.0^2$	SR $\geq 21.5^1$	SR $\geq 121.0^2$
Sensitivity (%)	100.0	100.0	94.2	14.5	90.7	14.0
Specificity (%)	21.2	23.8	40.4	96.2	47.6	95.4
PPV (%)	62.7	57.3	67.7	83.3	63.9	70.0
NPV (%)	100.0	100.0	84.0	45.9	83.3	52.0
Accuracy (%)	66.1	62.4	71.1	49.6	69.4	54.1

¹Internally derived optimal strain ratio (SR) cutoff for sensitivity (and accuracy).

²Internally derived optimal SR cutoff for specificity.

EUS: Endoscopic ultrasound; SR: Strain ratio; PPV: Positive predictive value; NPV: Negative predictive value; PM: Pancreatic masses.



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Figure 1 Distribution of strain ratio values among malignant (red) and nonmalignant (blue) pancreatic masses and their associated lymph nodes. ^aMann-Whitney U test. SR: Strain ratio.

(AUROC = 0.685) ($P = 0.7073$) (Figure 2A and B).

Among the 43 patients with associated LNs, the median age was 67.5 (39–95) years, and 14/43 (32.6%) were female. Histology confirmed malignancy in 22/43 (51.2%) patients, who were subsequently placed in the malignant group. There were no significant differences between the malignant and nonmalignant LN groups in LN location, diameter, EUS characteristics, Giovannini elastic score, or SR (Table 4). Specifically, the average SR was 30.0 (3.0–120.0) for malignant LNs and 40.0 (5.0–269.0) for nonmalignant LNs ($P = 0.7182$) (Figure 1). There was no association between LN SR and diameter ($\rho = -0.017$, 95%CI: -0.503–0.421; $P = 0.937$).

Qualitative EUS elastography analysis yielded a sensitivity, specificity, PPV, NPV, and accuracy of 68.1%, 38.1%, 53.6%, 53.3%, and 53.5%, respectively; these values were lower than those obtained using the structural characteristics detected *via* conventional B-mode scanning (Table 5). For the PMs, we obtained two SR cutoff values by identifying the values that yielded optimal sensitivity and specificity. Specifically, an SR cutoff value of 14.0 yielded a sensitivity, specificity, PPV, NPV and accuracy of 90.0%, 28.6%, 51.4%, 75.0% and 60.4, respectively; the corresponding values for an SR cutoff value of 155.0 were 4.5%, 95.2%, 50.0%, 48.8% and 48.8% (Table 5). The use of SR for diagnosing malignancy yielded an AUROC of 0.417 (Figure 2C).

DISCUSSION

In the present study, we found that qualitative EUS elastography analysis was highly sensitive for solid PMs. Moreover, in the quantitative assessment, an SR cutoff value of ≥ 21.5 had a 90% sensitivity for

Table 4 Baseline data, endoscopic ultrasound, and endoscopic ultrasound elastography diagnostic outcomes of the associated lymph nodes

	Malignancy (n = 22)	Nonmalignancy (n = 21)	P value
Age (yr), median (range)	76 (57–95)	65 (39–85)	0.2037 ^a
Sex (female), n (%)	8 (36.4)	6 (28.6)	0.5860 ^b
LN location, n (%)			0.4250 ^b
Esophagus	13 (59.1)	15 (71.4)	
Stomach	2 (9.1)	1 (4.8)	
Liver	1 (4.5)	-	
Pancreas	5 (22.7)	5 (23.8)	
Kidney	1 (4.5)	-	
LN diameter, median (range)	20.0 (4.0–50.0)	15.5 (7.0–21.6)	0.2662 ^a
EUS-LN characteristics, n (%)			
Irregular shape	11 (50.0)	10 (47.6)	0.8760 ^b
Undefined border	13 (59.1)	8 (38.1)	0.2730 ^b
Anechoic density	7 (31.8)	3 (14.3)	0.1740 ^b
Giovannini elastic score, n (%)			0.7970 ^b
Green (score 1 to 2)	1 (4.5)	2 (9.5)	
Cyan (score 3)	6 (27.3)	6 (28.6)	
Dark blue (score 4 to 5)	15 (68.2)	13 (61.9)	
Strain ratio, median (range)	30.0 (3.0–120.0)	40.0 (5.0–269.0)	0.7182 ^a
Histopathology, n (%)			< 0.001 ^b
Acute lymphadenitis	-	10 (47.6)	
Chronic lymphadenitis	-	11 (52.4)	
Lymphoma	2 (9.1)	-	
Metastasis	20 (90.9)	-	

^aMann-Whitney U test.^bPearson Chi-Quadrat Test.

EUS: Endoscopic ultrasound; LN: Lymph node.

defining malignancy in solid PMs (Figure 3). In contrast, a cutoff value of ≥ 121.0 had a 95% specificity for malignant PMs. For the evaluation of associated LNs, an SR of ≥ 14.0 had a 91% sensitivity, whereas an SR of ≥ 155.0 had a 95% specificity.

Various studies have shown the ability of EUS to distinguish between malignant and nonmalignant lesions. Itokawa *et al*[8] proposed that a Giovannini elastic score of 5 during EUS elastography evaluation is a characteristic of pancreatic malignancy[8,9], with 98.6% of patients having a score of five and a confirmed pancreatic malignancy. However, our study found that 91.4% of patients with malignant PMs had a score of 4 to 5.

The qualitative elastic score had a high sensitivity of 100.0% in our study for solid and solid-cystic PMs. On the other hand, Itokawa *et al*[8] found that a considerable number of nonmalignant cases scored 5, decreasing the specificity of the elastic score to 64.3%[2]. Our study found a specificity of 21.15% for solid and solid-cystic PMs and 23.81% for solid masses alone. No malignant pancreatic lesions had an elastic score of 1 or 2 following Giovannini's classification. According to the qualitative analysis, our cases reported high sensitivity and NPV.

Iglesias-Garcia *et al*[6], in a prospective study of 86 patients, described one of the highest diagnostic accuracy values based on qualitative and quantitative EUS elastography analysis. For the qualitative measurements, the sensitivity, specificity, PPV, NPV, and overall accuracy were 100%, 71%, 87%, 100%, and 90%, respectively. For the quantitative values, a lower SR cutoff value of > 6.0 had a sensitivity, specificity, PPV, NPV, and overall accuracy of 100%, 92%, 96%, 100%, and 97%, respectively[6].

Table 5 Diagnostic accuracy of conventional B-mode endoscopic ultrasound and qualitative and quantitative endoscopic ultrasound elastography analysis for malignancy in the associated lymph nodes ($n = 43$)

	Conventional B-mode EUS				EUS-elastography qualitative analysis	EUS-elastography quantitative analysis	
	Size	Shape	Border	Density		SR ≥ 14.0 ¹	SR ≥ 155.0 ²
Sensitivity (%)	59.1	50.0	59.1	31.8	68.1	90.9	4.5
Specificity (%)	42.9	52.4	61.9	85.7	38.1	28.6	95.2
PPV (%)	52.0	52.4	61.9	70.0	53.6	51.4	50.0
NPV (%)	50.0	50.0	59.1	54.6	53.3	75.0	48.8
Accuracy (%)	51.2	51.2	60.5	58.1	53.5	60.4	48.8

¹Internally derived optimal strain ratio cutoff for sensitivity (and accuracy).

²Internally derived optimal cutoff for specificity.

EUS: Endoscopic ultrasound; SR: Strain ratio; PPV: Positive predictive value; NPV: Negative predictive value.

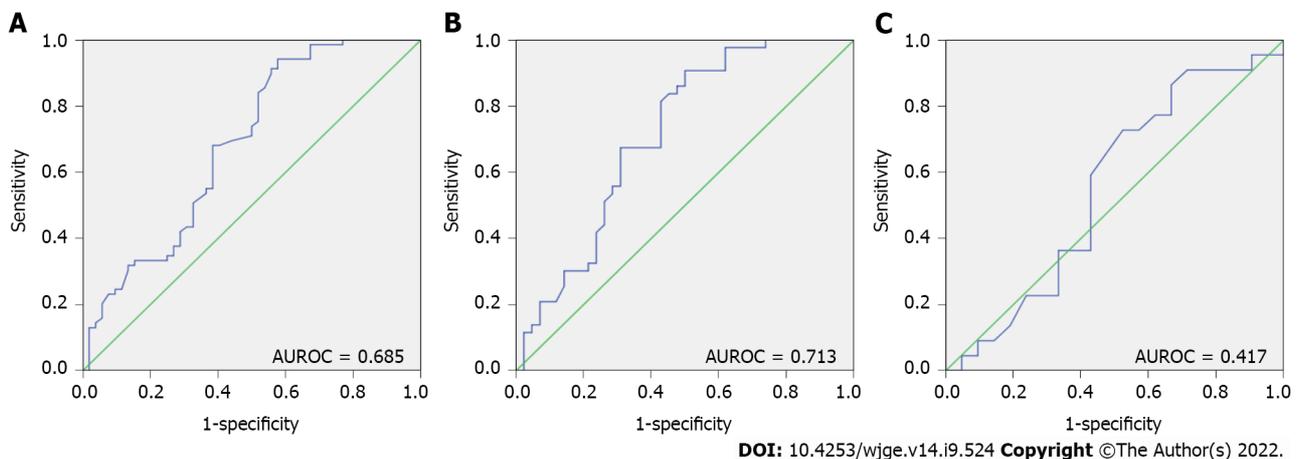


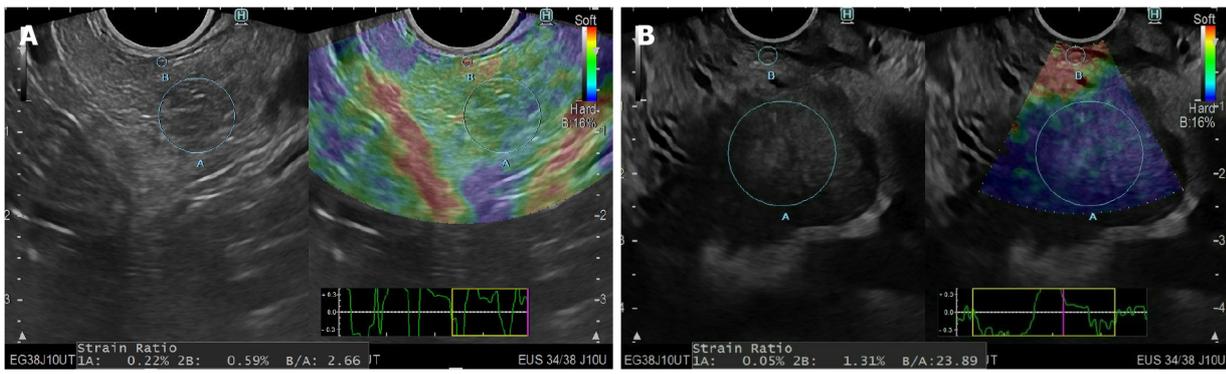
Figure 2 Areas under the receiver operating characteristic curve. A: Areas under the receiver operating characteristic curve (AUROC) of the strain ratio in the detection of malignancy in pancreatic masses [AUROC = 0.685 (0.586–0.783)]; B: AUROC of the strain ratio in the detection of malignancy in only solid pancreatic masses [AUROC = 0.713 (0.602–0.825)]; C: AUROC of the strain ratio in the detection of malignancy in associated lymph nodes [AUROC = 0.417 (0.076–0.757)]. There was no significant difference between AUROC-A and AUROC-B ($P = 0.7073$). AUROC: Areas under the receiver operating characteristic curve.

Dawwas *et al*[10] obtained a higher diagnostic accuracy for EUS elastography using an SR cutoff value of 4.65 to achieve a 100% sensitivity and a cutoff value of 59.25 to achieve a 100% specificity. Okasha *et al*[11] concluded that the best SR cutoff level was 7.8, which gave a sensitivity of 92%, a specificity of 77%, a PPV of 91%, an NPV of 80%, and an accuracy of 88%[11]. Our study achieved a higher sensitivity using a lower cutoff value. Factors such as tissue inflammation, fibrosis, necrosis, advanced age, or ethnicity may affect the hardness of tissue, explaining the difference in the cutoff values proposed in the literature[12–14]. Moreover, the size of the region of interest and tissue compression level could affect the quantitative evaluation of EUS elastography.

Additionally, a study published by Kongkam *et al*[15] showed that a cutoff SR level of 3.17 along with EUS-FNA provided a sensitivity, specificity, PPV, NPV and accuracy of 95.2%, 71.4%, 90.9%, 83.3%, and 89.3%, respectively, compared to the 90%, 100%, 100% 80% and 92.8% of EUS elastography alone. Based on these results, the authors raised the possibility of a future combination of both techniques for evaluating PMs[15].

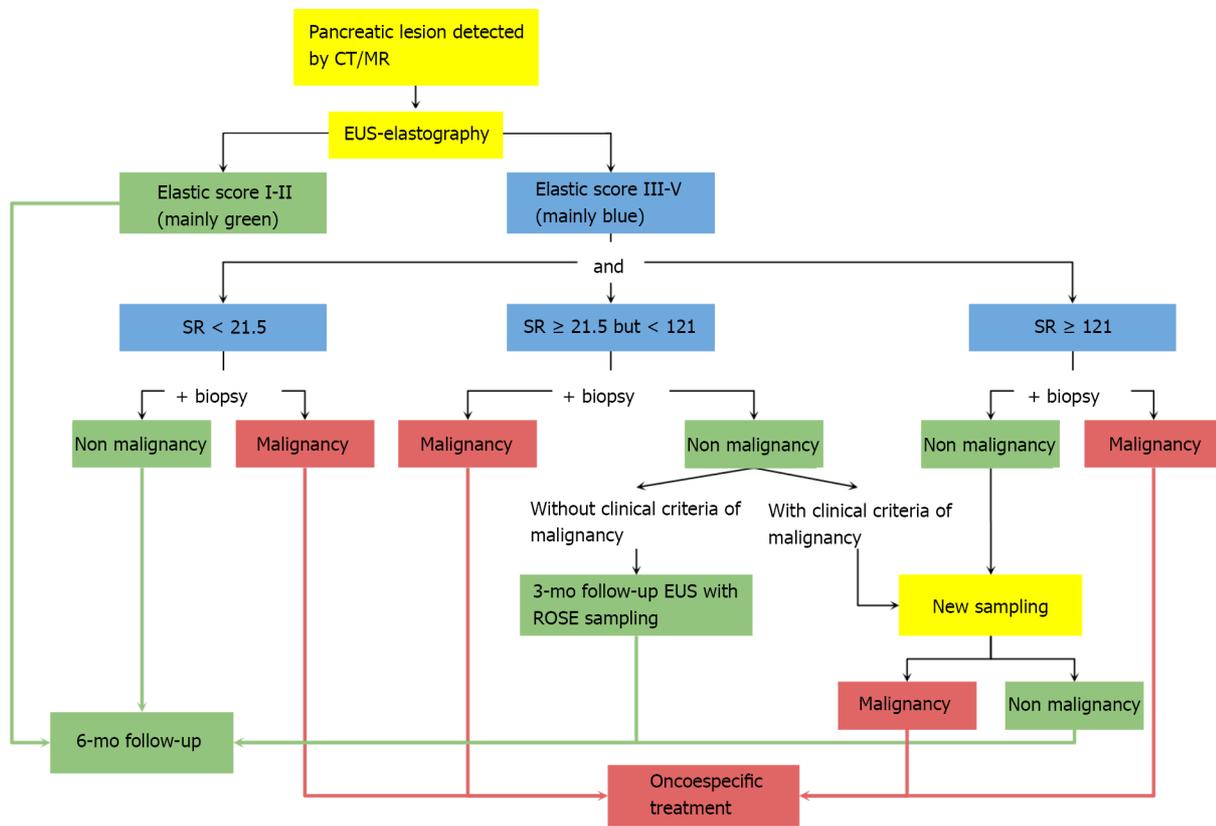
Paterson *et al*[12] focused their research on the utility of quantitative EUS elastography analysis for defining malignancy in the LNs related to esophageal and gastric cancer and compared this approach to an analysis using conventional EUS LN features. Compared to our results, they found a lower diagnostic accuracy for conventional EUS but a higher diagnostic accuracy for EUS elastography[12].

The present study has several limitations, including its retrospective design and single-center nature, leading to a limited number of operators. A few patients from the malignant case group underwent surgery, limiting the histological description of this research. The nonmalignant control group was defined as patients with nonmalignant masses instead of a healthy population. However, this study has



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Figure 3 Quantitative and qualitative endoscopic ultrasound elastography assessment. A: Case No. 84: A 26-year-old women with a pancreatic mass. A plain B-mode image (left) and a color-code strain image (right) are shown, strain ratio (SR) = 2.66, Giovannini elastic score of 2 (green). Biopsy confirmed chronic pancreatitis; B: Case No. 73: A 46-year-old man with a pancreatic mass. A plain B-mode image (left) and a color-coded strain image (right) are shown, SR = 23.8, Giovannini elastic score of 4 (dark blue). Biopsy confirmed pancreatic adenocarcinoma.



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Figure 4 Proposed algorithm for the workup of pancreatic masses. SR: Strain ratio; EUS: Endoscopic ultrasound; CT: Computed tomography; MR: Magnetic resonance.

the advantage of using the qualitative elastic score proposed by Giovannini[3]. For the interpretation of PMs and their associated LNs, instead of the 4-score by Furukawa *et al*[16], and may be one of the first studies to evaluate the utility of EUS elastography in Hispanic patients. Future research on this topic will be designed as diagnostic trials, considering the Giovannini score for PMs and associated LN descriptions.

Finally, hard PMs are not necessarily malignant all the time, whereas soft lesions are not necessarily nonmalignant[2,17]. Therefore, a validated cutoff value for defining malignancy in PMs and their associated LNs is imperative for obtaining an appropriate diagnosis and providing management guidance. Based on our findings, we recommend an SR cutoff values of > 121.0 and > 155.0 as criteria for supporting the need for FNA sampling of pancreatic lesions or their associated LNs, respectively. In

patients with SR values ranging from 21.5-121.0 and 14.0-155.0, sampling should be indicated if there is a high clinical suspicion of malignancy. [Figure 4](#) shows a proposed clinical algorithm using EUS elastography evaluations. We recommend starting with a qualitative measurement. For those with a low risk of malignancy (elastic score I-II), a 6-mo follow-up is necessary. However, for those with an elastic score between 3 and 5, a quantitative evaluation is required to define the SR measurement and determine the necessity of FNA and whether a malignancy is suspected.

CONCLUSION

We found that EUS combined with qualitative and quantitative elastography analysis *via* SR is a helpful resource when assessing PMs and their associated LNs. This approach is more effective and convenient than limiting the evaluation to only conventional EUS-fine needle aspiration for the detection of malignancy. Although histological analysis is mandatory for a final diagnosis, elastography should be included in the diagnostic workup of PMs and their associated LNs. However, validating this recommendation through a prospective, multi-center, controlled trial is preferable.

ARTICLE HIGHLIGHTS

Research background

Endoscopic ultrasound (EUS) elastography can be a useful technique for the evaluation of pancreatic masses (PMs) and their associated lymph nodes (LNs) through qualitative (analysis of color maps) and quantitative (assessing the strain ratio).

Research motivation

The accuracy of this technique in differentiating malignant from nonmalignant lesions has only been assessed for masses consisting of solid tissue. For the evaluation of solid-cystic lesions, the suitability of EUS-elastography has not been reported.

Research objectives

To determine the diagnostic accuracy of EUS elastography and the strain ratio (SR) cutoff value for malignant PMs and LNs in a Hispanic cohort.

Research methods

A retrospective study of patients who underwent EUS elastography for PMs between December 2013 and December 2014. A qualitative and quantitative (SR) analysis of PMs and their associated LNs was performed. The accuracy of EUS elastography in identifying malignant PMs and LNs and cutoff value for SR were analyzed. A PM and/or its associated LNs were considered malignant based on histopathological findings from fine-needle aspiration biopsy samples.

Research results

Malignant PMs have a superior median SR compared to nonmalignant lesions (50.4 *vs* 33.0, respectively) ($P < 0.001$). When analyzing LNs, there was no statistical significance (SR 30.0 for PMs *vs* 40.0 for LNs) ($P = 0.7182$). An SR cutoff value > 21.5 in PMs yielded a 94.2% sensitivity. Meanwhile, an SR cutoff value > 14.0 yielded a 90.9% sensitivity.

Research conclusions

The proposed EUS elastography SR cutoff values have a high sensitivity and specificity for the detection of malignancy.

Research perspectives

Future research evaluating the utility of EUS elastography in Hispanic patients through a prospective, multi-center, controlled trial is necessary to validate our data.

FOOTNOTES

Author contributions: Puga-Tejada M and Oleas R performed design of the work, acquisition, analysis, and interpretation of data, drafting and critical revision of the manuscript for important intellectual content, and final approval of the version to be published; Del Valle R, Egas-Izquierdo M, Ospina J and Soria-Alcivar M contributed to the acquisition of data for the work, critical revision of the manuscript for important intellectual content, and final approval of the version to be published; Egas-Izquierdo M performed the final database consolidation and

encryption; Arevalo-Mora M and Baquerizo-Burgos J contributed to the acquisition and analysis of data, drafting the manuscript, and final approval of the version to be published; Pitanga-Lukashok H contributed to the conception and design of the work, critical revision of the manuscript for important intellectual content, and final approval of the version to be published; Robles-Medranda C contributed to the conception and design of the work, drafting and critical revision of the manuscript for important intellectual content, and final approval of the version to be published.

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Informed consent statement: All study participants or their legal guardian provided informed written consent about personal and medical data collection prior to study enrolment.

Conflict-of-interest statement: Carlos Robles-Medranda is a key opinion leader and consultant for Pentax Medical, Boston Scientific, Steris, Medtronic, Motus, Microtech, G-Tech Medical Supply, CREO Medical, EndoSound, and Mdconsgroup. The other authors declare no conflicts of interest.

Data sharing statement: The Institutional Review Board approved the use and management of the corresponding data, and the study was conducted in accordance with the Declaration of Helsinki.

STROBE statement: The authors have read the STROBE Statement – checklist of items, and the manuscript was prepared and revised according to the STROBE Statement – checklist of items.

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