

Utility of quantitative elastography by Endoscopic Ultrasound (EUS) to diagnose solid pancreatic lesions (SPL)

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Abstract

Introduction: Endoscopic ultrasonography with fine-needle aspiration allows performing a diagnosis of solid pancreatic lesions with an approximate 85% sensitivity, as referenced in specialized literature, and even lower sensitivity as per local research. To yield better sensitivity and to improve the results, it is required to examine new elements (needles) and techniques like elastography. Elastography helps in the quantification of tissue stiffness with a high level of accuracy. Since 2001, elastography has been applied in diagnosing solid forms of cancer (tumors) that affect organs like breasts, the thyroid, and some muscles. This method which has been used to diagnose solid pancreatic lesions (SPL) since 2006 has proved to be useful as a complementary method to the existing diagnostic techniques. It improves the accuracy of the endoscopic ultrasound-guided fine-needle aspiration biopsy (EUS-FNA) by selecting the more suspicious area to be punctured, and it also guides the clinical treatment after getting a negative EUS-FNA or a non-conclusive result. **Objective:** To evaluate the diagnostical performance of the *strain ratio* (SR) quantitative elastography by ecoendoscopy in solid pancreatic lesions, considering the cytopathologic diagnostic as the gold standard. **Methods:** 71 patients (age range: 35-89 years old, mean: 62.2 years old); out of those 71 patients, The EUS to diagnose SPL, was performed on 35 women. This was a single-center, prospective cross-sectional study design. The EUS was performed with a Pentax linear endoscope and a Hitachi-Nobius ultrasound. The lesion (area A) and a reference area B were selected to calculate the deformation ratio (B/A, SR expressed as a percentage). SR > 22 was selected as a cut-off point to determine the malignant lesions (solid lesions), considering the evidence currently available. The results were compared with their cytopathology interpretation once that the EUS was performed. After the exclusion criteria was applied, a statistical analysis of 56 patients was performed, considering $p < 0,05$. The sensitivity, the specificity, the positive predictive value (PPV), the negative predictive value (NPV) and the diagnostic accuracy, were calculated, comparing the elastography SR with the final diagnostics with the cytopathology interpretation. **Results:** Quantitative elastography SR (%) allows to detect the malignant SPL with sensitivity 94.6% (95% confidence interval [CI]: 85.4%-98.2%), specificity of 89.3% (CI 95%: 78,5 %-95,0 %), PPV of 89.8% (CI 95 %: 79,5 %-95,3 %); NPV of 94.3% (IC 95 %: 84,6 %-98,1 %) and an accuracy of 92.0% (CI 95 %: 85,4 %-95,7 %). **Conclusion:** SR quantitative elastography by Endoscopic Ultrasound, EUS is a suitable complement method that improves the EUS-FNA accuracy, by selecting the most suspicious area to be punctured, and it also guides clinical treatment after getting a negative EUS-FNA or a non-conclusive result, due to its high sensitivity and specificity levels to diagnose malignant SPL.

Keywords

Elastography, Endoscopic ultrasound, Solid pancreatic lesion, Elasticity, Pancreas.

INTRODUCTION

The insertion into clinical practice of endoscopic ultrasonography (EUS) has allowed advancing the treatment of

a wide range of pathologies, significantly changing their diagnosis or management in 25%–50% of the cases^(1,2). In the pancreas, EUS obtains high-resolution images of the parenchyma and duct, so it is considered a method for

staging and diagnosing various entities, whether benign or malignant pancreatic diseases. Its role in the differential diagnosis of solid pancreatic lesions (SPL) stands out, representing a heterogeneous group of entities classified as neoplastic or non-neoplastic. Ductal adenocarcinoma is the most frequently detected malignant tumor, with up to 90% of all neoplastic pancreatic malignancies^(3,4).

Pancreatic cancer is a significant cause of mortality with a 5-year survival rate of less than 5%, reaching 20% in selected patients (non-invasive tumors undergoing surgical resection)⁽⁵⁾. EUS cannot always provide an accurate diagnosis using only images despite its demonstrated usefulness. So, obtaining tissue from the pancreas using endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) offers a good final diagnostic yield^(1,6,7), a sensitivity of approximately 85%–90%, false negatives of 15%, and specificities close to 100%^(7,8).

However, several factors substantially affect its yield since it is a demanding procedure from a technical point of view that may require multiple punctures to obtain a sufficient sample and make an adequate diagnosis⁽⁹⁾. Other factors that also affect it include interobserver variability, a non-standard technique, the endoscopist's experience, the position of the equipment, the time of day, the needle gauge used, the technique, the characteristics of lesions, the number of needle passes, the presence of the cytologist in the room, chronic pancreatitis, among others⁽¹⁰⁻¹⁷⁾. Therefore, new non-invasive methods have emerged to characterize these lesions more accurately, while EUS-FNA is limited to patients with highly-suspected malignant lesions. One of these techniques is *elastography*^(1,18), a non-invasive procedure emerging from the concepts that have been described since 1988, such as tissue deformability and elasticity of a solid tumor⁽¹⁹⁾. Later, in 1991, tissue elasticity was measured by evaluating a modulus of elasticity after exerting pressure. The term elastography was then used for the first time^(20,21), resulting in real-time B-mode ultrasound imaging development in 2001^(21,22). Since then, elastography has been applied to the diagnosis of solid tumors in various organs, such as the breast, thyroid, lymph nodes, and liver, but the use of elastography for SPL was reported for the first time in 2006^(21,23,24).

From a technical point of view, elastography is founded on the fact that the pressure exerted on a target lesion by an endoscopic ultrasound probe creates strain, which differs according to the hardness or softness of the tissue. So, it allows distinguishing the tissues considered benign—soft—from those malignant—hard—. The strain created in the tissues is represented through different colors based on elasticity (red is the softest tissue, and blue is the hardest tissue)^(21,25). There are two elastography systems available. The first is grounded on the qualitative assessment of the pattern obtained

from the elastographic study (qualitative elastography: If the color of the lesion is homogeneous blue, it suggests malignancy). The second quantifies stiffness using software (quantitative elastography)^(1,25). The most crucial advantage of EUS elastography is that it can provide the endoscopist with real-time data during diagnostic evaluation, assessing the nature of the patient's lesion and targeting it more accurately when taking the cytology sample by EUS-FNA, without a second endoscopic stage or additional diagnostic studies. It is noteworthy that EUS elastography is not yet considered a technique to replace biopsy. It may be a helpful complement since it improves the accuracy of the EUS-FNA biopsy by selecting the most suspicious area for puncture and guides further clinical management when EUS-FNA is negative or inconclusive^(18,25).

In Colombia, no clinical studies have shown the diagnostic yield of EUS elastography in SPL; therefore, this study evaluates the diagnostic yield of quantitative elastography or strain ratio (SR) in differentiating SPLs.

MATERIALS AND METHODS

Primary objective

To evaluate the diagnostic yield of the quantitative SR elastography obtained by EUS in SPLs using histopathological diagnosis as a standard.

Study design

This prospective cross-sectional study was conducted between January 2017 and January 2018 in a benchmark gastroenterology and endoscopic ultrasound unit. The unit's ethics committee approved the study, carried out under the Declaration of Helsinki and its amendments, and Good Clinical Practice guidelines⁽²⁶⁾.

Patients

A total of 682 endoscopic ultrasounds were performed in this period, of which 71 (10.56%) were patients referred for SPL puncture. We selected this group of patients considering the following inclusion criteria: patients older than 18 years of age with a diagnosis of SPL, endoscopic ultrasound report that included quantitative SR elastography and EUS-FNA, conclusive results of the cytopathology from puncture samples, and signed informed consent. The exclusion criteria were patients with performance status greater than 4 on the ECOG (Eastern Cooperative Oncology Group) scale (**Table 1**)⁽²⁷⁾, patients with bleeding risk (international normalized ratio [INR]) > 1.5 or platelet count < 50,000/mm², patients who take two or more

Table 1. ECOG Performance Status

Grade	Description
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities; up and about more than 50% of waking hours
3	Capable of only limited selfcare; confined to bed or chair more than 50% of waking hours
4	Completely disabled; cannot carry on any selfcare; totally confined to bed or chair
5	Dead

Taken from reference⁽²⁷⁾.

antiplatelet agents, patients with a pancreatic mass that cannot be detected by EUS, patients in whom puncture is not achievable due to anatomical variants (interposition of large vessels, altered surgical anatomy), pregnant women, patients under 18 years of age, and patients who did not authorize the inclusion of their data in the study. After following the criteria, we included 56 patients for analysis.

Statistical analysis

A fellow gastroenterology internist previously trained collected data from the included population through Google Drive virtual data tables filled in simultaneously with the procedure; these data were corrected and entered in the SPSS software (version 12.0; SPSS Inc.). SR data were tested using one-way analysis of variance, considering a p -value < 0.05 to indicate statistical significance. We present data as means, ranges, percentages, and 95% confidence intervals (CI), as appropriate. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy were calculated by comparing the diagnoses made by SR elastography and the final diagnoses provided by cytopathology, obtained through EUS-FNA.

Technique

EUS in all patients followed the quality indicators of the American Society for Gastrointestinal Endoscopy and the American College of Gastro-enterology⁽²⁸⁾. They were carried out in the gastroenterology ward of a benchmark unit under anesthesiologist-guided sedation, with a combination of propofol and remifentanyl titrated according to the characteristics of each patient. All procedures were performed with a Pentax linear echoendoscope (EG3870UTK; Pentax, Tokyo, Japan) combined with a Noblus portable

color Doppler ultrasound system (Hitachi Aloka Medical, Tokyo, Japan), including the elastography module, by an endoscopist experienced in interventional procedures, with more than 1,500 puncture endoscopic ultrasound procedures performed. Also, 22-gauge endoscopic ultrasound aspirating needles (Boston Scientific) were used.

According to the recommendations in the literature, the wet suction technique was employed to take biopsies, with a total of five passes and four motions within the lesion, given its higher diagnostic yield (85.2%) compared to the dry technique (71%) in our population (*results to be published*). In this technique, before puncturing the lesion, the stylet (22-gauge needle) is removed and pre-washed with 5 mL of saline solution to replace the air column with liquid. A 10 mL syringe is prefilled with 3 mL of saline solution and employed for subsequent aspiration when puncturing the lesion. Once the needle is inside, it is moved three times from one side to the other; this maneuver is repeated four times (passes) for a total of 12 motions. When the needle is withdrawn, the aspirate is released into a sheet by applying air⁽²⁹⁻³¹⁾. In addition to the higher diagnostic yield, a meta-analysis showed a lower rate of bleeding with this technique⁽³²⁾. The samples were fixed in ethyl alcohol and sent for cytopathological study by a pathology specialist.

For evaluating elastography, elasticity values were marked with different colors, resulting in different elastographic patterns that were superimposed on conventional B-mode EUS images, following the technical recommendations available in the literature published so far^(25,33). As a result, the color representation of hard, intermediate, and soft tissues was blue, green/yellow, and red, respectively. The linear echoendoscope was maneuvered towards the gastrointestinal lumen, administering the necessary strain to generate an optimal B-mode image at 7.5 MHz for elastography. The region of interest (ROI) for the elastographic

examination was chosen manually to cover the entire target area of the SPL (or most of it when the dimensions of the lesion did not allow it) and the surrounding tissues. The study required a five-second stable image for quantitative analysis and final definition of the pattern.

Two different ROI areas (A and B) were selected for quantitative elastographic analysis. Area A includes the entire lesion (when possible), while Area B includes the reference peripancreatic fatty area outside the tumor (fatty soft tissue)^(25,33,34). SR was calculated by the processor software expressed as a percentage, considering the ROIs, and calculating the B/A ratio^(25,35). We estimated their elasticity values three times in all patients to limit the selection bias of Areas A and B; the mean value of the three SR measures was deemed the analysis result. Values > 22 were taken as the cut-off point for SR to define malignant (hard) lesions, per the published data on the differential diagnosis of SPL, especially the cut-off point recently identified in a study carried out in 398 patients using SR values to detect pancreatic cancer. Specifically, they were 21.80 ± 12.23 ⁽³⁶⁾, a cut-off point similar to that found by Itokawa *et al*, and 39.08 ± 20.54 ⁽³⁷⁾. The published recommendations on the technique were considered⁽²⁵⁾.

RESULTS

A total of 682 endoscopic ultrasounds were performed between January 2017 and January 2018; 71 patients (10.56%) in an age range of 25-89 years (mean: 62.28 years) were diagnosed with SPL. The size of the evaluated lesions ranged between 15 and 60 mm (mean: 29.34 mm); the SR range (%) obtained was 12-189 (mean: 51.15). On the one hand, of these patients, 35 (49.3%) were female, in an age range of 25-89 years (mean: 63.32 years); the size of the lesion in this group was 15-55 mm (mean: 30.8041), and the SR range (%) was 13-189 (mean: 50.436). On the other hand, 36 (50.7%) patients were male, in an age range of 29-87 years (mean: 61.24); the size of the lesions in this group was 15-60 mm (mean: 27.97 mm), and the SR range (%) was 12-140 (mean: 51.86) (**Table 2**).

The puncture was performed in 100% of the patients, but in 11 (6 women and 5 men [15.5%]), the samples were not enough for pathology to reach a diagnostic conclusion. Two (2.8%) of the female patients did not give their authorization for the study, and we could not contact 2 patients (male and female; 2.8%) to know the results of the histopathological study. Statistical analysis was made on 56 patients, 24 females (42.8%) and 32 males (58.2%) (**Figure 1**). The endoscopic ultrasound diagnoses, their frequency, and the diagnoses found later in the histopathological study are summarized in **Table 2**.

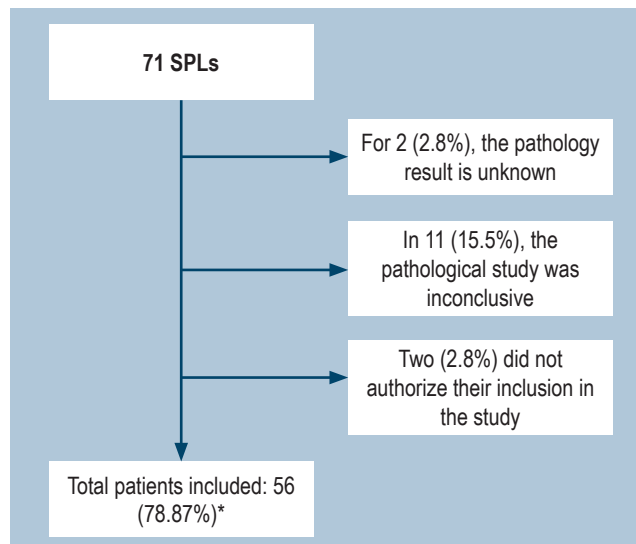


Figure 1. Flow diagram of patient inclusion in the study. *56 patients were included in the statistical analysis after meeting the inclusion and exclusion criteria proposed in the study's methodological design.

When performing the statistical analysis, we found that SR quantitative elastography (%) allows detecting malignant pancreatic masses with a sensitivity of 94.6% (95%CI: 85.4-98.2), specificity of 89.3% (95%CI: 78.5-95.0), PPV of 89.8% (95%CI: 79.5-95.3); NPV of 94.3% (95%CI: 84.6-98.1), and accuracy of 92.0% (95%CI: 85.4-95.7).

DISCUSSION

The prevalence of SPL is not as apparent. Strang *et al* reported a 0.6% prevalence of pancreatic masses in potentially healthy kidney donors⁽³⁸⁾; a similar prevalence of 0.49% was found among 2,941 patients undergoing 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) for unrelated causes⁽³⁹⁾. In Japan, of 39,785 FDG-PETs performed for cancer detection, the prevalence of pancreatic neoplasia was less than 0.001%⁽⁴⁰⁾, a figure more closely related to SEER (Surveillance, Epidemiology, and End Results program, United States), showing an overall incidence of 0.73% for 2013, which has increased⁽⁴¹⁾.

The differential diagnosis of SPLs is broad since they represent a heterogeneous group of entities classified as neoplastic and non-neoplastic. Neoplastic lesions (also called malignant) are the most common and include adenocarcinoma, neuroendocrine tumors, solid pseudopapillary tumor, pancreatoblastoma, lymphoma, metastases, and miscellaneous rarer neoplasias^(42,43). As mentioned, ductal adenocarcinoma is the most common malignant tumor of the pancreas and represents about 90% of all pancreatic

Table 2. Characteristics of the Patients

Sex	n	%	Age range (years)	Mean	Lesion size (range in mm)	Mean	SR (%)	Mean
Female	35	49.3	25-89	63.32671062	15-55	30.8041	13-189	50.436
Male	36	50.7	29-87	61.24544003	15-60	27.9732	12-140	51.867
Total	71	100	25-89	62.27738159	15-60	29.336	12-189	51.1516
Endoscopic ultrasound diagnosis								
- Cancer in the head of the pancreas	51	71.8						
- Cystadenocarcinoma	1	1.4						
- Injury to the head and body of the pancreas	2	2.8						
- Injury to the body of the pancreas	4	5.6						
- Focal injury to the head of the pancreas	6	8.4						
- Chronic pancreatitis	2	2.8						
- Frantz's tumor	2	2.8						
- Cancer in the tail of the pancreas	2	2.8						
- Injury to the neck of the pancreas	1	1.4						
- Total	71	100						
Histopathological diagnosis								
- Adenocarcinoma	48	67.6						
- No diagnosis	15	21.1						
- Chronic pancreatitis	4	5.6						
- Solid pseudopapillary tumor	2	2.8						
- Mesenchymal lesion with atypia	1	1.4						
- Oncocytic papillary neoplasia	1	1.4						
- Total	71	100						
- Do not meet the criteria for analysis	15	21.1						
- Total patients included in the statistical analysis	56	78.9						

malignant neoplasias^(3-5,44,45). The American Cancer Society estimates that 48,960 cases of pancreatic cancer developed in 2015 in the United States, and most patients (40,560) will die of the disease⁽⁴⁶⁾. The 5-year survival rate is less than 5%, reaching its highest point (20%) in selected patients with non-invasive tumors who underwent surgical resection⁽⁴⁷⁾.

Symptoms generally do not occur until the disease is advanced and frequently presents with obstructive jaundice, abdominal pain, anorexia, weight loss, acute pancrea-

titis, onset or poorly controlled diabetes, or steatorrhea. On physical examination, jaundice, muscle wasting, skin lesions, palpable lymphadenopathy, hepatomegaly, or palpable masses may be found. These lesions are sometimes found incidentally on control abdominal imaging, during the evaluation of abdominal pain, or in patients who present abnormalities on routine or diagnostic liver profiling tests. Remarkably, the increased levels of bilirubin and alkaline phosphatase may result in a diagnosis of cholesta-

sis due to biliary obstruction when the SPL is in the head of the pancreas; however, most patients present it without any symptoms, so the main objective is to detect it in its early stages. Currently, ultrasound, computerized axial tomography (CAT), and magnetic resonance imaging (MRI) are the mainstay in assessing 80%–85% of SPLs^(48,49).

The challenge of preoperative diagnosis of SPLs persists despite advances in imaging. EUS-FNA is considered the method of choice to detect and diagnose these lesions^(6,44). Diagnostic yield is highly sensitive and specific⁽⁵⁰⁾, but multiple factors affect its yield, driving the development of new diagnostic methods based on technological advances, such as elastography. The latter has been used successfully in examining organs other than the pancreas, such as breast, thyroid, prostate, cervix, liver, muscles, and others⁽⁵¹⁻⁵⁴⁾.

Elastography is based on the knowledge that different pathologies trigger processes such as fibrosis and inflammation, increasing the rigidity of tissues. Physiological vascular pulsations and respiratory movements provide the necessary vibrations and compressions that the software takes for the study; thus, elastography is built to mainly use the information from the aortic pulse wave^(1,55,56). Elastography can be performed in real-time using conventional endoscopic ultrasound equipment connected to a processor with specific software installed^(1,54-56). It is deemed an easy-to-use technique when performing an endosonography; it does not require additional preparation or changes in the patient's position or the anesthetic procedure.

There are two different generations in EUS elastography; the first generation allowed only qualitative assessment. Using this, Giovannini *et al*⁽⁵³⁾ published the first study on EUS-guided elastography in SPL. The sensitivity and specificity were reported for malignancy of 100% and 67%, respectively, considering the blue (hard) lesions as malignant. This study defined a scoring system (**Table 3**) to classify elastography less subjectively⁽⁵⁷⁾. In 2009, Giovannini *et al*, in a multicenter study with 121 cases, reported that EUS elastography in differentiating between benign and malignant pancreatic masses reached a sensitivity of 92.3%, with a specificity of 80.0%, PPV of 93.3%, NPV of 77.4%, and overall accuracy of 89.2%. Published that same year, Iglesias-García *et al*⁽⁵⁸⁾ evaluated 130 patients with solid pancreatic masses and 20 controls, defined four different elastography patterns, and reported a sensitivity of 100%, specificity of 85.5%, PPV of 90.7%, NPV of 100%, and accuracy of 94.0%. All subjects were evaluated by two endosonographers who made the same interpretation in 121 of 130 cases and 20 of 20 controls, with a 0.772 kappa index as a consistency evaluator. By 2015, Soares J-B *et al* appraised the interobserver consistency and concluded that EUS-guided elastography is reproducible in SPL assessment, even among inexperienced or little experienced echoendoscopists⁽⁵⁹⁾. Despite the

results described, it is a subjective and operator-dependent technique whose main problem is reproducing the image within the procedure, which is why research continued⁽⁶⁰⁾.

Table 3. Classification of Elastographic Patterns for EUS

Color and pattern	Rigidity	Malignancy
Homogeneous, green predominates	Soft	No
Heterogeneous, green predominates	Intermediate	No
Heterogeneous, blue predominates	Hard	Yes
Homogeneous, blue predominates	Hard	Yes
Heterogeneous, green and blue with no predominant color	Hard intermediate	Indeterminate

Taken from reference⁽⁵⁷⁾.

Currently, second-generation EUS elastography and qualitative assessment enable quantitative estimation of tissue stiffness with two different approaches: SR and strain histogram. SR is the most widely disseminated with the largest number of studies, for which it was taken as the base criterion of the study; SR compares the strain between target area A and other reference areas B to provide more objective qualitative data^(1,37). Multiple studies use SR to diagnose pancreatic carcinoma differentially^(53,61-67). All of them have variants in taking the areas of interest to ROI; some take healthy pancreatic tissue, peripancreatic tissue, and mesenteric fat, and others take the duodenal wall as a reference to obtain SR. In our study, peripancreatic fat was used to compare lesions (ROI B); it is a soft tissue that can be quickly evaluated in the same image or ultrasound cut given the anatomical proximity of these structures and for being the pattern for breast lesions, with which this technique was initially described⁽⁶⁸⁻⁷⁰⁾.

The diagnostic yield of SR qualitative elastography has been estimated over time in different meta-analyses. In 2012, elastography had a sensitivity of 95% (95%CI: 93–96) and a specificity of 69% (95%CI: 63–75)⁽⁷¹⁾. In 2013, 13 studies were assessed with 1,042 cases and a sensitivity of 95% (95%CI: 94–97), specificity of 67% (95%CI: 61–73), and odds ratio (OR) of 42.28 (95%CI: 26.90–66.46)⁽⁷²⁾. Also, in 2013, another meta-analysis included seven studies with 752 patients and found that the sensitivity of EUS elastography for the differential diagnosis of solid pancreatic masses was 97% (95%CI: 0.95–0.98), and the specificity was 76% (95%CI: 0.69–0.82). The area under the curve (AUC) was 0.9529. The positive probability ratio was 3.71 (95%CI: 2.72–5.07), and the negative probability ratio was 0.05 (95%CI: 0.02–0.13)⁽⁷³⁾. Another meta-analysis published in the same year included ten stu-

dies with a total of 781 patients and reported a sensitivity of 92% (95%CI: 0.89-0.95), specificity of 76% (95%CI: 0.67-0.83), positive likelihood ratio (*LR* [+]) of 2.84 (95%CI: 2.05-3.93), negative likelihood ratio (*LR* [-]) of 0.12 (95%CI: 0.08-0.19), and diagnostic OR of 24.69 (95%CI: 12.81-47.59)⁽⁷⁴⁾. Nonetheless, all these studies reveal significant heterogeneity due to the variability between controlled clinical trials included, mainly the selection of different ROIs (the *soft* reference area B). Other factors to consider are the distance of the reference area from the echoendoscope, which also significantly impacts SR measurements⁽⁷⁵⁾, various SR cut-off points, and the subjectivity of qualitative elastography.

More recently, in 2018, a new meta-analysis that included a total of 19 studies with 1,687 patients who underwent quantitative elastography showed a sensitivity of 95% (95%CI: 0.93–0.97), specificity of 61% (95%CI: 0.56–0.66), *LR* (+) of 2.64 (95%CI: 1.82–3.82), and *LR* (-) of 0.10 (95%CI: 0.06-0.16)⁽⁷⁶⁾. Our study found a sensitivity of 94.6% (95%CI: 85.4–98.2), matching the sensitivity figures reported in the meta-analyses; however, the specificity was 89.3% (95%CI: 78.5–95.0), which is slightly higher than that reported in the literature. This finding may be due to our patients having more advanced and larger lesions (30 mm on average), significantly increasing the possibility of malignancy (86.9%–93.2%)^(77,78). The age of the patients and the methodology reduced confounding factors previously identified in the literature, such as taking peripancreatic fat for comparison (*soft* tissue, ROI B), taking the average out of three different SRs in the same patient, using a previously evaluated standard cut-off point (> 22), the experience of the endosonographer, and using more technological equipment. Likewise, the reduction of confounding factors was also achieved

by following the recommendations on the technical principles of real-time tissue elastography recently described in detail by the European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) and the World Federation of Ultrasound in Medicine and Biology (WFUMB). In summary, these parameters comprise an appropriate transducer and the selection of the adequate frequency, number of frames per second, line density, probing speed and amplitude, noise filters (ultrasonographic), persistence, the dynamic range of elasticity, and other quality parameters (e.g., viewing the deformation graph)^(70,79-81). For its part, the *PPV* of 89.8% (95%CI: 79.5-95.3), *NPV* of 94.3% (95%CI: 84.6–98.1), and accuracy of 92.0% (95%CI: 85.4–95.7) are consistent with those found in a recently published retrospective study of 116 patients (97 with malignant lesions and 19 with benign lesions) with a median age of 55.9 years old; an SR cut-off point of 7.75 was used with a specificity of 99.9%, sensitivity of 90.7%, *PPV* of 99.9%, *NPV* of 67.9%, and accuracy of 92.2%⁽⁸²⁾.

CONCLUSION

Differential diagnosis of SPL remains one of the most difficult diagnostic challenges in clinical practice. EUS-FNA is the best method for diagnosing solid pancreatic tumors due to its high sensitivity and specificity when combined with quantitative elastography. However, EUS elastography is not yet considered a modality that can replace biopsy. It is a valuable complement since it improves the accuracy of the EUS-FNA biopsy by selecting the most suspicious area to be punctured. Additionally, it helps guide additional clinical management when EUS-FNA is negative or inconclusive because, as this paper shows, it is highly sensitive and specific in diagnosing malignant tumors of the pancreas.

REFERENCES

1. Iglesias-García J, Lariño-Noia J, Domínguez-Muñoz JE. New Imaging Techniques: Endoscopic Ultrasound-Guided Elastography. *Gastrointest Endosc Clin N Am*. 2017;27(4):551-567. <https://doi.org/10.1016/j.giec.2017.06.001>
2. Luthra AK, Evans JA. Review of current and evolving clinical indications for endoscopic ultrasound. *World J Gastrointest Endosc*. 2016;8(3):157-64. <https://doi.org/10.4253/wjge.v8.i3.157>
3. Kleeff J, Korc M, Apte M, La Vecchia C, Johnson CD, Biankin AV, Neale RE, Tempero M, Tuveson DA, Hruban RH, Neoptolemos JP. Pancreatic cancer. *Nat Rev Dis Primers*. 2016;2:16022. <https://doi.org/10.1038/nrdp.2016.22>
4. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2018;68(6):394-424. <https://doi.org/10.3322/caac.21492>
5. Xiao AY, Tan ML, Wu LM, Asrani VM, Windsor JA, Yadav D, Petrov MS. Global incidence and mortality of pancreatic diseases: a systematic review, meta-analysis, and meta-regression of population-based cohort studies. *Lancet Gastroenterol Hepatol*. 2016;1(1):45-55. [https://doi.org/10.1016/S2468-1253\(16\)30004-8](https://doi.org/10.1016/S2468-1253(16)30004-8)

6. Wang W, Shpaner A, Krishna SG, Ross WA, Bhutani MS, Tamm EP, Raju GS, Xiao L, Wolff RA, Fleming JB, Lee JH. Use of EUS-FNA in diagnosing pancreatic neoplasm without a definitive mass on CT. *Gastrointest Endosc.* 2013;78(1):73-80.
<https://doi.org/10.1016/j.gie.2013.01.040>
7. Hewitt MJ, McPhail MJ, Possamai L, Dhar A, Vlavianos P, Monahan KJ. EUS-guided FNA for diagnosis of solid pancreatic neoplasms: a meta-analysis. *Gastrointest Endosc.* 2012;75(2):319-31.
<https://doi.org/10.1016/j.gie.2011.08.049>
8. Bhatia V, Varadarajulu S. Endoscopic ultrasonography-guided tissue acquisition: How to achieve excellence. *Dig Endosc.* 2017;29(4):417-430.
<https://doi.org/10.1111/den.12823>
9. Polkowski M, Larghi A, Weynand B, Boustière C, Giovannini M, Pujol B, Dumonceau JM; European Society of Gastrointestinal Endoscopy (ESGE). Learning, techniques, and complications of endoscopic ultrasound (EUS)-guided sampling in gastroenterology: European Society of Gastrointestinal Endoscopy (ESGE) Technical Guideline. *Endoscopy.* 2012;44(2):190-206.
<https://doi.org/10.1055/s-0031-1291543>
10. Korenblit J, Tholey DM, Tolin J, Loren D, Kowalski T, Adler DG, Davolos J, Siddiqui AA. Effect of the time of day and queue position in the endoscopic schedule on the performance characteristics of endoscopic ultrasound-guided fine-needle aspiration for diagnosing pancreatic malignancies. *Endosc Ultrasound.* 2016;5(2):78-84.
<https://doi.org/10.4103/2303-9027.180470>
11. Ramesh J, Bang JY, Hebert-Magee S, Trevino J, Eltoun I, Frost A, Hasan MK, Logue A, Hawes R, Varadarajulu S. Randomized Trial Comparing the Flexible 19G and 25G Needles for Endoscopic Ultrasound-Guided Fine Needle Aspiration of Solid Pancreatic Mass Lesions. *Pancreas.* 2015;44(1):128-33.
<https://doi.org/10.1097/MPA.0000000000000217>
12. Madhoun MF, Wani SB, Rastogi A, Early D, Gaddam S, Tierney WM, Maple JT. The diagnostic accuracy of 22-gauge and 25-gauge needles in endoscopic ultrasound-guided fine needle aspiration of solid pancreatic lesions: a meta-analysis. *Endoscopy.* 2013;45(2):86-92.
<https://doi.org/10.1055/s-0032-1325992>
13. Kamata K, Kitano M, Yasukawa S, Kudo M, Chiba Y, Ogura T, Higuchi K, Fukutake N, Ashida R, Yamasaki T, Nebiki H, Hirose S, Hoki N, Asada M, Yazumi S, Takaoka M, Okazaki K, Matsuda F, Okabe Y, Yanagisawa A. Histologic diagnosis of pancreatic masses using 25-gauge endoscopic ultrasound needles with and without a core trap: a multicenter randomized trial. *Endoscopy.* 2016;48(7):632-8.
<https://doi.org/10.1055/s-0042-106294>
14. Nakai Y, Isayama H, Chang KJ, Yamamoto N, Hamada T, Uchino R, Mizuno S, Miyabayashi K, Yamamoto K, Kawakubo K, Kogure H, Sasaki T, Hirano K, Tanaka M, Tada M, Fukayama M, Koike K. Slow pull versus suction in endoscopic ultrasound-guided fine-needle aspiration of pancreatic solid masses. *Dig Dis Sci.* 2014;59(7):1578-85.
<https://doi.org/10.1007/s10620-013-3019-9>
15. Bang JY, Magee SH, Ramesh J, Trevino JM, Varadarajulu S. Randomized trial comparing fanning with standard technique for endoscopic ultrasound-guided fine-needle aspiration of solid pancreatic mass lesions. *Endoscopy.* 2013;45(6):445-50.
<https://doi.org/10.1055/s-0032-1326268>
16. Suzuki R, Irisawa A, Bhutani MS, Hikichi T, Takagi T, Sato A, Sato M, Ikeda T, Watanabe K, Nakamura J, Tasaki K, Obara K, Ohira H. Prospective evaluation of the optimal number of 25-gauge needle passes for endoscopic ultrasound-guided fine-needle aspiration biopsy of solid pancreatic lesions in the absence of an onsite cytopathologist. *Dig Endosc.* 2012;24(6):452-6.
<https://doi.org/10.1111/j.1443-1661.2012.01311.x>
17. Hébert-Magee S, Bae S, Varadarajulu S, Ramesh J, Frost AR, Eloubeidi MA, Eltoun IA. The presence of a cytopathologist increases the diagnostic accuracy of endoscopic ultrasound-guided fine needle aspiration cytology for pancreatic adenocarcinoma: a meta-analysis. *Cytopathology.* 2013;24(3):159-71.
<https://doi.org/10.1111/cyt.12071>
18. Cui XW, Chang JM, Kan QC, Chiorean L, Ignee A, Dietrich CF. Endoscopic ultrasound elastography: Current status and future perspectives. *World J Gastroenterol.* 2015;21(47):13212-24.
<https://doi.org/10.3748/wjg.v21.i47.13212>
19. Ueno E, Tohno E, Soeda S, Asaoka Y, Itoh K, Bamber JC, Blaszczyk M, Davey J, Mckinna JA. Dynamic tests in real-time breast echography. *Ultrasound Med Biol.* 1988;14 Suppl 1:53-7.
[https://doi.org/10.1016/0301-5629\(88\)90047-6](https://doi.org/10.1016/0301-5629(88)90047-6)
20. Ophir J, Céspedes I, Ponnekanti H, Yazdi Y, Li X. Elastography: a quantitative method for imaging the elasticity of biological tissues. *Ultrasound Imaging.* 1991;13(2):111-34.
<https://doi.org/10.1177/016173469101300201>
21. Chantarojanasiri T, Kongkam P. Endoscopic ultrasound elastography for solid pancreatic lesions. *World J Gastrointest Endosc.* 2017;9(10):506-513.
<https://doi.org/10.4253/wjge.v9.i10.506>
22. Shiina T, Nitta N, Ueno E, Bamber JC. Real time tissue elasticity imaging using the combined autocorrelation method. *J Med Ultrason (2001).* 2002;29(3):119-28.
<https://doi.org/10.1007/BF02481234>
23. Giovannini M, Hookey LC, Bories E, Pesenti C, Monges G, Delpero JR. Endoscopic ultrasound elastography: the first step towards virtual biopsy? Preliminary results in 49 patients. *Endoscopy.* 2006;38(4):344-8.
<https://doi.org/10.1055/s-2006-925158>
24. Gennisson JL, Deffieux T, Fink M, Tanter M. Ultrasound elastography: principles and techniques. *Diagn Interv Imaging.* 2013;94(5):487-95.
<https://doi.org/10.1016/j.diii.2013.01.022>

25. Costache MI, Dumitrescu D, Săftoiu A. Technique of qualitative and semiquantitative EUS elastography in pancreatic examination. *Endosc Ultrasound*. 2017;6(Suppl 3):S111-S114. https://doi.org/10.4103/eus.eus_75_17
26. Declaración de Helsinki de la AMM. Principios éticos para las investigaciones médicas en seres humanos [internet]. AMM [consultado el 10 de agosto de 2019]. Disponible en: www.wma.net/es/politicas-post/declaracion-de-helsinki-de-la-amm-principios-eticos-para-las-investigaciones-medicas-en-seres-humanos
27. Pérez Cruz PE, Acevedo F. Escalas de estado funcional (o performance status) en cáncer. *Gastroenterol Latinoam*. 2014;25(3):219-226.
28. Wani S, Wallace MB, Cohen J, Pike IM, Adler DG, Kochman ML, Lieb JG 2nd, Park WG, Rizk MK, Sawhney MS, Shaheen NJ, Tokar JL. Quality indicators for EUS. *Am J Gastroenterol*. 2015;110(1):102-13. <https://doi.org/10.1038/ajg.2014.387>
29. Villa NA, Berzosa M, Wallace MB, Raijman I. Endoscopic ultrasound-guided fine needle aspiration: The wet suction technique. *Endosc Ultrasound*. 2016;5(1):17-20. <https://doi.org/10.4103/2303-9027.175877>
30. Polkowski M, Jenssen C, Kaye P, Carrara S, Deprez P, Gines A, Fernández-Esparrach G, Eisendrath P, Aithal GP, Arcidiacono P, Barthet M, Bastos P, Fornelli A, Napoleon B, Iglesias-Garcia J, Seicean A, Larghi A, Hassan C, van Hooft JE, Dumonceau JM. Technical aspects of endoscopic ultrasound (EUS)-guided sampling in gastroenterology: European Society of Gastrointestinal Endoscopy (ESGE) Technical Guideline - March 2017. *Endoscopy*. 2017;49(10):989-1006. <https://doi.org/10.1055/s-0043-119219>
31. Attam R, Arain MA, Bloechl SJ, Trikudanathan G, Munigala S, Bakman Y, Singh M, Wallace T, Henderson JB, Catalano MF, Guda NM. "Wet suction technique (WEST)": a novel way to enhance the quality of EUS-FNA aspirate. Results of a prospective, single-blind, randomized, controlled trial using a 22-gauge needle for EUS-FNA of solid lesions. *Gastrointest Endosc*. 2015;81(6):1401-7. <https://doi.org/10.1016/j.gie.2014.11.023>
32. Lee JK, Choi JH, Lee KH, Kim KM, Shin JU, Lee JK, Lee KT, Jang KT. A prospective, comparative trial to optimize sampling techniques in EUS-guided FNA of solid pancreatic masses. *Gastrointest Endosc*. 2013;77(5):745-51. <https://doi.org/10.1016/j.gie.2012.12.009>
33. Dietrich CF, Bibby E, Jenssen C, Saftoiu A, Iglesias-Garcia J, Havre RF. EUS elastography: How to do it? *Endosc Ultrasound*. 2018;7(1):20-28. https://doi.org/10.4103/eus.eus_49_17
34. Dietrich CF, Săftoiu A, Jenssen C. Real time elastography endoscopic ultrasound (RTE-EUS), a comprehensive review. *Eur J Radiol*. 2014;83(3):405-14. <https://doi.org/10.1016/j.ejrad.2013.03.023>
35. Kamata K, Kitano M, Omoto S, Kadosaka K, Miyata T, Minaga K, Yamao K, Imai H, Kudo M. New endoscopic ultrasonography techniques for pancreaticobiliary diseases. *Ultrasonography*. 2016;35(3):169-79. <https://doi.org/10.14366/usg.15042>
36. Kim SY, Cho JH, Kim YJ, Kim EJ, Park JY, Jeon TJ, Kim YS. Diagnostic efficacy of quantitative endoscopic ultrasound elastography for differentiating pancreatic disease. *J Gastroenterol Hepatol*. 2017;32(5):1115-1122. <https://doi.org/10.1111/jgh.13649>
37. Itokawa F, Itoi T, Sofuni A, Kurihara T, Tsuchiya T, Ishii K, Tsuji S, Ikeuchi N, Umeda J, Tanaka R, Yokoyama N, Moriyasu F, Kasuya K, Nagao T, Kamisawa T, Tsuchida A. EUS elastography combined with the strain ratio of tissue elasticity for diagnosis of solid pancreatic masses. *J Gastroenterol*. 2011;46(6):843-53. <https://doi.org/10.1007/s00535-011-0399-5>
38. Strang AM, Lockhart ME, Kenney PJ, Amling CL, Urban DA, El-Galley R, Burns JR, Colli JL, Hammontree LN, Kolettis PN. Computerized tomographic angiography for renal donor evaluation leads to a higher exclusion rate. *J Urol*. 2007;177(5):1826-9. <https://doi.org/10.1016/j.juro.2007.01.007>
39. Pitts A, Nissen NN, Waxman A, Yu R. Unsuspected fluorodeoxyglucose positron emission tomography (FDG-PET)-positive pancreatic lesions: prevalence and significance. *Pancreas*. 2013;42(7):1191-3. <https://doi.org/10.1097/MPA.0b013e318287d06e>
40. Weckesser M, Schober O. Is whole-body FDG-PET valuable for health screening? Against. *Eur J Nucl Med Mol Imaging*. 2005;32(3):342-3. <https://doi.org/10.1007/s00259-005-1775-2>
41. Gordon-Dseagu VL, Devesa SS, Goggins M, Stolzenberg-Solomon R. Pancreatic cancer incidence trends: evidence from the Surveillance, Epidemiology and End Results (SEER) population-based data. *Int J Epidemiol*. 2018;47(2):427-439. <https://doi.org/10.1093/ije/dyx232>
42. Zárate X, Williams N, Herrera MF. Pancreatic incidentalomas. *Best Pract Res Clin Endocrinol Metab*. 2012;26(1):97-103. <https://doi.org/10.1016/j.beem.2011.06.005>
43. Low G, Panu A, Millo N, Leen E. Multimodality imaging of neoplastic and nonneoplastic solid lesions of the pancreas. *Radiographics*. 2011;31(4):993-1015. <https://doi.org/10.1148/rg.314105731>
44. Kamisawa T, Wood LD, Itoi T, Takaori K. Pancreatic cancer. *Lancet*. 2016;388(10039):73-85. [https://doi.org/10.1016/S0140-6736\(16\)00141-0](https://doi.org/10.1016/S0140-6736(16)00141-0)
45. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray F. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer*. 2015;136(5):E359-86. <https://doi.org/10.1002/ijc.29210>
46. ASGE Standards of Practice Committee, Eloubeidi MA, Decker GA, Chandrasekhara V, Chathadi KV, Early DS, Evans JA, Fanelli RD, Fisher DA, Foley K, Hwang JH, Jue

- TL, Lightdale JR, Pasha SF, Saltzman JR, Sharaf R, Shergill AK, Cash BD, DeWitt JM. The role of endoscopy in the evaluation and management of patients with solid pancreatic neoplasia. *Gastrointest Endosc.* 2016;83(1):17-28. <https://doi.org/10.1016/j.gie.2015.09.009>
47. Liles JS, Katz MH. Pancreaticoduodenectomy with vascular resection for pancreatic head adenocarcinoma. *Expert Rev Anticancer Ther.* 2014;14(8):919-29. <https://doi.org/10.1586/14737140.2014.919860>
 48. Hanada K, Okazaki A, Hirano N, Izumi Y, Teraoka Y, Ikemoto J, Kanemitsu K, Hino F, Fukuda T, Yonehara S. Diagnostic strategies for early pancreatic cancer. *J Gastroenterol.* 2015;50(2):147-54. <https://doi.org/10.1007/s00535-014-1026-z>
 49. Scialpi M, Reginelli A, D'Andrea A, Gravante S, Falcone G, Baccari P, Manganaro L, Palumbo B, Cappabianca S. Pancreatic tumors imaging: An update. *Int J Surg.* 2016;28 Suppl 1:S142-55. <https://doi.org/10.1016/j.ijso.2015.12.053>
 50. Bang JY, Hebert-Magee S, Navaneethan U, Hasan MK, Hawes R, Varadarajulu S. EUS-guided fine needle biopsy of pancreatic masses can yield true histology. *Gut.* 2018;67(12):2081-2084. <https://doi.org/10.1136/gutjnl-2017-315154>
 51. Meng FS, Zhang ZH, Ji F. New endoscopic ultrasound techniques for digestive tract diseases: A comprehensive review. *World J Gastroenterol.* 2015;21(16):4809-16. <https://doi.org/10.3748/wjg.v21.i16.4809>
 52. Hirooka Y, Itoh A, Hashimoto S, Kawashima H, Hara K, Kanamori A, Uchida H, Goto J, Ishikawa S, Ohmiya N, Niwa Y, Goto H. Utility of EUS: Elastography in the Diagnosis of Pancreatic Diseases. *Gastroenterology.* 2005;61(5):AB282. [https://doi.org/10.1016/S0016-5107\(05\)01447-1](https://doi.org/10.1016/S0016-5107(05)01447-1)
 53. Okasha H, Elkholy S, El-Sayed R, Wifi MN, El-Nady M, El-Nabawi W, El-Dayem WA, Radwan MI, Farag A, El-Sherif Y, Al-Gemeie E, Salman A, El-Sherbiny M, El-Mazny A, Mahdy RE. Real time endoscopic ultrasound elastography and strain ratio in the diagnosis of solid pancreatic lesions. *World J Gastroenterol.* 2017;23(32):5962-5968. <https://doi.org/10.3748/wjg.v23.i32.5962>
 54. Arcidiacono PG. Endoscopic ultrasound elastography. *Gastroenterol Hepatol (NY).* 2012;8(1):48-67.
 55. Sigrist RMS, Liao J, Kaffas AE, Chammas MC, Willmann JK. Ultrasound Elastography: Review of Techniques and Clinical Applications. *Theranostics.* 2017;7(5):1303-1329. <https://doi.org/10.7150/thno.18650>
 56. Săftoiu, A., Gheonea, D. I., Cârțână, T., & Streba, C. Advanced endoscopic ultrasound imaging: contrast-enhanced endoscopic ultrasound (low MI, high MI), including 3D techniques in Pancreatic imaging. *Video Journal and Encyclopedia of GI Endoscopy*, 2013, 1, 534-536.
 57. Janssen J, Schlörer E, Greiner L. EUS elastography of the pancreas: feasibility and pattern description of the normal pancreas, chronic pancreatitis, and focal pancreatic lesions. *Gastrointest Endosc.* 2007;65(7):971-8. <https://doi.org/10.1016/j.gie.2006.12.057>
 58. Iglesias-Garcia J, Larino-Noia J, Abdulkader I, Forteza J, Dominguez-Munoz JE. EUS elastography for the characterization of solid pancreatic masses. *Gastrointest Endosc.* 2009;70(6):1101-8. <https://doi.org/10.1016/j.gie.2009.05.011>
 59. Soares JB, Iglesias-Garcia J, Goncalves B, Lindkvist B, Lariño-Noia J, Bastos P, Caetano AC, Ferreira A, Pimentel-Nunes P, Lopes L, Moutinho-Ribeiro P, Dominguez-Muñoz JE. Interobserver agreement of EUS elastography in the evaluation of solid pancreatic lesions. *Endosc Ultrasound.* 2015;4(3):244-9. <https://doi.org/10.4103/2303-9027.163016>
 60. Giovannini M. What is the place of pancreatic endoscopic ultrasound elastography in 2018? *Endoscopy.* 2018;50(11):1051-1052. <https://doi.org/10.1055/a-0637-8840>
 61. Kongkam P, Lakananurak N, Navicharern P, Chantarojanasiri T, Aye K, Ridditid W, Kritisin K, Angsuwatcharakon P, Aniwon S, Pittayanon R, Sampatanukul P, Treeprasertsuk S, Kullavanijaya P, Rerknimitr R. Combination of EUS-FNA and elastography (strain ratio) to exclude malignant solid pancreatic lesions: A prospective single-blinded study. *J Gastroenterol Hepatol.* 2015;30(11):1683-9. <https://doi.org/10.1111/jgh.13067>
 62. Dietrich CF, Sahai AV, D'Onofrio M, Will U, Arcidiacono PG, Petrone MC, Hocke M, Braden B, Burmester E, Möller K, Săftoiu A, Ignee A, Cui XW, Iordache S, Potthoff A, Iglesias-Garcia J, Fusaroli P, Dong Y, Jenssen C. Differential diagnosis of small solid pancreatic lesions. *Gastrointest Endosc.* 2016;84(6):933-940. <https://doi.org/10.1016/j.gie.2016.04.034>
 63. Iglesias-Garcia J, Lindkvist B, Lariño-Noia J, Abdulkader-Nallib I, Dominguez-Muñoz JE. 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. <https://doi.org/10.1177/2050640616640635>
 64. Ignee A, Jenssen C, Arcidiacono PG, Hocke M, Möller K, Săftoiu A, Will U, Fusaroli P, Iglesias-Garcia J, Ponnudurai R, Petrone MC, Braden B, Burmester E, Dong Y, Atkinson NS, Dietrich CF. Endoscopic ultrasound elastography of small solid pancreatic lesions: a multicenter study. *Endoscopy.* 2018;50(11):1071-1079. <https://doi.org/10.1055/a-0588-4941>
 65. Iordache S, Costache MI, Popescu CF, Streba CT, Cazacu S, Săftoiu A. Clinical impact of EUS elastography followed by contrast-enhanced EUS in patients with focal pancreatic masses and negative EUS-guided FNA. *Med Ultrason.* 2016;18(1):18-24. <https://doi.org/10.11152/mu.2013.2066.181.ich>
 66. Carrara S, Auriemma F, Di Leo M, Rahal D, Preatoni P, Correale L, Anderloni A, Repici A. Endoscopic ultrasound-elastography (strain ratio) in the diagnosis of solid pancreatic lesions: A prospective cohort study. *Endosc Ultrasound.* 2017;6(Suppl 2):S54. <https://doi.org/10.4103/2303-9027.218430>

67. Hernández Mondragón OV, Velez Resendiz JM, Ruiz RR. Quantitative Elastography Versus Fine-needle Aspiration by Endoscopic Ultrasound for the Assessment of Pancreatic Solid Masses. *J Clin Gastroenterol.* 2019;53(7):e261-e268. <https://doi.org/10.1097/MCG.0000000000001017>
68. Ueno E, Umemoto T, Bando H, Tohno E, Waki K, Matsumura T. New quantitative method in breast elastography: fat-lesion ratio (FLR). En: Proceedings of the radiological society of North America scientific assembly and annual meeting. Chicago: Radiological Society of North America; 2007. p. 25-30.
69. Itoh Y, Itoh A, Kawashima H, Ohno E, Nakamura Y, Hiramatsu T, Sugimoto H, Sumi H, Hayashi D, Kuwahara T, Morishima T, Funasaka K, Nakamura M, Miyahara R, Ohmiya N, Katano Y, Ishigami M, Goto H, Hirooka Y. Quantitative analysis of diagnosing pancreatic fibrosis using EUS-elastography (comparison with surgical specimens). *J Gastroenterol.* 2014;49(7):1183-92. <https://doi.org/10.1007/s00535-013-0880-4>
70. Hirooka Y, Kuwahara T, Irisawa A, Itokawa F, Uchida H, Sasahira N, Kawada N, Itoh Y, Shiina T. JSUM ultrasound elastography practice guidelines: pancreas. *J Med Ultrason (2001).* 2015;42(2):151-74. <https://doi.org/10.1007/s10396-014-0571-7>
71. Pei Q, Zou X, Zhang X, Chen M, Guo Y, Luo H. Diagnostic value of EUS elastography in differentiation of benign and malignant solid pancreatic masses: a meta-analysis. *Pancreatol.* 2012;12(5):402-8. <https://doi.org/10.1016/j.pan.2012.07.013>
72. Mei M, Ni J, Liu D, Jin P, Sun L. EUS elastography for diagnosis of solid pancreatic masses: a meta-analysis. *Gastrointest Endosc.* 2013;77(4):578-89. <https://doi.org/10.1016/j.gie.2012.09.035>
73. Hu DM, Gong TT, Zhu Q. Endoscopic ultrasound elastography for differential diagnosis of pancreatic masses: a meta-analysis. *Dig Dis Sci.* 2013;58(4):1125-31. <https://doi.org/10.1007/s10620-012-2428-5>
74. Li X, Xu W, Shi J, Lin Y, Zeng X. Endoscopic ultrasound elastography for differentiating between pancreatic adenocarcinoma and inflammatory masses: a meta-analysis. *World J Gastroenterol.* 2013;19(37):6284-91. <https://doi.org/10.3748/wjg.v19.i37.6284>
75. Havre RF, Waage JR, Gilja OH, Ødegaard S, Nesje LB. Real-Time Elastography: Strain Ratio Measurements Are Influenced by the Position of the Reference Area. *Ultraschall Med.* 2012;33(6):559-568. <https://doi.org/10.1055/s-0031-1273247>
76. Zhang B, Zhu F, Li P, Yu S, Zhao Y, Li M. Endoscopic ultrasound elastography in the diagnosis of pancreatic masses: A meta-analysis. *Pancreatol.* 2018;18(7):833-840. <https://doi.org/10.1016/j.pan.2018.07.008>
77. Jafri M, Sachdev AH, Khanna L, Gress FG. The Role of Real Time Endoscopic Ultrasound Guided Elastography for Targeting EUS-FNA of Suspicious Pancreatic Masses: A Review of the Literature and A Single Center Experience. *JOP.* 2016;17(5):516-524.
78. Siddiqui AA, Brown LJ, Hong SK, Draganova-Tacheva RA, Korenblit J, Loren DE, Kowalski TE, Solomides C. Relationship of pancreatic mass size and diagnostic yield of endoscopic ultrasound-guided fine needle aspiration. *Dig Dis Sci.* 2011;56(11):3370-5. <https://doi.org/10.1007/s10620-011-1782-z>
79. Shiina T, Nightingale KR, Palmeri ML, Hall TJ, Bamber JC, Barr RG, Castera L, Choi BI, Chou YH, Cosgrove D, Dietrich CF, Ding H, Amy D, Farrokh A, Ferraioli G, Filice C, Friedrich-Rust M, Nakashima K, Schafer F, Sporea I, Suzuki S, Wilson S, Kudo M. WFUMB guidelines and recommendations for clinical use of ultrasound elastography: Part 1: basic principles and terminology. *Ultrasound Med Biol.* 2015;41(5):1126-47. <https://doi.org/10.1016/j.ultrasmedbio.2015.03.009>
80. Cosgrove D, Piscaglia F, Bamber J, Bojunga J, Correas JM, Gilja OH, Klausner AS, Sporea I, Calliada F, Cantisani V, D'Onofrio M, Drakonaki EE, Fink M, Friedrich-Rust M, Fromageau J, Havre RF, Jenssen C, Ohlinger R, Săftoiu A, Schaefer F, Dietrich CF; EFSUMB. EFSUMB guidelines and recommendations on the clinical use of ultrasound elastography. Part 2: Clinical applications. *Ultraschall Med.* 2013;34(3):238-53. <https://doi.org/10.1055/s-0033-1335375>
81. Hocke M, Braden B, Jenssen C, Dietrich CF. Present status and perspectives of endosonography 2017 in gastroenterology. *Korean J Intern Med.* 2018;33(1):36-63. <https://doi.org/10.3904/kjim.2017.212>
82. Altonbary AY, Hakim H, El-Shamy AM. Diagnostic Efficacy of Endoscopic Ultrasound Elastography in Differentiating Solid Pancreatic Lesions: A Single-Center Experience. *Clin Endosc.* 2019;52(4):360-364. <https://doi.org/10.5946/ce.2018.160>