

# EUS-FNA and ROSE in solid lesions of the pancreas; have the same diagnostic efficacy compared to pancreatic sites?

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## ABSTRACT

**OBJECTIVE:** Various techniques, needle types, and additional methods such as on-site pathological evaluation (ROSE) are used to increase the sensitivity of endoscopic ultrasound-fine needle aspiration (EUS-FNA), which is used in the diagnosis of pancreatic solid lesions. In this study, diagnosticity of the lesions according to the regions of the pancreas with EUS-FNA and ROSE performed with the slow pull technique using a 22 G needle will be evaluated.

**METHODS:** A total of 82 patients who underwent EUS-FNA between January 2, 2015, and March 14, 2020, were included in the study. General and clinical information of the patients were recorded retrospectively. The patients were diagnosed according to The Papanicolaou Society of Cytopathology System for Reporting Pancreaticobiliary Cytology Classification. If the diagnosis could not be made with EUS-FNA and ROSE, the diagnosis was made with alternative methods of surgery or percutaneous biopsy. Patients diagnosed as benign with EUS-FNA and ROSE were followed for at least 1 year and were accepted as benign.

**RESULTS:** The mean age of the patients was 63.2±10.5 years and 54 (69.6%) of them were male. The mean lesion size was 36.8 mm and the number of needle passes was 2.87. The overall sensitivity was 82.9% and the specificity was 100%. The sensitivity of EUS-FNA and ROSE in solid lesions in the head and body of the pancreas was higher than in lesions in the tail region (p=0.024).

**CONCLUSION:** EUS-FNA and ROSE are an effective method in the diagnosis of pancreatic solid lesions. The use of a 22 G needle may be more diagnostic in the head and body of the pancreas than in the tail region.

*Keywords: Endoscopic ultrasound; fine needle aspiration; pancreas; rapid on-site cytopathologic examination; slow pull technique.*

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Pancreatic cancer (PC) is the seventh leading cause of death from cancer worldwide. The 5-year survival rate for PC is about 6% [1]. A good prognosis is achieved by early diagnosis and surgical resection, especially for tumors smaller than 1 cm. Eight in ten cases have a

5-year survival rate [2]. Abdominal ultrasonography, computed tomography, magnetic resonance imaging, endoscopic ultrasound (EUS), and endoscopic retrograde cholangiopancreatography (ERCP) are used to diagnose PC. Advances in technology have paved the way for more



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precise imaging methods. EUS allows us to image the pancreas at high resolution. EUS has a sensitivity of 94% for the diagnosis of PC [3].

EUS-guided fine-needle aspiration (EUS-FNA) has been used since 1992 to sample pancreatobiliary tissues. It allows us to conduct a biopsy on EUS target lesions. It has been a popular method since fine-needle aspiration cytology/biopsy devices started to be used [4]. EUS-FNA may not always allow us to collect sufficient tissue from biopsy samples for pathological diagnosis. False-negative and non-diagnostic results can cause delays in treatment. Researchers have developed needles in different sizes and shapes and different techniques (suction, slow-pull, and aeration techniques) and methods (rapid on-site evaluation [ROSE]) to improve the diagnostic performance of EUS-FNA [5–9]. In this study, EUS-FNA was performed using a 22 gauge (G) calibrated needle and slow-pull technique, and aspirates were examined with ROSE. The diagnostic efficacy in solitary lesions according to the regions of the pancreas was analyzed.

## MATERIALS AND METHODS

This study was conducted at the Gastroenterology Clinic of Health Sciences University Umraniye Training and Research Hospital between January 2, 2015, and March 14, 2020. The study population consisted of 145 patients who underwent EUS FNA and ROSE. The sample consisted of 82 patients with solid lesion of the pancreas. Figure 1 shows the inclusion and exclusion criteria.

Informed consent was obtained from participants. Each participant was sedated with 2 mg/kg propofol by an anesthesiologist. EUS for guided puncture of the lesion was conducted using a Fujinon (Fujifilm, Tokyo, Japan, VP-4450 HD) EG 580UT gastroscope. Fine-needle aspiration was performed through a transgastric approach if the lesion involved the body and the tail. It was achieved through a transduodenal approach for lesions in the head and uncinat process. A 22 G needle was used for fine-needle aspiration. The slow-pull technique was used to collect samples.

In the ROSE examination, two primary staining methods are used to perform basic cytology. After aspiration, one or two smears were prepared immediately and stained with diff-quick stain for a pathologist to evaluate adequacy on-site. The others were fixed with alcohol and stained with Papanicolaou staining in a pathology

### Highlight key points

- EUS-FNA and ROSE are an effective method in the diagnosis of solid lesions of the pancreas.
- The risk of complications is low with the slow pull technique and 22G needle use in EUS-FNA procedure.
- EUS-FNA performed with a 22 G needle may make more effective diagnosis lesions in the head and body of the pancreas than lesions in the tail region.

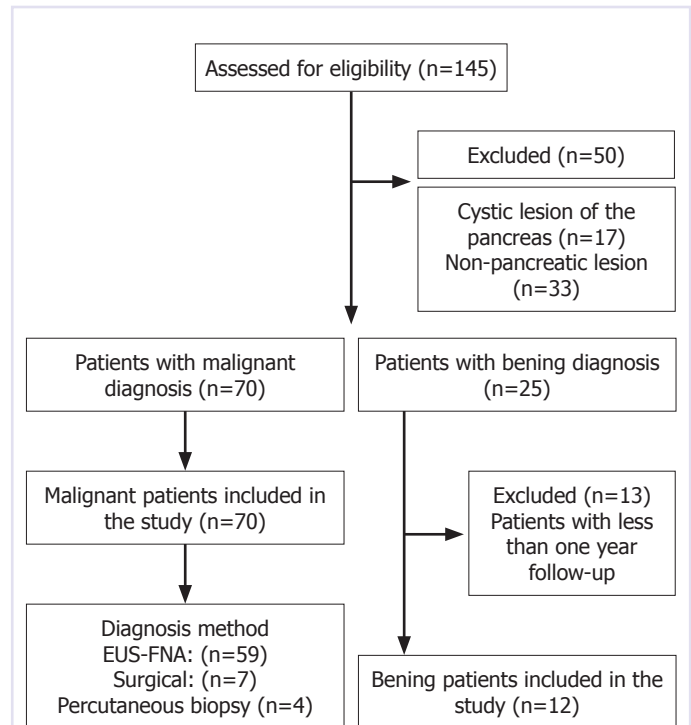


FIGURE 1. Inclusion and exclusion criteria.

laboratory. The aspiration needle was further washed in 10% formol in test tubes for cell block preparation. A pathologist evaluated the smears and sections of the cell block to confirm the on-site diagnosis and render the final diagnosis, which was then recorded according to the classification of the Papanicolaou Society of Cytopathology System for Reporting Pancreaticobiliary Cytology (PSCPC). According this system, category I is non-diagnostic, II is negative (for malignancy), III is atypical, IV is neoplastic: benign or other, V is suspicious for malignancy, and VI is positive/malignant. A PSCPC category of V or VI was regarded as malign [10].

Age, sex, hospital admission symptom, location of the lesion in the pancreas, EUS lesion size, CA 19.9 levels at diagnosis, and diagnosis of malignant patients were recorded retrospectively.

**TABLE 1.** General characteristics, clinical symptoms, and diagnostic methods

Parameters	
Age±	63.2±10.5
Gender (%)	
Female	30.4
Male	69.6
Symptom at admission (%)	
Icterus	41.4
Abdominal pain	26.8
Weight loss	12.1
Weakness	8.5
Other	10.9
Lesion size mm	36.8 (14–80)
Lesion location (%)	
Head	67.1
Body	23.2
Tail	9.8
Malignant patient (%)	85.4
Benign patient (%)	14.6
Diagnostic method	
EUS-FNA (%)	86.6
The average number of needle passes	2.87
*Surgical (%)	8.5
*Percutaneous biopsy (%)	4.9

\*: Patients with clinical suspicion of severe malignancy who could not be diagnosed with the EUS-FNA method were diagnosed with alternative methods.

The study endpoints were tissue diagnosis with EUS-FNA and ROSE in malignant patients and diagnosis by percutaneous biopsy or surgery in cases tissue could not be identified through EUS-FNA and ROSE. A lesion was benign if it did not change in size at a 1-year follow-up. This study was conducted following the principles of the Helsinki Declarations revised in 2013; designed retrospectively and approved by the ethics committee of Health Sciences University Umraniye Training and Research Hospital (date: 27.05.2021, no:B.10.1.TK H.4.34.H.GP.01/167).

### Statistical Analysis

All statistical procedures were performed using SPSS software (version 25.0, SPSS Inc., Chicago, IL, institutionally registered software). The Shapiro–Wilk test was used for normality testing. Median, minimum, maximum, and frequency were used for descriptive sta-



**FIGURE 2.** At the head of the pancreas 33×30 mm in size hypoechoic irregularly circumscribed lesion.

tistics. The Kruskal–Wallis H test was used for non-parametric data. The Chi-square (Fisher's Exact) test was used to analyze categorical data.  $P < 0.05$  was considered significant.

### RESULTS

Eighty-two patients underwent EUS-FNA due to solid lesions in the pancreas. Participants had a mean age of  $63.2 \pm 10.5$  years. More than half the participants were men (69.6%;  $n = 54$ ). Table 1 shows the patients general characteristics, clinical symptoms, and diagnostic methods.

Gender, lesion size, CA 19.9 and diagnosis, PSCPC categories, sensitivity, and specificity values of patients with malignant lesions according to the regions of the pancreas are shown in Table 2. EUS-FNA and ROSE were found to have higher diagnostic sensitivity in solid lesions in the head and body of the pancreas than in the tail region ( $p = 0.024$ ). Eleven patients with PSCPC Category I and III were diagnosed with adenocarcinoma by alternative diagnostic methods. In addition, all remaining patients could be diagnosed with EUS-FNA and ROSE method. A total of three patients were diagnosed with neuroendocrine tumor (NET) by EUS-FNA and ROSE. One patient was diagnosed with a well-differentiated NET, so it was considered category IV. The other two patients with NET were considered category V because they contained solid-cellular clearly neoplastic epithelial proliferation [10].

**TABLE 2.** Evaluation of lesion characteristics and diagnosticity by pancreatic regions

Parameters	Head	Body	Tail	P
Malignant patients (%)	68.6	21.4	10	
Gender (%)				
Male	67.4	25.6	7	
Female	70.4	14.8	14.8	
Lesion size mm	35 (14–65)*	40 (30–60)*	42 (32–80)*	0.130 <sup>†</sup>
Malignant diagnoses (%)				
Adenocarcinoma	62.9	21.4	8.6	
SCC	1.4	–	–	
RCC metastasis	1.4	–	–	
NET	2.9	–	1.4	
Benign (%)	58.3	33.3	8.3	
CA 19.9 pg/mL <sup>‡</sup>	780 (2–176170)*	385 (31–1834)*	278 (24–1642)*	0.300 <sup>†</sup>
PSCPC category (%)				
I	6.3	6.7	0.0	
III	4.2	13.3	42.9	
IV	2.1	0.0	0.0	0.024 <sup>§</sup>
V	27.1	20.0	42.9	
VI	60.4	60.0	14.3	
Sensitivity (%)	87.5	80	57.1	
Specificity (%)	100	100	100	
Total sensitivity (%)	82.9			
Total specificity (%)	100			

PSCPS: Papanicolaou Society of Cytopathology System for Reporting Pancreaticobiliary Cytology; SCC: Squamous cell carcinoma; RCC: Renal cell carcinoma; NET: Neuroendocrine tumor; \*: Minimum maximum value; †: Kruskal Wallis test; §: Fisher's exact test; ‡: CA 19.9 level was calculated in patients with adenocarcinoma.

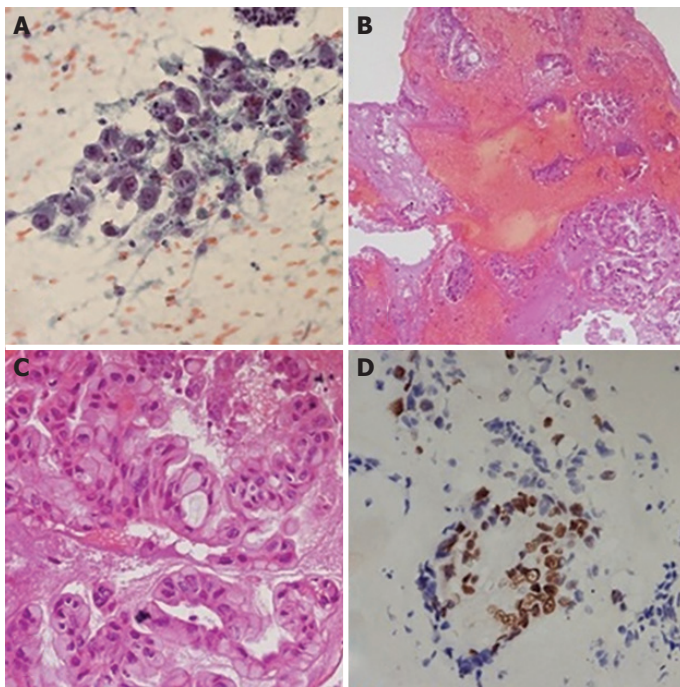
## DISCUSSION

The latest international guidelines on PC stipulate that pancreatic carcinoma should be diagnosed pathologically before chemotherapy. Therefore, EUS-guided sampling is recommended for locally advanced patients, who are candidates for neoadjuvant therapy, and those with metastatic disease. These two groups account for 80–85% of all PC patients [11, 12]. EUS-FNA can diagnose pancreatic lesions with high sensitivity and specificity through cytological and/or histological samples [13]. Fine-needle biopsy (FNB) needles have been developed to increase diagnostic sensitivity in solid pancreatic lesions. However, most research shows no difference in sensitivity between FNB and FNA [14–17]. We think that EUS-FNA and ROSE are an effective method in solid lesions of the pancreas. In the evaluation of a patient of our study; EUS image of a lesion in the head region of the pancreas is shown in Figure 2. Diagnosis of adenocarcinoma with the

ROSE is shown in Figure 3. This study reported the results of patients who underwent EUS-FNA and ROSE.

In the patients in this study; first three symptoms at admission were icterus (41.4%), abdominal pain (26.8%), and weight loss (12.1%). Most patients with malign lesions were diagnosed with adenocarcinoma (92.9%). More than half the lesions were at the head of the pancreas (68.6%). Less than a quarter of the lesions were at the body of the pancreas (21.4%). The remaining lesions were at the tail of the pancreas (10%). The symptoms at admission and lesion locations and diagnosis were consistent with the literature [18–20]. In general, due to presenting with early symptoms, head lesions have been diagnosed as smaller than the other localization of the pancreas, at diagnosis [21]. However, in our study, we found no statistical difference regarding lesion diameter among sites of pancreatic lesions. We think that it may be associated with, most of our patients, first diagnostic workout done in many different centers and referred to our tertiary referral center.





**FIGURE 3.** Cytopathological evaluation. **(A)** Atypical pancreatic ductal cells **(B, C)** Mucinous tumor aggregates on cell block ( $\times 20$  HPF,  $\times 40$  HPF) **(D)** Strong, diffuse p53 staining ( $\times 40$  HPF). HPF: High power field.

Hewitt et al. [22] conducted a meta-analysis on 33 studies with a total sample size of 4984 patients and reported 85% sensitivity (95CI%: 84–86%) and 98% specificity (95CI%: 97–99%) for EUS-FNA malignant cytology. We also reported 82.9% sensitivity and 100% specificity. Our results are consistent with the literature [22–24]. The number of needle passes is another factor affecting diagnosis in EUS FNA. LeBlanc et al. [25] reported that the ideal number of EUS-FNA needle passes to obtain a diagnosis ranged from 2 to 6. Fewer needle passes mean shorter operation time, reducing anesthesia time, medical costs, and adverse events [26]. EUS-FNA-related major complications are bleeding, perforation, infection, and acute pancreatitis [27]. 19G–25G caliber needles are generally used for the EUS-FNA examination of solid pancreatic lesions, and ROSE examination is recommended to increase diagnostic efficiency [28, 29]. However, research shows no difference in sensitivity and complication development between 22 G and 25 G needles in the EUS-FNA procedure of solid pancreatic lesions [23, 30]. Nakai et al. [31] found that the slow pull technique had better diagnostic efficiency than the suction technique. We used 22 G needles to perform the slow pull technique. The mean number of needle

passes was 2.87. We performed ROSE on all patients. None of the patients developed complications. EUS-FNA showed higher sensitivity in malignant lesions at the head and body of the pancreas than in those at the tail of the pancreas ( $p=0.024$ ). There was no significant difference in lesion sizes ( $p=0.130$ ). This may be because trans-gastric passage is more difficult than trans-duodenal passage and imaging of pancreatic tail lesions is more suboptimal than pancreatic head and body lesions. To the best of our knowledge, this is the first study with PSCPC category to compare the sensitivity of EUS-FNA by the regions of the pancreas. This study had two limitations. First, it was a retrospective study. Second, it was conducted in one center.

### Conclusion

EUS-FNA and ROSE are effective methods to diagnose solid pancreatic lesions. 22 G needles may be better at diagnosing lesions at the head and body of the pancreas than those at the tail. ROSE may be associated with a decrease in the number of needle passes. EUS-FNA with ROSE may be associated with a reduced risk of complications, regardless of needle diameter.

**Ethics Committee Approval:** The Health Sciences University Umraniye Training and Research Hospital Clinical Research Ethics Committee granted approval for this study (date: 27.05.2021, number: B.10.1.TKH.4.34.H.GP.01/167).

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