Effect of histological examination on the diagnosis of pancreatic mass using endoscopic ultrasound fine-needle aspiration

Seong Ji Choi[1,A,C,D], Jae Min Lee[2,A,C,F], Kang Won Lee[2,B,C], Hyuk Soon Choi[2,B,C], Eun Sun Kim[2,B,C], Bora Keum[2,C,D], Jai Hoon Yoon[1,C,D], Yoon Tae Jeen[2,E,F], Hoon Jai Chun[2,E,F], Hong Sik Lee[2,E,F], Ho Soon Choi[1,C,F]

[1] Department of Internal Medicine, College of Medicine, Hanyang University, Seoul, South Korea
[2] Division of Gastroenterology and Hepatology, Department of Internal Medicine, Korea University College of Medicine, Seoul, South Korea

A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of the article

Advances in Clinical and Experimental Medicine, ISSN 1899–5276 (print), ISSN 2451–2680 (online) *Adv Clin Exp Med*. 2021;30(9):885–891

Address for correspondence
Jae Min Lee
E-mail: jmlee1202@gmail.com

Funding sources
None declared

Conflict of interest
None declared

Acknowledgements
This study was supported by the Korea University grant (No. K1824371); 2018 Weolbong grant from the Korean Gastrointestinal Endoscopy Research Foundation; and the National Research Foundation of Korea (NRF) grant funded by the Korea government Ministry of Science and ICT – MSIT (No. NRF-2021M3E5D1A01015177).

Received on February 26, 2021
Reviewed on March 21, 2021
Accepted on April 29, 2021

Published online on August 18, 2021

Cite as
Choi SJ, Lee JM, Lee KW, et al. Effect of histological examination on the diagnosis of pancreatic mass using endoscopic ultrasound fine-needle aspiration. *Adv Clin Exp Med*. 2021;30(9):885–891. doi:10.17219/acem/136278

DOI
10.17219/acem/136278

Abstract

Background. Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) is a well-established method for the diagnosis of solid pancreatic lesions. However, the diagnostic yield of EUS-FNA for pancreatic lesions varies at around 70–90%. Samples from EUS-FNA consist of cells and tissues that can be analyzed separately, and the results can be combined for a final diagnosis.

Objectives. To investigate the effect of cytological and histological analysis of EUS-FNA samples on the final diagnosis, and identify factors that may affect the accuracy of the cytological, histological, and overall analysis.

Materials and methods. A single-center prospective observational study was conducted at a tertiary university hospital from July 2018 to June 2019. Patients who underwent EUS-FNA for pancreatic solid lesions with a 22-gauge EUS-FNA needle were included in our study. Liquid-based cytological analysis of the specimen and histological analysis of the whitish core were performed, and factors that affected the diagnostic accuracy of each analysis were evaluated.

Results. In 63 EUS-FNA samples, the overall diagnostic accuracy was 87.3%, which was significantly higher than the cytological accuracy of 73.8% ($p = 0.031$) and the histological accuracy of 69.8% ($p = 0.001$). Factors that affected the results differed in each group: 1) cytological analysis: size, location, and approach method; 2) histological analysis: specimen weight; and 3) overall analysis: size, location, and approach method.

Conclusions. Histologic evaluation of core material obtained from EUS-FNA improved diagnostic accuracy, and factors that affected each result were analyzed. Further studies with prospective randomized trials are recommended to support our data.

Key words: endosonography, diagnosis, pancreatic neoplasms, endoscopic ultrasound-guided fine-needle aspiration

Background

Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) is a well-established and safe method for tissue acquisition from solid pancreatic lesions. Ever since Vilmann et al. first reported the use of EUS-FNA in a solid pancreatic lesion, it has become one of the most important endoscopic procedures in the diagnosis of benign and malignant tumors, as well as in the staging of malignancies of the gastrointestinal tract and adjacent structures, including the pancreas.[1] However, the diagnostic yield of the procedure varies at around 70–90%, and is affected by several factors such as lesion location or size, characteristics of the target lesion, various procedural techniques and devices, tissue-processing method, the availability of cytology staff or rapid on-site evaluation (ROSE), and the experience of the endosonographer.[2,3] The fact that the diagnostic yield is sometimes as low as 70% in expert hands can result in high medical costs from extra procedures and/or imaging studies, and the uncertainty in diagnosis can also cause treatment delay.

Many studies have been performed to overcome the limitations of EUS-FNA and improve diagnostic yield. The development of diagnostic techniques, such as the fanning technique and the slow-pull technique, and new endoscopic ultrasound-guided fine-needle biopsy (EUS-FNB), have brought a certain degree of success in this regard.[2,4,5] Even though recent meta-analysis results have not been consistent enough to confirm the superiority of EUS-FNB over EUS-FNA, its ability to provide core tissue specimens with preserved architecture provides advantages, especially in diagnosing lymphoma, gastrointestinal stromal tumors (GIST) and autoimmune pancreatitis, as well as in molecular and genetic analyses for precision medicine.[2,6,7] However, the EUS-FNB needle has several technical disadvantages compared to the EUS-FNA needle due to its stiffness and targeting difficulties, especially during the transduodenal approach, and an ideal technique for EUS-FNB has not yet been established.[8,9]

Although it is easy to think otherwise due to the nomenclature, biopsy specimens can also be obtained from EUS-FNA, and several articles have shown no difference between EUS-FNA and EUS-FNB in histologic core procurement.[6,10,11] In EUS-FNA without ROSE, the number of EUS-FNA passes and the end of the procedure are decided by the endosonographer on the basis of macroscopic evaluation of the FNA specimen.[11]

Objectives

In this study, we aimed to compare the results of liquid-based preparation (LBP) cytology alone and LBP cytology with histopathological study, to assess whether histologic evaluation of core tissue obtained from EUS-FNA using a 22-gauge needle could improve the diagnostic accuracy of EUS-FNA for solid pancreatic lesions in the absence of ROSE. The influence of the characteristics of the lesion and core tissue derived from EUS-FNA on diagnostic yield was also evaluated.

Materials and methods

Patient eligibility

In this prospective observational study, we collected data from 70 consecutive patients who underwent EUS-FNA for solid pancreatic lesions from July 2018 to June 2019. Eligible individuals were patients older than 20 years with a suspected solid pancreatic tumor measuring ≥10 mm. Exclusion criteria were as follows: 1) previous history of intra-abdominal surgery or cancer; 2) bleeding tendency (platelet count ≤50,000, prothrombin time-international normalized ratio (PT-INR) ≥1.8); 3) no confirmed final diagnosis; 4) cystic lesion on EUS; 5) repeated procedures due to inadequate samples; 6) pregnancy; and 7) refusal to participate. Patient demographics, laboratory test results and follow-up clinical data were collected. The lesion size and location (head/body/tail), approach method (transduodenal/transgastric), needle device, number of needle passes, depth of the needle from the margin, suction technique (syringe/slow-pull), the weight of the specimen, cytology results, histology results, and the final diagnosis were recorded with regard to the procedure. The study was conducted in accordance with the Declaration of Helsinki and was approved by the Korea University Anam Hospital Institutional Review Board (approval No. 2019AN0406). Written informed consent was obtained from all patients before the procedure.

EUS-FNA procedure and sample handling

The EUS-FNA procedures were performed by 2 experienced endosonographers at Korea University Anam Hospital, Seoul, South Korea, from July 2018 to June 2019. The procedures were performed using an electronic curvilinear echoendoscope (GF-UCT 240; Olympus Corp., Tokyo, Japan), a standard endoscopic system (EVIS LUCERA ELITE CV-260/CLV-260, CV-290/CLV-290SL; Olympus Medical Systems, Co. Ltd.) and the ProSound α10 premier (ALOKA, Co. Ltd., Tokyo, Japan). The EUS-FNA needles used for the procedure were either 22-gauge Expect™ Slimline FNA needles (Boston Scientific, Boston, USA) or 22-gauge EchoTip® Ultra FNA needles (Cook Medical, Bloomington, USA), as per the preference of the endosonographer. The precision balance used in our study was the FX-200i Precision Balance (A&D Medical, Chicago, USA). Endoscopic procedures were

performed under a moderate degree of procedural sedation using intravenous injection of propofol.

The lesion and the surrounding structures were closely reviewed under EUS and color Doppler mode. All lesions at the head were approached in a transduodenal manner, and all lesions in the body and tail were approached in a transgastric manner. Under real-time EUS imaging, the EUS-FNA needle was inserted through the working channel of the echoendoscope, where it punctured the target lesion. The mean lesion diameter and the maximum puncture depth of the needle from the surface of the lesion were measured. Once the needle was advanced into the target lesion, a suction technique, either application of a 10-milliliter syringe with negative pressure or slow withdrawal of the stylet, was decided by the endosonographer. An assistant nurse applied the suction and 10 to-and-fro movements using a fanning technique, with a maximum of 3 passes, for sample collection were performed under the endosonographer's discretion.

After the sampling procedure, the whole needle was removed from the echoendoscope, and the content inside the needle was directly placed into a translucent bottle with a cellular preservative fluid (CytoRichRed; Becton Dickinson, Franklin Lakes, USA) for primary rinsing, inspection, weight measurement, and subsequent LBP cytology. The specimen obtained from the procedure was slowly pushed out of the needle, using a needle stylet. Before the placement of the specimen, the precision balance was rescaled to zero with the preservative bottle, so only the weight of the specimen was measured. The endosonographer carefully assessed the specimen macroscopically, and if thread-like, tan-pink/red, thick, and granular material was observed, it was considered a visible histologic core, which was harvested and placed into a formalin bottle for subsequent histologic evaluation. For the confirmation of adequate sampling, macroscopic examination of the specimen was performed by the endosonographer who performed the procedure, along with another endosonographer who had not participated in the procedure. The ROSE was not available in any of the cases.

Cytologic and histologic analyses

The collected remnant samples in the cellular preservative fluid were sent for LBP cytology and preparation of a cell block. The slide was prepared by a completely automated preparation technique for LBP cytology, and cell blocks were prepared using residual samples. The sections were stained with hematoxylin and eosin (H&E), and both slides were reviewed by a pathologist for cytological analysis. The core specimens transferred from the preservative fluid into the 20% buffered formalin bottle were embedded in paraffin, and these sections were also stained with H&E, which were reviewed by a pathologist for histologic analysis.

Data analyses

The adequacies of both samples were determined by pathologists. Overall, samples were considered adequate if either the cytology or histology was considered adequate. Both cytologic and histologic results were reported as: 1) definite malignancy; 2) suspicious of malignancy; 3) atypical cells present; 4) benign cytology/histology; or 5) inadequate. We considered patients as having a malignancy when their results were either 1) or 2).[12] The final diagnosis was confirmed according to the following criteria: 1) positive cytologic or histologic results of EUS-FNA with compatible clinical features; 2) histologic diagnoses from other sources like surgery or biopsy; or 3) negative EUS-FNA results with clinical follow-up of at least 6 months with compatible benign clinical features.

Statistical analyses

Descriptive statistics for continuous variables are presented as means and standard deviations (SD) or medians and ranges. Categorical variables are presented as counts and percentages. Continuous and categorical variables were analyzed using the Student's t-test and χ^2 test, respectively. The diagnostic sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV) were measured, and the diagnostic accuracies of the samples were compared using McNemar's test. Potential factors that might have affected the diagnostic accuracy were evaluated. A p-value <0.05 was considered statistically significant. The IBM SPSS Statistics for Windows v. 21.0 (IBM Corp., Armonk, USA) was used for all analyses.

Results

Among the 70 patients who were eligible for our study, 7 were excluded: 3 patients with cystic lesions, 2 patients without confirmation of final diagnosis, and 2 patients with re-study. After the exclusion, 63 patients who underwent EUS-FNA for pancreatic solid lesions were analyzed. Thirty-three males (52.4%) were included in the study, and the mean age of patients was 70.2 ±10.7 years. The mean lesion size was 3.9 ±1.6 cm, and the lesions were located in the head (n = 21, 35.9%), body (n = 30, 47.6%) or tail (n = 20, 33.3%). The final diagnoses included 2 focal chronic pancreatitis and 61 adenocarcinomas. Table 1 shows the baseline characteristics of the participants. Procedure-related characteristics are listed in Table 2. Twenty-one procedures were performed using the transduodenal approach and 42 procedures were performed using the transgastric approach. Two different needle devices were used: Expect™ Slimline (n = 35, 55.6%) and EchoTip® Ultra (n = 28, 44.4%). The median number of needle passes was 2 (range 1–3), and the mean needle depth was 15.6 ±4.1 mm. Two suction techniques were used: negative

Table 1. Baseline characteristics of the participants

Variables	FNA (n = 63)
Age [years], mean ±SD	70.2 ±10.7
Lesion size [cm], mean ±SD	3.9 ±1.6
Sex	
Male, n (%)	33 (52.4)
Female, n (%)	30 (47.6)
Location	
Head, n (%)	21 (35.9)
Body, n (%)	22 (30.8)
Tail, n (%)	20 (33.3)
Final diagnosis	
Benign, n (%)	2 (3.2)
Adenocarcinoma, n (%)	61 (96.8)

FNA – fine-needle aspiration; SD – standard deviation.

Table 2. Procedure-related characteristics

Variables	FNA (n = 63)
Approach method	
Transduodenal, n (%)	21 (33.3)
Transgastric, n (%)	42 (66.7)
Needle device	
Expect™ Slimline, n (%)	35 (55.6)
EchoTip® Ultra, n (%)	28 (44.4)
Needle passes, n	2.4 ±0.5
Needle depth [mm], mean ±SD	15.6 ±4.1
Suction technique	
Syringe, n (%)	29 (46.0)
Slow-pull, n (%)	34 (54.0)
Specimen weight [mg], mean ±SD	183.5 ±120.0

FNA – fine-needle aspiration; SD – standard deviation.

suction with a 10-mL syringe (n = 29, 46.0%) and the slow-pull technique (n = 34, 54.0%). The mean specimen weight was 183.5 ±120.0 mg.

Positive results were seen in 47 cytologic samples and 44 histologic samples, and 55 patients showed positive results on the final diagnosis. For evaluation, 96.8% of cytology samples, 85.7% of histology samples and 98.4% of the overall samples were adequate. Most diagnostic discrimination values for the cytologic analysis were slightly higher than those for the histologic analysis: sensitivity 73.8% compared to 68.9%; specificity 100% compared to 100%; accuracy 74.6% compared to 69.8%; PPV 100% compared to 100%; and NPV 11.1% compared to 9.5%. Overall results were the combined cytologic and histologic analyses showing: sensitivity 86.9%; specificity 100%; accuracy 87.3%; PPV 100%; and NPV 20.0% (Table 3).

Table 4 summarizes the comparison of the diagnostic accuracies; the overall accuracy was significantly higher than the accuracy of cytology (p = 0.031) and that of histology (p = 0.001). The accuracy of cytology was higher than the accuracy of histology, but the difference was not significant (p = 0.332).

Univariate analysis was performed to evaluate the factors affecting the results in different specimen types (Table 5). With cytology, the positive group was significantly larger than the negative group (p = 0.02), and there were differences related to the location (p = 0.02), such that the diagnostic accuracy was in the following order: body (86.4%), tail (75.5%), and head (52.4%). The approach method was also significant (p = 0.00). With histology, specimens that showed positive results tended to weigh more than those with negative results (199.8 ±129.6 mg compared to 145.7 ±85.5 mg; p = 0.04). Overall, the size and location of the lesion significantly affected obtaining positive results from EUS-FNA (both p = 0.04).

Discussion

Because pancreatic cancer has a dismal prognosis, accurate diagnosis is crucial for patients to receive adequate treatment without delay. The EUS-FNA is a safe, accurate

Table 3. Cytology, histology and overall outcomes of endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA)

Samples	Positive, n	Negative, n	Adequacy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	PPV (%)	NPV (%)
Cytology	47	16	96.8 (61/63)	73.8 (45/61)	100.0 (2/2)	74.6 (47/63)	100.0 (45/45)	11.1 (2/18)
Histology	44	19	85.7 (54/63)	68.9 (42/61)	100.0 (2/2)	69.8 (44/63)	100.0 (42/42)	9.5 (2/21)
Overall	55	8	98.4 (62/63)	86.9 (55/61)	100.0 (2/2)	87.3 (55/63)	100.0 (53/53)	20.0 (2/10)

PPV – positive predictive value; NPV– negative predictive value.

Table 4. Comparison of the diagnostic yield of cytology and histology with overall result

Result		Cytology		p-value	Result	Histology		p-value
		positive, n	negative, n			positive, n	negative, n	
Overall	positive	47	8	0.031*	positive	44	11	0.001*
	negative	0	8		negative	0	8	

* statistically significant (McNemar's test).

Table 5. Univariate analysis of factors affecting the results in different types of specimen

Variables	Cytology			Biopsy			Overall		
	positive (n = 47)	negative (n = 16)	p-value	positive (n = 44)	negative (n = 19)	p-value	positive (n = 5)	negative (n = 8)	p-value
Sex male, n female, n	 25 22	 8 8	0.83	 23 21	 10 9	0.98	 29 26	 4 4	0.89
Age [years], mean ±SD	70.7 ±9.3	68.9 ±12.8	0.53	69.6 ±11.1	71.8 ±7.8	0.43	70.1 ±10.3	71.5 ±10.0	0.72
Size [mm], mean ±SD	40.7 ±16.4	31.3 ±9.7	0.03	37.9 ±16.1	39.4 ±14.3	0.71	39.8 ±15.8	28.3 ±8.4	0.04
Location, n (head/body/tail)	11/19/17	10/3/3	0.02*	12/17/15	9/5/5	0.34*	15/21/19	6/1/1	0.04*
Approach method, n (transduodenal/transgastric)	11/36	10/6	0.00	12/32	9/10	0.15	15/40	6/2	0.05
Needle device, n (Expect™/EchoTip®)	28/19	7/9	0.28	23/21	12/7	0.43	30/25	5/3	0.76
Needle passes, n, median (range)	2 (1–5)	2 (1–5)	1.00	2 (1–5)	2 (1–5)	1.00	2 (1–5)	2 (1–5)	1.00
Needle depth [mm], mean ±SD	15.6 ±4.7	16.1 ±2.8	0.64	15.2 ±4.5	16.7 ±3.4	0.24	15.5 ±4.2	16.5 ±3.0	0.40
Suction technique, n (syringe/slow-pull)	22/25	7/9	0.84	19/25	10/9	0.50	25/30	4/4	0.81
Specimen weight [mg], mean ±SD	189.6 ±103.9	181.4 ±126.0	0.82	199.8 ±129.6	145.7 ±85.5	0.04	180.0 ±120.3	202.0 ±122.8	0.55

SD – standard deviation; * statistically significant.

and cost-effective diagnostic modality for pancreatic tumors, especially in providing specimens for cytological evaluation. However, it is sometimes difficult to distinguish adenocarcinoma from reactive changes on cytologic evaluation because of their overlapping features.[13] It is widely accepted that the presence of ROSE during EUS-FNA improves diagnostic yield, but the total procedure time and costs increase, and more importantly, this method is not available in many centers.[14] Special needles for biopsy were developed and they showed promising results in many studies by obtaining adequate histologic cores. Yet, they have limitations, including the tip hardness, cost and the lack of any set standard technique. We conducted a prospective observational study of EUS-FNA to evaluate the effects of cytological and histological examination on diagnostic accuracy, and the factors that affected each sample.

In our study, the diagnostic accuracy of cytology was higher than that of histology but the difference was not significant (74.6% compared to 69.8%), and the diagnostic accuracy of the final result of combined cytology and histology was significantly higher than that of cytology or histology alone. Even though the histologic evaluation alone yielded fewer results than cytologic evaluation, both cytology and histology specimens were important in EUS-FNA, as their results were complementary towards the diagnosis of the lesion. These results are consistent with those of previous studies.[15,16]

Because acquiring cytohistologic specimens is critical for diagnosis, many studies have been performed to evaluate the factors that affect the diagnostic accuracy of EUS-FNA. Though there is a lack of consensus over the findings of the reports, the presence of ROSE and size and location of the tumor are widely accepted factors that influence diagnostic accuracy.[2,9,17–20] In our study, tumor size, location and the approach method were significant factors that affected the rendering of positive cytologic results, and the specimen weight was a significant factor for positive histologic results. With combined analysis, the tumor size and location of the lesion were significant factors for a positive diagnosis.

Even though the tumor size was important, the mean needle depth from the margin of the lesion was not significantly greater in the positive group, and was even slightly lesser. The larger the tumor size, the more possible it is to insert the needle from various angles avoiding nearby vascular structures. Alternatively, more vigorous fanning techniques could be applied, and these factors might be the cause of this result. Regardless of specimen, in our study, diagnostic accuracy was the highest in the body, followed by the tail and then, the head. This was largely affected by the approach method. The transduodenal approach showed a significantly lower positive rate for cytology, and this may be due to disruption of the needle from its original arrangement.[21] Further research is needed in this regard.

Among the 16 and 19 negative results from cytology and histology, respectively, the ratio of atypical cells was higher with histology (n = 15, 78.9%) than cytology (n = 10, 62.5%). Atypical cells do not contribute to a definite diagnosis for malignancy; however, they can help clinicians suspect malignancy in false-negative cases and plan further more aggressive diagnostic procedures or approaches, rather than observation.[12]

The length of the tissue core is reported to be a significant factor for diagnosis in several studies, and our study is the first to analyze the sample weight and its correlation with diagnostic accuracy.[11,22] The weight of cytologic samples might not be accurate because of factors such as blood contamination or tissue fragments, and the result was not significant. The weight of the histologic core was also measured and was significantly higher in the positive group ($p = 0.04$). In particular, patients who underwent the slow-pull technique for suction showed significantly higher histologic core weight compared to those who underwent the negative syringe technique (201.3 ±138.6 mg compared to 130.1 ±61.8 mg; $p = 0.04$). This result suggests that although the slow-pull technique does not significantly improve the accuracy of EUS-FNA, positivity of histologic results can be predicted in advance through the weight of the sample in cases of EUS-FNA with the slow-pull technique. Further validation and study of thresholds are needed to confirm our suggestion.

Our study evaluated cytology with LBP and cellblock-processed samples. In our institute, the entire specimen is placed in cellular preservative fluid for better visualization of the core after rinsing. Although the diagnostic outcome of the conventional smear method is reported to be better than that of LBP cytology, it is not applicable in some hospitals because of pathologists' preferences and hospital settings.[23,24] However, our study results were similar to those of a previous study using the smear method.[15] To exclude the effects of various factors that are still controversial in their influence on the diagnostic accuracy of EUS-FNA, variables such as needle caliber (22-gauge), tissue acquisition method (fanning technique) and presence of stylet were controlled in our study.

Our study suggests that vigorous collection of tissue core and its analysis would be a method of increasing the diagnostic yield in cases of pancreatic head lesions without ROSE. In addition, EUS-FNA for collecting tissue samples may be helpful, but further studies are needed, considering the poor maneuverability of the needle in a bent, torqued position.

Limitations

Our study has several limitations. First, the study was performed in a single tertiary center. In addition, the weight of the specimen may not exactly correlate with the quantity of the specimen because of blood contamination or fibrosis, that may have been included. Other solid pancreatic lesions, such as neuroendocrine tumors or cystic pancreatic lesions were not evaluated. Also, the number of true-negative lesions was small, resulting in a low NPV. A larger prospective multicenter study is needed to provide more evidence for our results.

Conclusions

Our findings suggest that histologic evaluation of core material obtained from EUS-FNA improved diagnostic sensitivity, accuracy and NPV. Previous studies have focused on improving diagnostic accuracy by analyzing its factors, but our study shows that the factors influencing the results of cytology and histology are slightly different. Thus, overall diagnostic accuracy can be improved by improving each factor. Measuring the weight of the sample could be a method of obtaining sufficient samples during EUS-FNA, along with the slow-pull technique to increase histologic accuracy and, thus, the overall accuracy. Follow-up studies with prospective randomized trials are recommended to support our data.

ORCID iDs

Seong Ji Choi https://orcid.org/0000-0002-1969-516X
Jae Min Lee https://orcid.org/0000-0001-9553-5101
Kang Won Lee https://orcid.org/0000-0002-5902-9700
Hyuk Soon Choi https://orcid.org/0000-0002-4343-6950
Eun Sun Kim https://orcid.org/0000-0003-1820-459X
Bora Keum https://orcid.org/0000-0003-0391-1945
Jai Hoon Yoon https://orcid.org/0000-0003-3194-5149
Yoon Tae Jeen https://orcid.org/0000-0003-0220-3816
Hoon Jai Chun https://orcid.org/0000-0002-5539-361X
Hong Sik Lee https://orcid.org/0000-0001-9726-5416
Ho Soon Choi https://orcid.org/0000-0003-3746-8742

References

1. Vilmann P, Jacobsen GK, Henriksen FW, Hancke S. Endoscopic ultrasonography with guided fine needle aspiration biopsy in pancreatic disease. *Gastrointest Endosc*. 1992;38(2):172–173. doi:10.1016/s0016-5107(92)70385-x
2. Khan MA, Grimm IS, Ali B, et al. A meta-analysis of endoscopic ultrasound-fine-needle aspiration compared to endoscopic ultrasound-fine-needle biopsy: Diagnostic yield and the value of onsite cytopathological assessment. *Endosc Int Open*. 2017;5(5):E363–E375. doi:10.1055/s-0043-101693
3. Itoi T, Sofuni A, Itokawa F, Irisawa A, Khor CJ, Rerknimitr R. Current status of diagnostic endoscopic ultrasonography in the evaluation of pancreatic mass lesions. *Dig Endosc*. 2011;23(Suppl 1):17–21. doi:10.1111/j.1443-1661.2011.01132.x
4. 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):445–450. doi:10.1055/s-0032-1326268
5. Lee JM, Lee HS, Hyun JJ, et al. Slow-pull using a fanning technique is more useful than the standard suction technique in EUS-guided fine needle aspiration in pancreatic masses. *Gut Liver*. 2018;12(3):360–366. doi:10.5009/gnl17140
6. Bang JY, Hawes R, Varadarajulu S. A meta-analysis comparing ProCore and standard fine-needle aspiration needles for endoscopic ultrasound-guided tissue acquisition. *Endoscopy*. 2016;48(4):339–349. doi:10.1055/s-0034-1393354
7. Larsen MH, Fristrup CW, Detlefsen S, Mortensen MB. Prospective evaluation of EUS-guided fine needle biopsy in pancreatic mass lesions. *Endosc Int Open*. 2018;6(2):E242–E248. doi:10.1055/s-0043-124078
8. Panic N, Larghi A. Techniques for endoscopic ultrasound-guided fine-needle biopsy. *Gastrointest Endosc Clin N Am*. 2014;24(1):83–107. doi:10.1016/j.giec.2013.08.010
9. Attili F, Fabbri C, Yasuda I, et al. Low diagnostic yield of transduodenal endoscopic ultrasound-guided fine needle biopsy using the 19-gauge Flex needle: A large multicenter prospective study. *Endosc Ultrasound*. 2017;6(6):402–408. doi:10.4103/eus.eus_54_17

10. Bang JY, Hebert-Magee S, Trevino J, Ramesh J, Varadarajulu S. Randomized trial comparing the 22-gauge aspiration and 22-gauge biopsy needles for EUS-guided sampling of solid pancreatic mass lesions. *Gastrointest Endosc*. 2012;76(2):321–327. doi:10.1016/j.gie.2012.03.1392
11. Iwashita T, Yasuda I, Mukai T, et al. Macroscopic on-site quality evaluation of biopsy specimens to improve the diagnostic accuracy during EUS-guided FNA using a 19-gauge needle for solid lesions: A single-center prospective pilot study (MOSE study). *Gastrointest Endosc*. 2015;81(1):177–185. doi:10.1016/j.gie.2014.08.040
12. Layfield LJ, Schmidt RL, Hirschowitz SL, Olson MT, Ali SZ, Dodd LL. Significance of the diagnostic categories "atypical" and "suspicious for malignancy" in the cytologic diagnosis of solid pancreatic masses. *Diagn Cytopathol*. 2014;42(4):292–296. doi:10.1002/dc.23078
13. Kato K, Kamada H, Fujimori T, Aritomo Y, Ono M, Masaki T. Molecular biologic approach to the diagnosis of pancreatic carcinoma using specimens obtained by EUS-guided fine needle aspiration. *Gastroenterol Res Pract*. 2012;2012:243524. doi:10.1155/2012/243524
14. Ganc RL, Carbonari AP, Colaiacovo R, et al. Rapid on-site cytopathological examination (ROSE) performed by endosonagraphers and its improvement in the diagnosis of pancreatic solid lesions. *Acta Cir Bras*. 2015;30(7):503–508. doi:10.1590/S0102-865020150070000009
15. Yang L, Iwai T, Kida M, et al. Analysis of the diagnostic yield of endoscopic ultrasonography-guided fine-needle aspiration in patients with a suspected pancreatic malignancy. *Rev Esp Enferm Dig*. 2018;110(9):544–550. doi:10.17235/reed.2018.5455/2017
16. Moller K, Papanikolaou IS, Toermer T, et al. EUS-guided FNA of solid pancreatic masses: High yield of 2 passes with combined histologic-cytologic analysis. *Gastrointest Endosc*. 2009;70(1):60–69. doi:10.1016/j.gie.2008.10.008
17. Crino SF, Conti Bellocchi MC, Bernardoni L, et al. Diagnostic yield of EUS-FNA of small (≤15 mm) solid pancreatic lesions using a 25-gauge needle. *Hepatobiliary Pancreat Dis Int*. 2018;17(1):70–74. doi:10.1016/j.hbpd.2018.01.010
18. Li HZ, Peng CY, Shen SS, et al. Factors affecting the accuracy of endoscopic ultrasound-guided fine needle aspiration for the diagnosis of small (≤20 mm) pancreatic lesions. *J Dig Dis*. 2020;21(7):416–421. doi:10.1111/1751-2980.12875
19. Polkowski M, Jenssen C, Kaye P, et al. 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. doi:10.1055/s-0043-119219
20. Hwang CY, Lee SS, Song TJ, et al. Endoscopic ultrasound guided fine needle aspiration biopsy in diagnosis of pancreatic and peripancreatic lesions: A single center experience in Korea. *Gut Liver*. 2009;3(2):116–121. doi:10.5009/gnl.2009.3.2.116
21. de Nucci G, Petrone MC, Imperatore N, et al. Feasibility and accuracy of transduodenal endoscopic ultrasound-guided fine-needle aspiration of solid lesions using a 19-gauge flexible needle: A multicenter study. *Clin Endosc*. 2021;54(2):229–235.doi:10.5946/ce.2020.056
22. Iglesias-Garcia J, Dominguez-Munoz E, Lozano-Leon A, et al. Impact of endoscopic ultrasound-guided fine needle biopsy for diagnosis of pancreatic masses. *World J Gastroenterol*. 2007;13(2):289–293. doi:10.3748/wjg.v13.i2.289
23. Lee JK, Choi ER, Jang TH, et al. A prospective comparison of liquid-based cytology and traditional smear cytology in pancreatic endoscopic ultrasound-guided fine needle aspiration. *Acta Cytol*. 2011;55(5):401–407. doi:10.1159/000330811
24. Biermann K, Lozano Escario MD, Hebert-Magee S, Rindi G, Doglioni C. How to prepare, handle, read, and improve EUS-FNA and fine-needle biopsy for solid pancreatic lesions: The pathologist's role. *Endosc Ultrasound*. 2017;6(Suppl 3):S95–S98. doi:10.4103/eus.eus_71_17