# Influence of On-Site Cytopathology Evaluation on the Diagnostic Accuracy of Endoscopic Ultrasound-Guided Fine Needle Aspiration (EUS-FNA) of Solid Pancreatic Masses

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OBJECTIVES: **The aim of this study was to evaluate the influence of on-site cytopathological evaluation on the diagnostic yield of endoscopic ultrasound (EUS)-guided fine needle aspiration (FNA) for the differential diagnosis of solid pancreatic masses in an unselected series of consecutive patients.**

METHODS: **Patients undergoing EUS-guided FNA of solid pancreatic lesions over a 2-year study period were included. Samples were either evaluated on site by a cytopathologist or processed by the endoscopist and sent to the pathology department for evaluation. Diagnostic accuracy for malignancy, number of needle passes, adequate-specimen collection rate, cytological diagnosis, and final diagnosis, and complication rate according to the presence or absence of on-site cytopathologist were evaluated.**

RESULTS: **A total of 182 patients were included. An on-site cytopathologist was available in 95 cases (52.2%). There was no difference between groups in terms of age, sex, location, and size of the lesions. A significantly higher number of needle passes was performed when an on-site cytopathologist was not available (3.5±1.0 vs. 2.0±0.7; $P<0.001$). The presence of an on-site cytopathologist was associated with a significantly lower number of inadequate samples (1.0 vs. 12.6%, $P=0.002$), and a significantly higher diagnostic sensitivity (96.2 vs. 78.2%; $P=0.002$) and overall accuracy (96.8 vs. 86.2%; $P=0.013$) for malignancy. Three patients developed complications (two acute pancreatitis, one local bleeding), all of them belonging to the group without on-site cytopathology.**

CONCLUSIONS: **On-site cytopathological evaluation improves the diagnostic yield of EUS-guided FNA for the cytological diagnosis of solid pancreatic masses. This is associated with a significantly lower number of inadequate samples and a lower number of needle passes.**

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## INTRODUCTION

Differential diagnosis of pancreatic masses is a frequent clinical challenge. Therapeutic decision in this context is mainly based on the ability to establish or exclude malignancy (1). Although ductal adenocarcinoma is the most frequent cause of pancreatic mass, other neoplasms (e.g., lymphoma, cystic tumors, and metastasis) and benign conditions (e.g., chronic pancreatitis) with different prognoses and treatment options can arise within the pancreas (2). A pathological diagnosis becomes therefore relevant for an optimal therapeutic decision (3).

Endoscopic ultrasound (EUS)-guided fine needle aspiration (FNA) has been proven to be a safe and useful method for tissue sampling of intramural and extramural gastrointestinal lesions including the pancreas (4,5). Several studies have evaluated the accuracy of cytology after EUS-guided FNA for the diagnostic evaluation of pancreatic masses (6–19). According to these reports, an adequate cytological specimen can be obtained in 82–91% of cases, providing a diagnostic sensitivity for malignancy ranging from 64 to 96%. In previous studies, 3–6 needle passes through the lesion (9–21) and the on-site cytopathological evaluation of the tissue sample for adequacy (7–9,22–28) were

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considered as essential for obtaining an appropriate high diagnostic accuracy of EUS-guided FNA. Reports on the need of on-site cytological evaluation during the procedure are however scarce. In fact, although experts recommend the on-site cytopathological assessment of tissue samples to maximize the diagnostic yield of EUS-guided FNA, the influence of this recommendation on the diagnostic accuracy of the procedure has not been properly addressed.

The aim of this study was to evaluate the influence of on-site cytopathological evaluation on the diagnostic yield of EUS-guided FNA for the differential diagnosis of solid pancreatic masses in an unselected series of consecutive patients.

## METHODS

### Subjects

Patients who underwent EUS-guided FNA of solid pancreatic lesions over a 2-year study period were retrospectively identified from a prospectively collected endoscopy database, and included in the study. EUS-guided FNAs of solid pancreatic lesions performed previously ($n=258$) were excluded to avoid bias related to learning curve of both endoscopists and cytopathologists. Patients were scheduled for EUS by a secretary of the Endoscopy Unit, who had no information about availability of on-site cytopathologist. In addition, information regarding availability of on-site cytopathology was unknown in advance, at the time of scheduling patients for EUS.

### Methods

***EUS-guided FNA***. EUS was daily performed from Monday to Friday every week. According to our protocol, pancreatic EUS-guided FNA was consistently performed if a pancreatic mass was detected during EUS.

Once the corresponding signed informed consent was obtained, EUS was performed under conscious sedation by two operators (J.I.-G. and J.L.-N.). A standard blood coagulation analysis was consistently performed before EUS-guided FNA, and an uncorrectable coagulation profile (prothrombin time <60%) was considered as a contraindication for the procedure.

EUS was performed using a convex array echoendoscope (Pentax EG-3870UTK; Pentax Europe GmbH, Hamburg, Germany) connected to an ultrasound equipment, Hitachi-8500 (Hitachi Medical Systems Europe, Zug, Switzerland). FNA was performed with a standard 22-gauge needle (Wilson-Cook Medical, Winston-Salem, NC). These needles are equipped with a round nitinol stylet covered by a protective metal spiral coil sheath. The needle can be advanced up to 8.5 cm from the spiral sheath. The target lesion was endosonographically visualized and the region was scanned for vessels using color and pulsed Doppler. FNA was performed from the duodenum or the stomach according to the location of the lesion in the head or the body/tail of the pancreas, respectively. Before puncture, the stylet was withdrawn several millimeters, thereby exposing the sharp needle tip. The needle was then advanced into the target tissue under endosonographic guidance (**Figure 1**). Once the lesion was penetrated, the stylet was advanced to the original position to "unplug" the needle and to push out any potentially needle-clogging tissue or body fluids. The stylet was then removed and suction

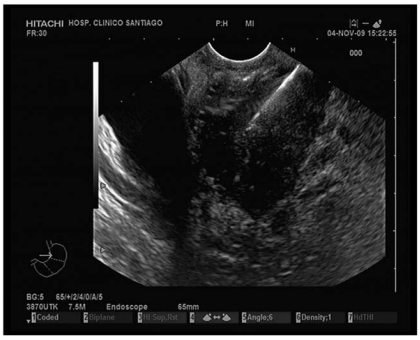


**Figure 1.** Endoscopic ultrasound image of a mass in the head of the pancreas. Fine needle aspiration of the mass confirmed the diagnosis of pancreatic adenocarcinoma.

was applied using a 5 ml syringe while moving the needle to and fro within the lesion. Suction was released before removing the needle.

All patients were observed prospectively for postprocedure complications. Clinical symptoms were carefully evaluated. Pancreatitis as a potential postprocedure complication was defined by the presence of abdominal pain and a threefold increase of serum amylase and/or lipase within 24 h after the procedure.

***Sample processing and cytological evaluation***. The presence of the cytopathologist in the EUS room was decided by the pathology department according to weekly internal organization. Based on that, an expert cytopathologist was available at the endoscopy room for on-site evaluation of EUS-guided FNA samples 2 to 3 days a week. After each needle pass, the cytopathologist processed the sample and provided an immediate evaluation of cellularity of air-dried smear stained with a Romanowski stain (Diff-Quick; Merck KGaA, Darmstadt, Germany). Punctures were repeated until the cytopathologist considered the sample as adequate for providing a diagnosis (**Figure 2**).

On the remaining days, when on-site cytopathology was not available, samples were spread on the slides and fixed in 96% ethanol by experienced endoscopists, and sent to the pathology department for evaluation. On-site microscopic evaluation of sample adequacy was thus not performed on those days. To increase the probability of obtaining an adequate sample for diagnosis, puncture was repeated at least three times when possible. All samples were thereafter processed for cytological study by Papanicolau staining (**Figure 3**). The same two experienced cytopathologists examined cytological smears of all patients.

Cytological diagnoses were categorized into nondiagnostic, negative for malignancy, and positive for malignancy according to previously reported specific protocols (28–30) and the corresponding guidelines of the Papanicolau Society of Cytopathology (31). Samples considered as malignant or suspicious for malignancy were categorized as positive for malignancy, whereas samples considered as benign, indeterminate, or atypical were categorized as negative for malignancy.

***Gold standard for final diagnosis***. Cytological findings were compared with histology of surgical specimens as gold standard in patients who were further operated upon. In nonoperated

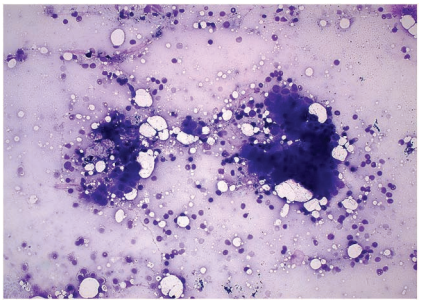

**Figure 2.** On-site cytological evaluation of a pancreatic sample obtained by endoscopic ultrasound (EUS)-guided fine needle aspiration (FNA), supporting the final diagnosis of pancreatic adenocarcinoma (Diff-Quick ×20).

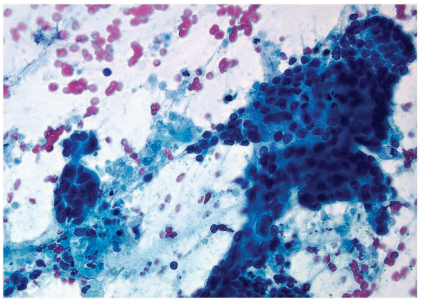

**Figure 3.** Cytological evaluation of a pancreatic sample obtained by endoscopic ultrasound (EUS)-guided fine needle aspiration (FNA). The presence of marked cellular atypia supports the diagnosis of adenocarcinoma of the pancreas (Papanicolau staining, ×40).

patients, a global clinical, morphological (EUS and computed tomography scan), and biochemical evaluation (including serum levels of Ca19.9) over a minimum follow-up of at least 12 months was considered as gold standard.

***Data analysis***. The major end point of the study was the difference in diagnostic accuracy of EUS-guided FNA according to the presence or absence of the cytopathologist on site. The following data were consistently recorded: demographic characteristics of patients, EUS diagnosis, location and size of the lesion, number of needle passes, adequate specimen collection rate, cytological diagnosis, final diagnosis, and complications. Data are shown as mean and range, mean±s.d., and percentages and 95% confidence intervals (CIs) as appropriate. Categorized variables were analyzed by Fisher's exact test or $\chi^2$ test, as appropriate. After confirming a normal distribution of data, quantitative variables were analyzed using the two-sample Student's *t*-test. Sensitivity, specificity, overall accuracy, and positive and negative predictive values for malignancy were calculated. To minimize the impact of a potentially insufficient sample size, accuracy data are shown with a 95% CI.

## RESULTS

### Patient characteristics and final diagnoses

A total of 182 patients underwent EUS-guided FNA of solid pancreatic lesions over the study period. On-site cytopathologist was present in 95 cases (52.2%), whereas EUS-guided FNA was performed in the remaining 87 cases (47.8%) without on-site cytopathologist. There was no difference between both groups in terms of age, sex, and location and size of the lesions (**Table 1**).

**Table 1. The demographic and tumor characteristics of the patients**

| | With on-site pathologist (*n*=95) | Without on-site pathologist (*n*=87) | *P* value |
|---|---|---|---|
| Number of patients | 95 | 87 | NS |
| Mean age (range) | 62 years (24–84) | 59 years (20–83) | NS |
| Sex (male/female) | 57/38 | 52/35 | NS |
| *Localization of the lesion within the pancreas* | | | |
| Head | 69 | 64 | |
| Body | 20 | 19 | NS |
| Tail | 6 | 4 | |
| Mean size of the lesion (mean±s.d.) | 31.7±13.6 mm | 30.7±12.9 mm | NS |

NS, not significant.

Final diagnoses according to the presence or absence of on-site cytopathology are shown in **Table 2**. Mean follow-up of patients with benign lesions was 15 months (range 12–23 months).

### Outcome of EUS-guided FNA

A higher number of needle passes was performed when on-site cytopathologist was not available (3.5±1.0 vs. 2.0±0.7; $P<0.001$; **Figure 4**). Adequate cytological samples were obtained more frequently when on-site cytopathologist was available (98.9%, 95% CI 98.4–99.5) compared with procedures performed without on-site cytopathological evaluation (87.4%, 95% CI 86.7–88.0; $P=0.002$). Except for the proportion of inadequate samples, distribution of patients according to cytological result was not influenced by the presence or absence of on-site cytopathology (**Table 3**).

Out of the 79 malignant masses evaluated by EUS-guided FNA with on-site cytopathology, 76 were correctly classified as malignant (sensitivity 96.2%; 95% CI 95.5–96.9), compared with 43 out of the 55 malignant masses correctly classified as malignant by EUS-guided FNA without on-site cytopathology (sensitivity 78.2%; 95% CI 77.2–79.2; $P=0.002$). No false-positive result for malignancy was observed among the 51 cases of benign pancreatic masses independently of whether on-site cytopathologist was available or not. Diagnostic accuracy of EUS-guided FNA with and without on-site cytopathology is shown in **Table 4**.

### Complications related to the technique

Two patients (1.1%) suffered from mild acute pancreatitis related to the procedure, and they required hospitalization for 4 and 5 days, respectively. One patient (0.55%) developed bleeding at the site of gastric puncture, which was successfully managed endo-

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**Table 2. Final diagnoses of solid pancreatic masses (*n*) in this study**

| Final diagnosis | With on-site cytopathologist (*n*=95) | Without on-site cytopathologist (*n*=87) | Total (*n*=182) |
|---|---|---|---|
| Pancreatic adenocarcinoma | 66 | 49 | 115 |
| Inflammatory mass | 16 | 24 | 40 |
| Neuroendocrine tumor | 8 | 3 | 11 |
| Serous cystadenoma with solid appearance | 0 | 8 | 8 |
| Metastasis[a] | 2 | 2 | 4 |
| Cystadenocarcinoma with solid appearance | 2 | 0 | 2 |
| Lymphoma | 0 | 1 | 1 |
| Teratoma | 1 | 0 | 0 |

[a]Three metastases of lung oat cell cancer and one of epidermoid carcinoma.
Data are shown according to the presence or absence of on-site cytopathology evaluation of endoscopic ultrasound (EUS)-guided fine needle aspiration (FNA) samples.

scopically. All three complications occurred in patients in whom a high number of needle passes was required related to the absence of on-site cytopathologist. Thus, the rate of complications was 3.4 and 0% in EUS-guided FNAs without and with on-site cytopathological evaluation, respectively ($P=0.1$). There was no death associated with the technique.

## DISCUSSION

This study in a large series of consecutive patients provides strong evidence supporting EUS-guided FNA as a very accurate and useful tool for the cytological diagnosis of solid pancreatic masses. It points out that on-site cytopathological evaluation is needed to improve the diagnostic yield of EUS-guided FNA in this setting. On-site cytopathological evaluation of EUS-guided FNA samples for adequacy is associated with a significantly lower number of inadequate samples, lower number of needle passes required, and higher diagnostic sensitivity and overall accuracy for malignancy. Complications were infrequent and occurred only in the group without on-site cytopathology, but the difference between groups was not statistically significant.

The accuracy of EUS-guided FNA for the cytological diagnosis of pancreatic masses has been widely analyzed. The overall accuracy of this method ranges from 64 to 96% in different series (6–19). Obtaining an appropriate sample for cytological evaluation is absolutely needed for an adequate diagnostic accuracy (19). This supports the concept of rapid on-site cytopathological evaluation of EUS-guided FNA for sample adequacy (7–9,22–29).

The influence of on-site cytopathological interpretation on the diagnostic yield of percutaneous ultrasound-guided FNA of lymph nodes and breast, thyroid, and lung masses is well established (32–36). Based on that, experts advocate on-site cytopathological assessment for tissue sample adequacy also after EUS-guided FNA

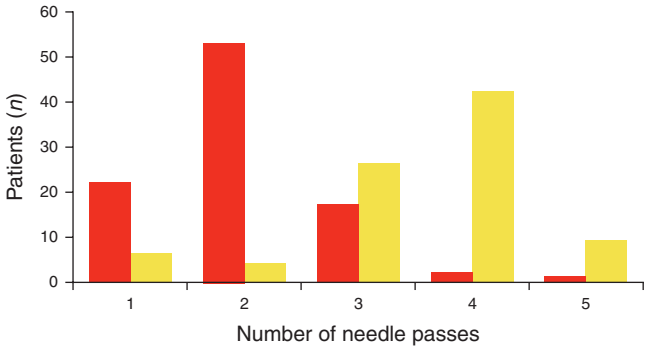


**Figure 4.** Distribution of patients (*n*) according to the number of needle passes performed during endoscopic ultrasound (EUS)-guided fine needle aspiration (FNA) for cytological diagnosis of solid pancreatic masses. EUS-guided FNAs with on-site cytopathologist are shown in red bars, and without on-site cytopathologist in yellow bars. Statistical difference between the two groups: $P<0.001$.

(21,24,26,27). Actually, several studies on the diagnostic accuracy of EUS-guided FNA have included on-site cytopathological evaluation as part of their methodology (7–9,25). However, studies specifically designed with the aim of evaluating the influence of on-site cytopathological interpretation of EUS-guided FNA samples on diagnostic accuracy are scarce.

Klapman *et al.* (23) compared the diagnostic yield of EUS-guided FNA from two different hospitals, with and without on-site cytopathology, respectively. They showed that EUS-guided FNAs performed with on-site cytopathology were less likely to produce an unsatisfactory tissue specimen and more frequently had a cytological diagnosis. However, as the study compares two groups of patients who were recruited at two different hospitals, a center-related bias cannot be excluded. Actually, the two groups of patients were not similar, and pancreas was significantly the most common target site at the center without on-site cytopathology, whereas more accessible thoracic and/or abdominal nodes were the most common target sites at the center with on-site cytopathology.

More recently, Hikichi *et al.* (28) evaluated the diagnostic accuracy of EUS-guided FNA with on-site assessment of sample adequacy either by endosonographers or cytopathologists in patients with solid pancreatic masses from two different periods of time. As no differences were observed, they recommended on-site sample evaluation by the endosonographer if no cytopathologist is available. However, these two approaches of on-site sample evaluation were carried out at two different 2-year periods of time, with on-site sample evaluation by endosonographer being the last period. Experience could be thus a bias, mainly taking into account that sample size was low, with 73 EUS-guided FNAs of pancreatic masses performed over 4 years (average of 18 procedures performed per year). Contrary results were reported by Alsohaibani *et al.* (29) in a retrospective study comparing two consecutive periods of time, in which interpretation of EUS-guided FNA samples was performed on-site by a cytotechnologist or an endoscopy nurse, respectively. Although the number of needle passes performed in the two study periods was similar (2.1 and 2.6 as a mean, respectively), the diagnostic yield of

**Table 3. Distribution of patients (*n*) based on cytological finding according to the final diagnosis (malignant or benign masses)**

| Cytological finding | With on-site cytopathologist | | Without on-site cytopathologist | |
|---|---|---|---|---|
| | Malignant masses | Benign masses | Malignant masses | Benign masses |
| Positive for malignancy | 70 | 0 | 34 | 0 |
| Suspicious for malignancy | 6 | 0 | 9 | 0 |
| Negative for malignancy | 0 | 16 | 0 | 24 |
| Indeterminate or atypical | 2 | 0 | 1 | 8 |
| Inadequate sample | 1 | 0 | 11 | 0 |

**Table 4. Diagnostic accuracy of EUS-FNA for pancreatic malignancy according to the presence or absence of on-site pathologist**

| | With on-site pathologist (*n*=95) | Without on-site pathologist (*n*=87) | *P* value |
|---|---|---|---|
| Sensitivity | 96.2% (95.5–96.9) | 78.2% (77.2–79.2) | 0.002 |
| Specificity | 100% (96.9–100) | 100% (98.4–100) | NS |
| Positive predictive value | 100% (99.3–100) | 100% (98.8–100) | NS |
| Negative predictive value | 84.2% (81.5–86.9) | 72.7% (71.5–73.9) | NS |
| Overall accuracy | 96.8% (96.3–97.4) | 86.2% (85.6–86.8) | 0.013 |

EUS-FNA, endoscopic ultrasound-guided fine needle aspiration; NS, not significant.
95% Confidence intervals are shown in brackets.

EUS-FNA was significantly improved by evaluation of sample adequacy by a cytotechnologist (29). Similar results were also reported by Savoy *et al.* (37) in a prospective double-blind controlled trial. They found a higher diagnostic accuracy when EUS-guided FNA samples were evaluated on-site for adequacy by cytotechnologists compared with endosonographers. Nevertheless, diagnostic accuracy of EUS-guided FNA without on-site sample assessment was not evaluated in any of these three studies (28,29,37).

Compared with previous studies, all EUS and EUS-guided FNAs were performed by the same two endoscopists in this study. They had a previous EUS experience of several years and more than 250 EUS-guided pancreatic FNAs performed. Similarly, the same two experienced cytopathologists evaluated all FNA samples. A further strength of this study is that the diagnostic accuracy of EUS-guided FNA with and without on-site cytopathology was evaluated in one center over the same period of time. All this allows excluding experience of both endoscopists and cytopathologists as a potential bias of the reported results. Finally, this study is focused on the evaluation of a large number of unselected, consecutive patients with solid pancreatic masses, avoiding bias associated with a limited number of cases, a selected series of cases, or different target sites.

Differences in diagnostic accuracy of EUS-guided FNA according to the presence or absence of on-site cytopathologist could be explained at least partially by differences in the sample processing method. However, although Diff-Quick, used for on-site cytological evaluation, and Papanicolau stains, used after alcohol fixation of the samples, are considered as complementary and highlight different cellular details, they offer a similar diagnostic accuracy (24). Moreover, studies evaluating the rapid on-site cytological interpretation of EUS-guided FNA specimens reported a high accuracy compared with final cytological diagnosis by using similar sample preparations as those used in this study (38).

In this study, an adequate sample was obtained with just one or two needle passes in the majority of patients when samples were evaluated on-site by the cytopathologist, compared with three to four passes that were usually performed in order to increase the probability of adequate sample when no on-site cytopathology was available. Conversely, four or even five needle passes had to be performed in some cases before an adequate sample was called by the cytopathologist, which was very helpful and could not have been done in his absence. In addition, the area of puncture is changed according to the information provided by the on-site cytopathologist in cases of inadequate samples. This may impact the number of passes needed to obtain an appropriate sample too.

The potential for patients' selection bias in our study could be an issue. Actually, it could be argued that we could be more prone to schedule cases where a pathological diagnosis is critical on days with on-site cytopathology. As information regarding availability of on-site cytopathologist was unknown at the time of scheduling patients for EUS, we believe the potential of patient selection bias in this study is minimal. In addition, patients were scheduled for EUS by a secretary, who had no information about availability of on-site cytopathologist.

A final important issue to be discussed is safety. It is well known that EUS-guided FNA of the pancreas is a safe technique (39–41), with slightly higher complication rate related to the use of trucut needles (22). This study supports the safety of the technique, and only three major complications (1.65%) developed over the study period. Although complications are expected to occur in relation to a higher number of needle passes, because of the low complication rate of FNA, the size of this study is inadequate to show statistical differences in complications between groups with and without on-site cytopathology.

In conclusion, this study demonstrates that on-site cytopathological evaluation reduces the number of inadequate FNA samples and improves the sensitivity and overall accuracy of EUS-guided FNA for the diagnosis of malignancy in patients with solid pancreatic masses. Hence, we recommend the use of on-site cytopathological evaluation during EUS-guided FNA of pancreatic masses.

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## CONFLICT OF INTEREST

**Guarantor of the article:** Julio Iglesias-Garcia, MD.

**Specific author contributions:** Julio Iglesias-Garcia: conception and design, analysis and interpretation of data, and drafting the article; J. Enrique Dominguez-Munoz: conception and design, critical revision of the article for important intellectual content, and final approval of the article; Ihab Abdulkader, Jose Larino-Noia, Elena Eugenyeva, and Antonio Lozano-Leon: analysis and interpretation of data; Jeronimo Forteza: analysis and interpretation of data, and critical revision of the article for important intellectual content.

**Financial support:** None.

**Potential competing interests:** None.

## Study Highlights

### WHAT IS CURRENT KNOWLEDGE

- ✓ Endoscopic ultrasound (EUS)-guided fine needle aspiration (FNA) has been proven to be a safe and useful method for tissue sampling of intramural and extramural gastrointestinal lesions including the pancreas.
- ✓ Reports on the need of on-site cytopathological evaluation during the procedure are scarce.

### WHAT IS NEW HERE

- ✓ On-site cytopathological evaluation reduces the number of inadequate FNA samples and improves the sensitivity and overall accuracy of EUS-guided FNA for the diagnosis of malignancy in patients with solid pancreatic masses.

## REFERENCES


1. Tamm E, Charnsangavej C. Pancreatic cancer: current concepts in imaging for diagnosis and staging. Cancer J 2001;7:298–311.
2. Iglesias-Garcia J, Larino-Noia J, Abdulkader I *et al.* Quantitative endoscopic ultrasound elastography: an accurate method for the differentiation of solid pancreatic masses. Gastroenterology 2010;139:1172–80.
3. Cohen SJ, Pinover WH, Watson JC *et al.* Pancreatic cancer. Curr Treat Options Oncol 2000;1:375–86.
4. Rösch T. Endoscopic ultrasonography. Br J Surg 1997;84:1329–31.
5. Hawes RH. Endoscopic ultrasound. Gastrointest Endosc Clin N Am 2000;10:161–74.
6. Voss M, Hammel P, Molas G *et al.* Value of endoscopic ultrasound guided fine needle aspiration biopsy in the diagnosis of solid pancreatic masses. Gut 2000;46:244–9.
7. Wiersema MJ, Kochman ML, Cramer HM *et al.* Endosonography-guided real-time fine-needle aspiration biopsy. Gastrointest Endosc 1994;40:700–7.
8. Chang KJ, Katz KD, Durbin TE *et al.* Endoscopic ultrasound-guided fine-needle aspiration. Gastrointest Endosc 1994;40:694–9.
9. Erickson RA, Sayage-Rabie L, Beisner RS. Factors' predicting the number of EUS-guided fine-needle passes for diagnosis of pancreatic malignancies. Gastrointest Endosc 2000;51:184–90.
10. Binmoeller KF, Rathod VD. Difficult pancreatic mass FNA: tips for success. Gastrointest Endosc 2002;56:S86–93.
11. Bhutani MS, Hawes RH, Baron PL *et al.* Endoscopic ultrasound guided fine needle aspiration of malignant pancreatic lesions. Endoscopy 1997;29:854–8.
12. Harewood GC, Wiersema MJ. Endosonography-guided fine needle aspiration biopsy in the evaluation of pancreatic masses. Am J Gastroenterol 2002;97:1386–91.
13. Giovannini M, Seitz JF, Monges F *et al.* Fine-needle aspiration cytology guided by endoscopic ultrasonography: results in 141 patients. Endoscopy 1995;27:171–7.
14. Gress FG, Hawes RH, Savides TJ *et al.* Endoscopic ultrasound-guided fine-needle aspiration biopsy using linear array and radial scanning endosonography. Gastrointest Endosc 1997;45:243–50.
15. Raut CP, Grau AM, Staerkel GA *et al.* Diagnostic accuracy of endoscopic ultrasound-guided fine-needle aspiration in patients with presumed pancreatic cancer. J Gastrointest Surg 2003;7:118–26.
16. Wiersema MJ, Vilmann P, Giovannini M *et al.* Endosonography-guided fine-needle aspiration biopsy: diagnostic accuracy and complication assessment. Gastroenterology 1997;112:1087–95.
17. Chhieng DC, Jhala D, Jhala N *et al.* Endoscopic ultrasound-guided fine-needle aspiration biopsy: a study of 103 cases. Cancer 2002;96:232–9.
18. LeBlanc JK, Ciaccia D, Al-Assi MT *et al.* Optimal number of EUS-guided fine needle passes needed to obtain a correct diagnosis. Gastrointest Endosc 2004;59:475–81.
19. 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;13:289–93.
20. Williams DB, Sahai AV, Aabakken L *et al.* Endoscopic ultrasound guided fine needle aspiration biopsy: a large single center experience. Gut 1999;44:720–6.
21. Erickson RA. EUS-guided FNA. Gastrointest Endosc 2004;60:267–79.
22. Varadarajulu S, Fraig M, Schmulewitz N *et al.* Comparison of EUS-guided 19-gauge Trucut needle biopsy with EUS-guided fine-needle aspiration. Endoscopy 2004;36:397–401.
23. Klapman JB, Logroño R, Dye CE *et al.* Clinical impact of on-site cytopathology interpretation on endoscopic ultrasound-guided fine needle aspiration. Am J Gastroenterol 2003;98:1289–94.
24. Jhala NC, Jhala DN, Chhieng DC *et al.* Endoscopic ultrasound-guided fine needle aspiration. A cytopathologist's perspective. Am J Clin Pathol 2003;120:351–67.
25. Chang KJ, Nguyen P, Ericsson RA *et al.* The clinical utility of endoscopic ultrasound-guided fine needle aspiration in the diagnosis and staging of pancreatic carcinoma. Gastrointest Endosc 1997;45:387–93.
26. Yamao K, Sawaki A, Mizuno N *et al.* Endoscopic ultrasound fine-needle aspiration biopsy (EUS-FNAB): past, present, and future. J Gastroenterol 2005;40:1013–23.
27. Logrono R, Waxman I. Interactive role of the cytopathologist in EUS-guided fine needle aspiration: an effective approach. Gastrointest Endosc 2001;54:485–90.
28. Hikichi T, Irisawa A, Buthani MS *et al.* Endoscopic ultrasound-guided fine needle aspiration of solid pancreatic masses with rapid on-site cytological evaluation by endosonographers without attendance of cytopathologist. J Gastroenterol 2009;44:322–8.
29. Alsohaibani F, Girgis S, Sandha GS. Does onsite cytotechnology evaluation improve the accuracy of endoscopic ultrasound-guided fine needle aspiration biopsy? Can J Gastroenterol 2009;23:26–30.
30. Robins DB, Katz RL, Evans DB *et al.* Fine needle aspiration of the pancreas. In quest of accuracy. Acta Cytol 1995;39:1–10.
31. Suen KC, Abdul-Karim FW, Kaminsky DB *et al.* Guidelines of the Papanicolau Society of Cytopathology for fine needle aspiration procedure and reporting: the Papanicolau Society of Cytology Task Force on Standards of Practice. Diagn Cytopathol 1997;17:239–47.
32. Hall TL, Layfield LJ, Philippe A *et al.* Sources of diagnostic error in fine needle aspiration of the thyroid. Cancer 1989;63:718–25.
33. Austin JH, Cohen MB. Value of having a cytopathologist present during percutaneous fine needle aspiration biopsy of lung: report of 55 cancer patients and meta-analysis of the literature. AJR Am J Roentgenol 1993;160:175–7.
34. Miller DA, Carrasco CH, Katz RL *et al.* Fine needle aspiration biopsy: role of immediate cytological assessment. AJR Am Roentgenol 1986;147:155–8.
35. Palombini L, Fulciniti F, Vertani A *et al.* Fine needle aspiration of breast masses: a critical review of 1956 cases in 8 years (1977–1984). Cancer 1988;61:2273–7.
36. Nasuti JF, Yu G, Boudousquie A *et al.* Diagnostic value of lymph node fine needle aspiration cytology: an institutional experience of 387 cases observed over a 5 year period. Cytopathology 2000;11:18–31.
37. Savoy AD, Raimondo M, Woodward TA *et al.* Can endosonographers evaluate on-site cytologic adequacy? A comparison with cytotechnologist. Gastrointest Endosc 2007;65:953–7.
38. Eloubeidi MA, Tamhane A, Jhala N *et al.* Agreement between rapid onsite and final cytologic interpretations of EUS-guided FNA specimens: implications for the endosonographer and patient management. Am J Gastroenterol 2006;101:2841–7.
39. O'Toole D, Palazzo L, Arotçarena R *et al.* Assessment of complications of EUS-guided fine-needle aspiration. Gastrointest Endosc 2001;53:470–4.
40. Micames C, Jowell PS, White R *et al.* Lower frequency of peritoneal carcinomatosis in patients with pancreatic cancer diagnosed by EUS-guided FNA *vs* percutaneous FNA. Gastrointest Endosc 2003;58:690–5.
41. Eloubeidi MA, Tamhane A, Varadarajulu S *et al.* Frequency of major complications after EUS-guided FNA of solid pancreatic masses: a prospective evaluation. Gastrointest Endosc 2006;63:622–9.