

Yield of Endoscopic Ultrasound–Guided Fine-Needle Aspiration Biopsy in Patients with Suspected Pancreatic Carcinoma

Emphasis on Atypical, Suspicious, and False-Negative Aspirates

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BACKGROUND. Although atypical or suspicious cytology may support a clinical diagnosis of a malignancy, it is often not sufficient for the implementation of therapy in patients with pancreatic carcinoma. Endoscopic ultrasound–guided fine-needle aspiration biopsy (EUS-FNAB) is a relatively new method for obtaining cytology samples, and one that may decrease the number of atypical/suspicious diagnoses. The goals of the current study were to prospectively evaluate the yield of EUS-FNAB in the diagnosis of patients presenting with solid pancreatic lesions and to evaluate the significance of atypical, suspicious, and false-negative aspirates.

METHODS. All patients who presented with a solid pancreatic lesion and underwent EUS-FNAB over a 13-month period were included in the current study. One endoscopist performed all EUS-FNABs. On-site evaluation of specimen adequacy by a cytopathologist was available for each case. Follow-up included histologic correlation ($n = 21$) and clinical and/or imaging follow-up ($n = 80$), including 38 patients who died of the disease.

RESULTS. EUS-FNABs were obtained from 101 patients (mean age, 62 ± 11.8 years; age range, 34–89 years). The male-to-female ratio was 2:1. Sixty-five percent of the lesions were located in the head of the pancreas, 12% were located in the uncinate, 17% were located in the body, and 6% were located in the tail. The mean size of the tumors was 3.3 cm (range, 1.3–7 cm). A median of 4 needle passes were performed (range, 1–11 needle passes). Sixty-two biopsies (61.4%) were interpreted as malignant on cytologic evaluation, 5 (5%) as suspicious for a malignancy, 6 (5.9%) as atypical/indeterminate, and 26 (25.7%) as benign processes. Of the 76 malignant lesions, 71 were adenocarcinomas, 3 were neuroendocrine tumors, 1 was a lymphoma, and 1 was a metastatic renal cell carcinoma. All except one of the suspicious/atypical aspirates were subsequently confirmed to be malignant. Agreement was complete for the atypical cases. Among the suspicious cases, 2 of the 5 were identified as carcinoma by one cytopathologist and as suspicious lesions by the other, yielding a 40% disagreement rate between the 2 cytopathologists. Therefore, for the 10 atypical or suspicious cases that later were confirmed to be malignant, the final diagnosis of malignant disease was not made due to scant cellularity that could be attributed to sampling error in 8 cases and to interpretative disagreement in 2 cases (20%). All four false-negative diagnoses were attributed to sampling error. Two percent of all biopsies were inadequate for interpretation. Of the 99 adequate specimens, 72 yielded true-positive results, 23 yielded true-negative results, and 4 yielded false-negative results. No false-positives were encountered. Therefore, the sensitivity, specificity, positive predictive value, and negative predictive value of EUS-FNAB for solid pancreatic masses were 94.7% (95% confidence

interval [CI], 89.7–99.8%), 100%, 100%, and 85.2% (95% CI, 71.8–98.6%), respectively.

CONCLUSIONS. EUS-FNAB is a safe and highly accurate method for tissue diagnosis of patients with solid pancreatic lesions. Patients with suspicious and atypical EUS-FNAB aspirates deserve further clinical evaluation. *Cancer (Cancer Cytopathol)* 2003;99:285–92. © 2003 American Cancer Society.

KEYWORDS: endoscopic ultrasound, needle biopsy, pancreas, adenocarcinoma, pitfalls, interobserver variation.

Solid masses of the pancreas represent a variety of benign and malignant neoplasms of the exocrine and endocrine tissues of the pancreas. A tissue diagnosis is often required to direct therapy in the face of uncertain diagnosis or if the patient is not a surgical candidate either due to advanced disease or comorbidities.^{1–3} Endoscopic ultrasound (EUS) is a relatively new technology that employs endoscopy and high-frequency ultrasound (US). EUS involves imaging of the pancreatic head and the uncinate from the duodenum and imaging of the body and tail from the stomach. It has been shown to be a highly sensitive method for the detection of pancreatic masses.^{4,5} It is superior to extracorporeal US and computed tomographic (CT) scans, especially when the pancreatic tumor is smaller than 2–3 cm.^{6,7} Although EUS is highly sensitive in detecting pancreatic solid masses, its ability to differentiate between inflammatory masses and malignant disease is limited.⁴

Endoscopic retrograde cholangiopancreatography (ERCP) brushing, CT-guided biopsies, and transabdominal ultrasound (US) have been the standard nonsurgical methods for obtaining a tissue diagnosis of pancreatic lesions, but a substantial false-negative rate has been reported.⁸ Transabdominal US-guided fine-needle aspiration biopsy (US-FNAB) has been used for tissue diagnosis in patients with suspected pancreatic carcinoma.^{9–12} It has been shown to be highly specific, with no false-positive diagnoses. The overall sensitivity of TRUS-FNAB in one study was 81%, with a specificity of 100% and an overall specimen adequacy rate of 80%.¹⁰

With the advent of curvilinear echoendoscopes, transgastric and transduodenal EUS-FNAB of the pancreas have become a reality.^{7,13–17} In the current study, we prospectively evaluated the cellular yield of EUS-FNAB in patients with solid pancreatic masses who were clinically suspected to have pancreatic carcinoma. We also evaluated the clinical significance of an atypical or suspicious cytologic diagnosis and investigated the causes of false-negative results.

MATERIALS AND METHODS

EUS was introduced to the University of Alabama at Birmingham in July 2000. Since that time to August

2001, we prospectively evaluated the use of EUS-FNAB in 101 consecutive patients with suspected pancreatic carcinoma based on clinical results and/or other imaging studies. None of the patients had previously undergone chemotherapy or radiotherapy. We excluded cystic lesions of the pancreas from the current analysis because their diagnosis and management differ from solid pancreatic lesions. Patients who required a tissue diagnosis or who failed other attempts by ERCP, CT-guided biopsy, and/or US-guided biopsy were included in the current study. The institutional review board of the University of Alabama at Birmingham approved the current study. Informed consent was obtained from all patients before they underwent the procedure.

One attending gastroenterologist performed all EUS-FNABs (MAE). Standard EUS was performed on an outpatient basis under conscious sedation using a radial echoendoscope (model GF-UM130; Olympus, Melville, NY) for evaluating and staging the pancreatic lesion. Once a lesion was identified, EUS-FNAB was performed with a curvilinear echoendoscope (model UC-30P; Olympus). Patients with solid masses in the head and uncinate of the pancreas underwent biopsies via a transduodenal approach. Masses in the neck, body, or tail of the pancreas were targeted via a transgastric approach. Color flow and Doppler sonography were performed to exclude vascular structures and to choose a vessel-free needle track. All FNABs were performed with a 22-gauge needle (Echotip; Wilson-Cook, Winston Salem, NC) inserted through the working channel of the echoendoscope as previously described.^{17,20}

Attending cytopathologists were present for all procedures in the endoscopy suite to determine specimen adequacy. All pathologists with similar experience in cytopathology agreed on definitions of chronic pancreatitis and pancreatic adenocarcinoma and prospectively rendered diagnosis based on well-established, previously reported criteria.¹⁸ Cases diagnosed as atypical or suspicious later were reviewed by two blinded cytopathologists with similar experiences and specific interest in pancreatic FNABs. The cytologic diagnoses were classified as either malignant or be-

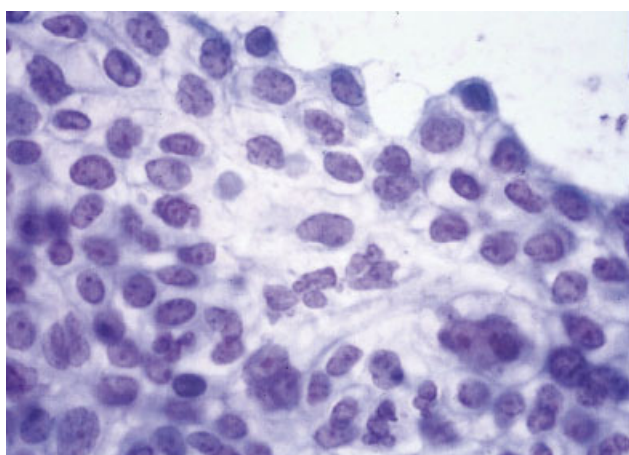


FIGURE 1. Smear from endoscopic ultrasound-guided fine-needle aspiration biopsy shows drunken honeycomb appearance of a well-differentiated pancreatic adenocarcinoma. Note the cohesive cell group with cellular crowding, loss of cellular polarity, and irregular nuclear membrane (Papanicolaou stain, original magnification $\times 40$).

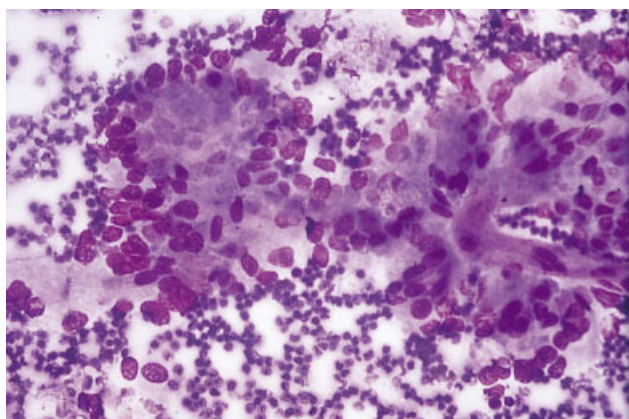


FIGURE 2. Smear reveals many single cells and abortive gland with marked cellular pleomorphism, altered nuclear-to-cytoplasmic ratio, and nuclear membrane irregularity characteristic for pancreatic adenocarcinoma (Diff-Quik stain, original magnification $\times 40$).

nign (including chronic pancreatitis) based on these same well-established cytologic criteria.¹⁸ Pancreatic adenocarcinomas were identified based on architectural and cellular characteristics. Aspirates from pancreatic adenocarcinomas (Figs. 1, 2) revealed increased cellularity demonstrating a combination of architectural features that include large crowded sheets of ductal cells ("drunken honey comb" appearance), three-dimensional groups, and many single atypical cells. Individual cells demonstrated nuclear enlargement, increased nuclear-to-cytoplasmic (N/C) ratio, anisocytosis and anisonucleosis, irregular nuclear membranes, and coarsely clumped chromatin patterns. Mitoses, especially abnormal mitoses, fa-

vored malignancy. Malignant cells also may show macronucleoli and cytoplasmic vacuolation. The background may show tumor diathesis and mucin production. Chronic pancreatitis (Fig. 3) was identified using a combination of features that include the presence of polymorphous cells including ductal and acinar cells. The ductal cells predominantly exhibit two-dimensional, tightly cohesive grouping. Individual ductal cells reveal a preserved N/C ratio and a regular nuclear membrane. Nucleoli are inconspicuous. Occasional individual ductal cells may also be observed. In addition, chunks of connective tissue may also be observed. Necrosis and chronic inflammatory cells in the background may be seen. When all features of adenocarcinoma were not identified, including increased cellularity, a smear was rendered and a diagnosis of either atypical or suspicious for adenocarcinoma was made (Fig. 4).

Other malignancies noted in pancreatic FNAB from neuroendocrine tumors (Fig. 5) were confirmed based on cellular characteristics, as has been well reported¹⁸ and on confirmatory immunohistochemical stains¹⁹ (chromogranin and synaptophysin) performed on the cell block preparation. Similarly, a combination of history of previous malignancy, cell characteristics, immunohistochemical stain, and flow cytometry analysis confirmed the diagnosis of metastatic renal cell carcinoma and malignant lymphoma.

The aspirate was expressed on to glass slides. Both air-dried and alcohol-fixed smears were prepared. Air-dried smears were stained with Diff-Quik (Baxter, McGraw Park, IL) and reviewed immediately by a cytopathologist to ensure specimen adequacy. A preliminary diagnosis was also rendered when possible. The remaining material was then flushed out and collected in Cytolyt preservative (Cytoc, Boxborough, MA) for subsequent preparation of a ThinPrep slide (Cytoc) and a cell block. At least five passes were obtained for each target lesion unless a cytologic evaluation performed on site confirmed the presence of malignant cells. Alcohol-fixed smears were later stained with the standard Pap stain. Immunocytochemistry was performed on the cell block preparation using a standard immunoperoxidase protocol when indicated.

The cytologic diagnoses were categorized into the following groups: positive for malignancy, suspicious for malignancy, atypical cells-indeterminate for malignancy, benign/reactive process, or nondiagnostic. Nondiagnostic specimens were defined either as aspirates in which the cytologic specimen was inadequate to characterize the lesion or the materials were not believed to be representative of the target lesion. Nondiagnostic cases were not included in the statistical

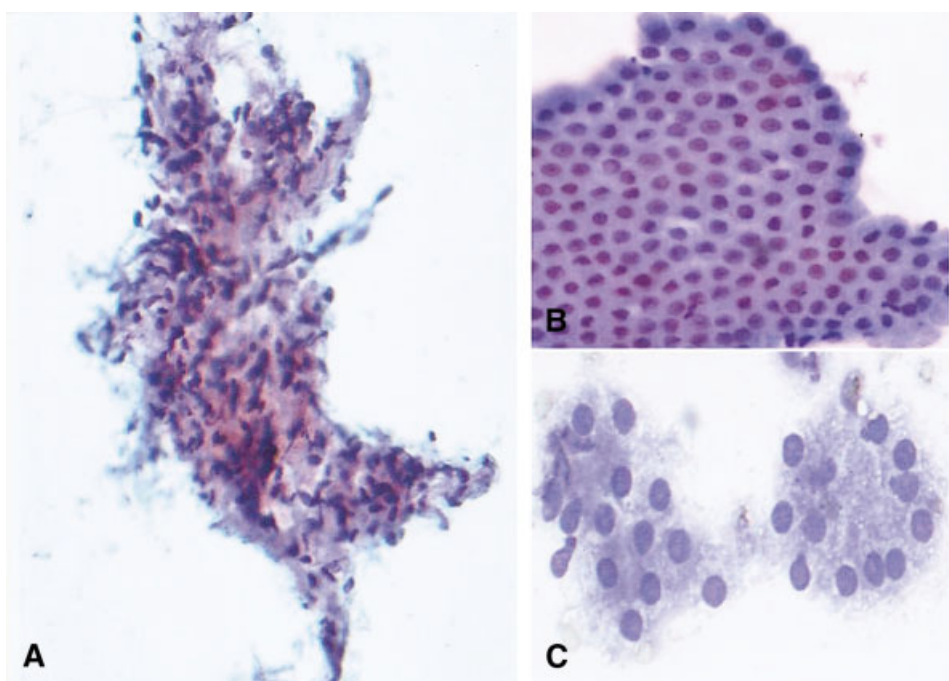


FIGURE 3. (A) Endoscopic ultrasound-guided fine-needle aspiration biopsy sample from a patient with chronic pancreatitis reveals fibrosis. (B) A tightly cohesive 2-dimensional group of ductal cells, with individual cells showing a regular nuclear membrane and an evenly distributed chromatin pattern, and (C) acinar cells with granular cytoplasm. Papanicolaou stains; original magnification $\times 20$ (A, B); $\times 40$ (C).

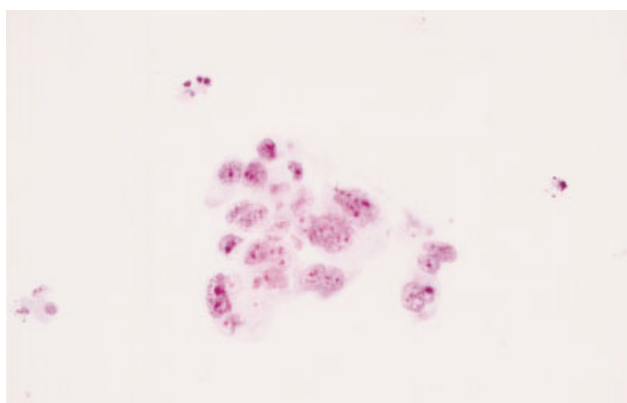


FIGURE 4. Smear reveals rare single cells with cellular atypia. Smear was considered suspicious but not diagnostic for malignancy (ThinPrep [Cytoc, Boxborough, MA] preparation; Papanicolaou stain, original magnification $\times 20$).

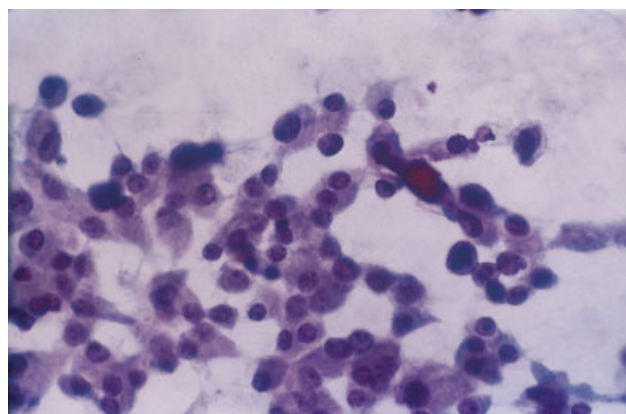


FIGURE 5. Smear from pancreatic neuroendocrine tumor reveals monomorphic single cells with occasional rosette formation and calcification. Also noted are cells with conspicuous nucleoli (Papanicolaou stain, original magnification $\times 40$).

calculation of sensitivity, specificity, and diagnostic accuracy.

The final diagnosis of pancreatic carcinoma was confirmed by histologic evidence or by clinical and/or imaging follow-up that showed death from disease or clinical progression. Lesions were considered to be benign if there was a lack of progression or spontaneous resolution in conjunction with continued patient well-being. Clinical follow-up was obtained for 80 patients (including 38 patients who died of the disease) and histologic correlation was obtained for 21 patients. Follow-up continued until February 2002.

Statistical Analysis

Continuous variables were reported as means and standard deviations (SD) or as median and range if data were not normally distributed. To determine the operating characteristics of EUS-FNABs in detecting pancreatic malignancy, their sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and corresponding 95% binomial exact confidence intervals (CIs) were calculated. Initially, all suspicious and atypical lesions were categorized as true-positives because patients had cancer on follow-up. However, we recalculated our values considering

TABLE 1
Comparison of Interobserver Agreement upon Review of Atypical and Suspicious Cytologic Findings

Observer	Atypical	Suspicious	Carcinoma
Observer 1	6	5	0
Observer 2	6	3	2

only suspicious lesions as true-positive. We also recalculated our values based on one false-positive diagnosis. The current analysis allows comparison to other studies. All statistical analyses were performed using SAS software (Version 6.12; SAS Institute, Cary, NC).

RESULTS

EUS-FNAB was performed in 101 patients with clinically suspected pancreatic carcinoma. The mean age of the patients was 62 years (SD \pm 11.8 years; range, 34–89 years), and the male-to-female ratio was 2:1. The median follow-up was 233 days (SD \pm 172 days). Seventy-six percent (77 of 101 patients) were Caucasian, 22.8% (23 of 101 patients) Black, and 1% (1 of 101) Asian. The mass location was the head of the pancreas in 65.3%, the uncinate in 11.9%, the body in 16.8%, and the tail in 5.9% of patients. The mean tumor size was 3.3 cm (range, 1.3–7 cm). A median of 4 EUS-FNAB needle passes were performed (range, 1–11 needle passes, SD \pm 2.54). Only 1 of 101 patients developed self-limited abdominal pain after the procedure. No other complications were reported.

EUS-FNAB was nondiagnostic in 2 patients (2%) due to the lack of adequate cellularity, as a result of technical difficulties. Sixty-two patients (61.4%) had a malignant cytologic diagnosis, 5 (5%) were interpreted as suspicious for a malignancy, 6 (5.9%) as atypical/indeterminate, and 26 (25.7%) had a benign/reactive process. Ten of 11 FNAB smears interpreted as either suspicious ($n = 5$) or atypical ($n = 6$) later were confirmed as positive for malignancy based on clinical follow-up or progression of disease ($n = 5$), surgical exploration with tissue confirmation ($n = 2$), or death from disease ($n = 3$). One patient with an atypical aspirate was later found to have chronic pancreatitis after surgical exploration. The results of the independent review by two blinded cytopathologists are shown in Table 1. Agreement was complete for the atypical cases. Among the suspicious cases, 2 of the 5 were read as carcinoma by one and as suspicious by the other, leading to a 40% disagreement rate between the 2 cytopathologists. Therefore, for the 10 atypical or suspicious cases that were later confirmed to be cancerous, the final diagnosis of cancer was not reached due to scant cellularity that could be attributed to

sampling error in 8 cases and to interpretative disagreement in 2 cases (20%). The false-negative diagnosis in all four patients was attributed to sampling error due to intervening venous or arterial structures such as the hepatic artery or periduodenal varices. EUS-FNAB was repeated for the four suspicious cases and pancreatic adenocarcinoma was confirmed, thus facilitating initiation of chemotherapy and radiotherapy.

Of all the solid pancreatic masses, 72 yielded true-positive results, 23 yielded true-negative results, and 4 yielded false-negative results. No false-positive results were encountered. (Table 2) Therefore, the sensitivity, specificity, PPV, and NPV of EUS-FNAB for pancreatic solid masses were 94.7% (95% CI, 89.7–99.8%), 100%, 100%, and 85.2% (95% CI, 71.8–98.6%), respectively. When we considered only suspicious cases as true-positive, the specificity and the PPV remained robust. However, the sensitivity and the NPV changed to 94.3% and 84.6% respectively. When we classified the only atypical aspirate with chronic pancreatitis as a false-positive result, the PPV changed to 98%, the NPV was 84.6%, and the specificity was 95.7%. The sensitivity remained unchanged. Of the 76 malignant lesions on final diagnosis, 71 were adenocarcinomas, 3 were neuroendocrine tumors, 1 was a lymphoma, and 1 was a metastatic renal cell carcinoma (Table 2). The lymphoma case was confirmed by surgical open biopsy and flow cytometry from peritoneal fluid. All the neuroendocrine tumors as well as the renal cell carcinoma were confirmed by immunohistochemical stains. One patient with a neuroendocrine tumor underwent surgical resection, further confirming our cytologic diagnosis. At the time of last follow-up, 38 patients died of the disease, 21 patients had undergone surgical exploration, and 42 patients had clinical follow-up and/or repeat imaging. Of these, 55% experienced disease progression whereas the rest either remained unchanged or improved.

DISCUSSION

EUS is increasingly used in the diagnosis and staging of pancreatic carcinoma.^{17,20,21} It is superior to other imaging modalities, especially when tumors are smaller than 2 cm.^{7,22} Based on imaging alone, whereas EUS is highly sensitive in detecting malignancy, it is not specific.^{4,7} In a study of 115 patients with histologic confirmation, EUS had a high sensitivity (95%) but a very low specificity (53%) for differentiating malignancy from focal masses caused by chronic pancreatitis.⁴ In addition, clinically unsuspected neuroendocrine tumors were misjudged in all 10 cases. A definitive tissue diagnosis of pancreatic carcinoma is required to direct future therapy in patients with inoperable disease because of locally ad-

TABLE 2
Comparison of Results of Endoscopic Ultrasound–Guided Fine-Needle Aspiration Biopsy with Results of Surgical Pathology, Cytology, and Extended Clinical/Repeat Imaging Follow-Up in Patients with Solid Pancreatic Masses

EUS-FNAB cytology	Final diagnosis		Final diagnosis for malignant findings
	Benign	Malignant	
Nondiagnostic (technical failure)	0	2	Adenocarcinoma
Atypical	1	5	All adenocarcinoma except for one lymphoma ^a
Suspicious	0	5	Adenocarcinoma
Benign	22	4	Adenocarcinoma
			All adenocarcinoma, except for three neuroendocrine tumors, and one renal cell carcinoma ^b
Malignant	0	62	
Total	23	78	

EUS-FNAB: endoscopic ultrasound–guided fine-needle aspiration biopsy.

^a The cytology from the lymphoma case was reported as atypical lymphoproliferative disorder and was confirmed by flow cytometry and surgical biopsy.

^b Neuroendocrine tumors and renal cell carcinoma were confirmed by immunohistochemical stains. A neuroendocrine tumor from one patient also was confirmed by surgery.

vanced disease and the presence of metastatic disease and comorbidities. With the advent of curvilinear echoendoscopes capable of performing puncture and tissue acquisition, pancreatic masses can be sampled using EUS-FNABs.

In the current study, we reviewed our experience with EUS-FNAB in 101 patients with solid pancreatic masses. The sensitivity, specificity, PPV, and NPV of EUS-FNAB in solid pancreatic masses were 94.7%, 100%, 100%, and 85.2%, respectively. These results compare very favorably with those of a multicenter EUS-FNAB study of solid pancreatic masses, which reported a sensitivity of 86%, a specificity of 94%, a PPV of 100%, and an NPV of 86%.²⁰ In the current study, 10.9% of pancreatic aspirates were reported as either atypical or suspicious. This compares with 7.8%²³ and an 8% rate of atypical/suspicious diagnosis from other centers.²⁰

All suspicious cytologic diagnoses were confirmed subsequently to be malignant. Two of the 5 (40%) cases reported as suspicious for malignancy in our report resulted from interobserver variation between pathologists. In these two cases, one pathologist rendered a diagnosis of positive for malignancy and the other independently rendered a diagnosis of suspicious for malignancy due to a few cells observed in the smear. In one case, there were only a few highly atypical cells admixed in the background of groups of reactive ductal epithelial cells. In contrast, in another case, marked necrosis was observed in most of the smears with rare, single, highly atypical ductal epithelial cells. These results suggest an inherent interobserver variation between pathologists in making a conclusive diagnosis of malignancy. In the event of scant cellularity, the combination of qualitative diagnostic criteria could be used to enhance the diagnostic

accuracy. Robins et al.²⁴ suggested that major diagnostic criteria (nuclear crowding, nuclear contour irregularity, and irregular chromatin distributions) and minor criteria (nuclear enlargement, single epithelial cells, and necrosis) were the most important predictors of malignancy. In each of our cases—although not in an explicit or a quantitative approach—we used these diagnostic criteria for evaluation during routine sign-out. Robins et al. showed that the sensitivity of diagnosing pancreatic carcinoma increased from 70% to 90% when a combination of cytologic criteria was used.

Similar to our observation, other investigators reported an 8% rate of EUS-FNAB classified as suspicious. All suspicious cases were later proven to be malignant on follow-up. However, unlike our report, earlier studies^{18,21} did not discuss the reasons for rendering suspicious or atypical diagnoses.

It also is possible that multiple attempts are necessary to obtain adequate cells for a definitive diagnosis. Another EUS-FNAB was performed on four of the five suspicious lesions, which confirmed malignancy. One patient was treated with chemotherapy based on a suspicious cytologic diagnosis. It is known that pancreatic adenocarcinoma induces a tumor-associated sclerotic response, which may contribute to scarce cellularity and may result in a nondiagnostic specimen.

Six patients had atypical cytology. One was determined to be a lymphoma and one was determined to be chronic pancreatitis at surgery; both were confirmed histologically. The remaining four were determined to be adenocarcinoma on subsequent follow-up. Of the four false-negative diagnoses, benign tissue was obtained due to a hepatic artery-encased tumor in one, periduodenal varices in a second, and the inabil-

ity to position the echoendoscope in a third. The presence of an intervening vascular structure between the transducer and the pancreatic mass precludes adequate targeting of the substance of the mass and, therefore, leads to either a nonrepresentative sample or, occasionally, to bloodier samples. We have shown, however, that in the presence of periduodenal collaterals, EUS-FNAB is feasible and safe.²⁵ A mass lesion was detected by EUS in all of these patients and surgical exploration was recommended. The fourth patient had an infiltrating tumor hidden within a background of chronic pancreatitis and did not have a definitive mass. The patient underwent a Whipple procedure based on the ERCP appearance of a common bile duct stricture. Frozen sections were consistent with chronic pancreatitis. Additional sections, however, revealed infiltrating carcinoma. These results suggest that all false-negative cases were due to sampling errors rather than to interpretation errors.

The results of EUS-FNAB in solid pancreatic masses presented in the current study compare favorably to those obtained by other techniques such as extracorporeal (CT or US) FNAB and brush cytology during ERCP.²⁶ More specifically, EUS-FNAB has a higher yield for cancer and less atypical, suspicious, or false-negative aspirates than other techniques. Enayati et al.²⁶ reported on the meaning of equivocal pancreatic cytology (FNAB or brush cytology) in patients believed to have pancreatic carcinoma.²⁶ In their large 6-year experience from the Virginia Mason Clinic, the authors retrospectively reviewed 224 cytologic specimens. Forty-three percent of all the cytologic specimens were read as malignant, 8% as suspicious, 13% as atypical, and 34% as negative. All cases of malignant and suspicious cytology were proven to be malignant. In their study, 55% of all atypical cytologic studies were malignant. More importantly, 49% of those samples read as benign were later confirmed to be malignant, pointing out the advantage of EUS-FNAB (an NPV of 86% in the current study) in preventing subsequent and needless resource utilization for tissue diagnosis.

The NPV of EUS-FNAB in the current study is superior to that reported for CT-guided FNAB (42%), brush cytology (68%), or the combination of both procedures (51%).²⁶ In another large multicenter retrospective study of CT-guided FNAB of 364 patients with pancreatic lesions, David et al.²⁷ reported that 6% of all aspirates were suspicious and another 6% of the aspirates were unsatisfactory. Eighty-one percent of all suspicious aspirates were ultimately diagnosed as malignant. The NPV of EUS-FNAB in the current study is superior to the NPVs reported by other experienced centers that perform EUS-FNAB.^{13,17} EUS-FNAB can

be utilized as a rescue modality when other techniques fail.²³

Increased yield and cellularity, which are required for adequate interpretation, are a consequence of the technique utilized, the operator, and the presence of a cytopathologist in the EUS suite. In one study, the diagnostic accuracy of neuroendocrine tumors by EUS-FNAB in the absence of a cytopathologist on site was only 47%. In the current study, similar to an earlier observation,¹⁹ we encountered no difficulty in differentiating between neuroendocrine tumors and primary adenocarcinomas. The presence of a cytopathologist to evaluate the aspirate on site allows the collection of additional material for ancillary studies. After rapid interpretation and initial cytologic impression of a neuroendocrine tumor, extra passes were made to ensure that a sufficient sample was available for immunocytochemistry. This was emphasized by the finding that we were able to diagnose correctly all our neuroendocrine tumors based on EUS-FNAB specimens. Similarly, we diagnosed correctly a case of metastatic renal cell carcinoma to the pancreas by EUS-FNAB.²⁸

In summary, EUS-FNAB is a safe and highly effective method for securing tissue diagnosis in patients with suspected pancreatic carcinoma. Almost all patients with suspicious and atypical cytology were subsequently proven to harbor cancer in the current study. Newer strategies, such as the addition of ancillary studies (e.g., tumor markers), are needed to further improve the yield and minimize suspicious, atypical, and false-negative results. Patients with suspicious or atypical EUS-FNAB aspirates warrant further clinical evaluation.

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