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The value of concurrent endoscopic ultrasound-guided fine needle aspirates and needle core biopsies in the diagnosis of pancreatic neoplasms

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Abstract

Background: Endoscopic ultrasound (EUS) fine needle aspiration (FNA) is highly sensitive and specific in the detection and diagnosis of pancreatic neoplasms. EUS-guided needle core biopsy has been used alone or as an adjunct to maximize diagnostic yield. This study compared the use of FNA versus needle core biopsy in the diagnosis of pancreatic neoplasms.

Methods: From January 1, 2018 through December 21, 2020, the Cytopathology Laboratory processed 374 FNAs from solid pancreatic masses of which 332 (89%) had concurrent pancreatic biopsies and form the basis of this study.

Results: Of the 332 FNAs, 173 (52%) were positive/suspicious for pancreatic adenocarcinoma, 33 (10%) were positive for a neoplasm, 20 (6%) were atypical 19 (6%) were negative and 87 (26%) were non-diagnostic. Biopsies were concordant in 248 (75%) cases and discordant in 84 (25%) cases. Of the 84 discordant cases, 29 (35%) had neoplastic cells on FNA of which 14 were atypical, 11 were negative and 4 were nondiagnostic on core biopsy. Of the 18 (21%) FNAs with atypical cells, 8 showed adenocarcinoma on core biopsy. Thirty-seven nondiagnostic FNAs showed adenocarcinoma on 25 (70%) core biopsies. If nondiagnostic FNAs were included, FNA sensitivity was 89% and specificity; 100%, and both were 100%, if the nondiagnostic cases were excluded. The needle core biopsy sensitivity was 91% and specificity; 100%.

Conclusion: Both FNAs and core biopsies show high sensitivity and specificity in the detection of pancreatic neoplasms. However, combining the techniques enhances cellular yields and provides material for ancillary tests.

KEYWORDS
diagnostic accuracy, fine needle aspiration, needle core biopsies, pancreatic neoplasms

1 | INTRODUCTION

Pancreatic carcinoma is an aggressive malignancy and, at present, the seventh leading cause of cancer-related death globally.[1,2] It presents insidiously with nonspecific symptoms and is often diagnosed at a late stage with a poor prognosis. Therefore, a diagnosis at an early stage of disease is an important determinate of patient prognosis, staging and management. Previous studies report that endoscopic ultrasound (EUS) fine needle aspiration (FNA) is 80%–90% sensitive and nearly 100% specific for the diagnosis of pancreatic malignancy.[3,4] The majority of pancreatic mass lesions are due to primary adenocarcinoma and 10%–15% are due to other lesions including neuroendocrine tumors and cystic neoplasms.

In addition to EUS-FNA, EUS-guided needle core biopsy is utilized as an effective diagnostic tool for sampling pancreatic lesions.[4] This study compares the use of FNA versus needle core biopsy in the diagnosis of pancreatic neoplasms.

2 | MATERIALS AND METHODS

From January 1, 2018 through December 31, 2020, the Cytopathology Laboratory of the University of Wisconsin Madison Hospital and Clinics processed 374 FNAs from solid pancreatic masses of which 332 (89%) had concurrent pancreatic biopsies and form the basis of this study. Pancreatic cyst aspirates were not included due to their low cellularity.

3 | PROCEDURAL INFORMATION

EUS was performed with the patient in the decubitus position and under conscious sedation consisting of intravenous midazolam and fentanyl. Patients first underwent EUS examination using a radial echoendoscope (GF-UM130 or GF-UE160, Olympus, USA) for evaluation and staging of target pancreatic lesions. Subsequently, a curvilinear echoendoscope (GF-UC140P-ALK5, Olympus) was used to evaluate and perform FNA of suspicious lesions. FNA was performed via standard technique using a 22- or 25-gauge needle (Echotip, Wilson-Cook, USA). Generally, a 22-gauge needle was used first. A 25-gauge needle was selected in cases of poor initial cellular return. A 19-gauge FNA needle (Quick-Core, Wilson-Cook, USA) was used to obtain core biopsies of tissue. On average, 3–4 aspirates were performed per pancreatic mass. From each pass, two slides were prepared. One slide was alcohol-fixed for Papanicolaou staining and the other slide was air-dried and immediately stained with Hema-Diff stain for adequacy assessment by a cytotechnologist. The cytotechnologist reviewed those cases that showed atypical cells to adenocarcinoma with the cytopathologist via telectyology and a preliminary diagnosis was provided. On completion of the procedure, the FNA slides were transported to the cytology laboratory by the cytotechnologist for final processing and additional staining by the Papanicoulaou method. The biopsies were fixed in 10% buffered formalin and sent to the histology laboratory in surgical pathology for routine processing and staining. Briefly, the biopsies were embedded in paraffin and 3-μm-thick sections were cut and stained with hematoxylin–eosin (H&E).

The pancreatic aspirates were screened by six experienced cytotechnologists and signed out by five board certified cytopathologists. Six subspecialty trained gastrointestinal pathologists reviewed and signed out the pancreatic biopsies without prior knowledge of the FNA cytology results. Cytohistologic correlation was conducted for this study in addition to standard quality improvement requirements.

4 | CYTOLOGIC REPORTING SYSTEM

Cytologic diagnoses were classified using the Papanicolaou Society of Cytopathology Terminology System as malignant, suspicious, neoplastic other, atypical, negative, or nondiagnostic.[5] Nondiagnostic samples were defined as those with no or very scant cellular material insufficient for analysis. A negative cytologic sample is synonymous with the absence of malignancy and cellular atypia and contains benign cellular material.

Molecular testing for mismatch repair proteins, MLH-1, MSH_2, MSH_6, and PMS_2, utilizing immunohistochemical analysis was performed on the positive needle core biopsies via the Ventana Benchmark Ultra IHC Automated platform according to the manufacturer's instructions. The amount of tissue was adequate for MMR analysis in 95% of the cases.

Specimen Evaluation Pathology reports were reviewed for all specimens. For statistical purposes, lesions considered positive included specimens diagnostic of a neoplasm.

The results of the FNAs and needle core biopsies were confirmed by additional available modalities including Whipple procedures, percutaneous biopsies, radiologic studies, clinical follow-up and/or death from disease. Sensitivity and specificity were calculated for EUS-guided FNAs and EUS-guided needle core biopsies.

For calculations, utilizing the resection specimen diagnosis, or if not available, clinical follow-up of at least 6 months was considered the gold standard for final diagnosis. Specimens diagnosed as malignant or suspicious were considered true positives if the final diagnosis was malignant and false positives if the final diagnosis was benign. Lesions diagnosed as atypical were considered true negatives if the final diagnosis was benign and false negatives if the final diagnosis was malignant. So too were the calculations for negative and nondiagnostic cases. For the purposes of this study, nondiagnostic cases were included in the calculations, as neoplastic cells were found on concurrent needle core biopsies.

5 | RESULTS

In the current study (Table 1), 173 (52%)/332 FNAs were positive/suspicious for pancreatic adenocarcinoma, 28 (8%) were positive for a neoplasm; 14 neuroendocrine tumors (NETs), 12 mucinous neoplasms

TABLE 1 Cytohistologic correlation

FNA	Pancreatic Biopsy						
	Number of Cases	Adeno-carcinoma	NET	IPMN	Atypical Cells	Negative	Non-Diagnostic
Adenocarcinoma	152	135	-	-	9	7	1
Suspicious for Adenocarcinoma	21	18	-	-	1	-	2
Neoplastic, Other							
NET	14	-	12	-	1	-	1
Mucinous Neoplasms	12	1	–	5	3	3	–
IPMN	2	–	–	2	–	–	–
Neoplasm, NOS	5	–	4	–	–	1	–
Atypical cells	20	8	–	–	2	7	3
Negative	19	–	–	–	–	19	–
Nondiagnostic	87	25	2	1	3	6	50
Total	332	187	18	8	19	43	57

Abbreviations: IPMN, intraductal papillary mucinous neoplasm; NET, neuroendocrine tumor; NOS, not otherwise specific.

TABLE 2 FNA/Needle Core Biopsy Accuracy Compared to Gold Standard Follow-up

FNA/NCB	Gold standard	
	Positive cases	Negative cases
Positive/suspicious	206	0
Atypical	10	10
Negative	0	19
Nondiagnostic	31	56
Total	247	85

Abbreviations: FNA, fine needle aspiration; NCB, needle core biopsy.

and 2 intraductal papillary mucinous tumors (IPMNs) and 5 neoplasms, not otherwise specified (NOS). Twenty (6%) FNAs were atypical, 19 (6%) were negative and 87 (26%) were nondiagnostic. Biopsies were concordant in 248 (75%) cases. Of the 248 concordant diagnoses 177 (71%) were positive/suspicious for neoplastic cells; these included primary pancreatic adenocarcinoma (153/177; 86%), NET (12/177; 7%), mucinous neoplasm (6/177; 3%), IPMN (2/177; 1%) and neoplasm, NOS (4/177; 2%). Follow-up for all concordant available cases correlated with the primary FNA and core needle biopsy. Sixty-nine (28%) of the 248 cases were negative/nondiagnostic by FNA and needle core biopsy. The majority of the negative cases represented pancreatitis and the nondiagnostic cases consisted of scanty cellular material insufficient for diagnosis. The two atypical cases favored an inflammatory/reactive process.

Eighty-four (25%) cases were discordant. Of the 84 discordant cases, 29 (35%) had neoplastic cells on FNA of which 14 were atypical, 11 were negative, and 4 were nondiagnostic on core biopsy. Of the 18 (21%) FNAs with atypical cells, 8 showed adenocarcinoma on core biopsy, 7 were negative and 3 were nondiagnostic. Thirty-seven (44%) nondiagnostic FNAs showed pancreatic adenocarcinoma on 25 core biopsies, 2 NETs, 1 IPMN, 3 atypical cells and 6 negative.
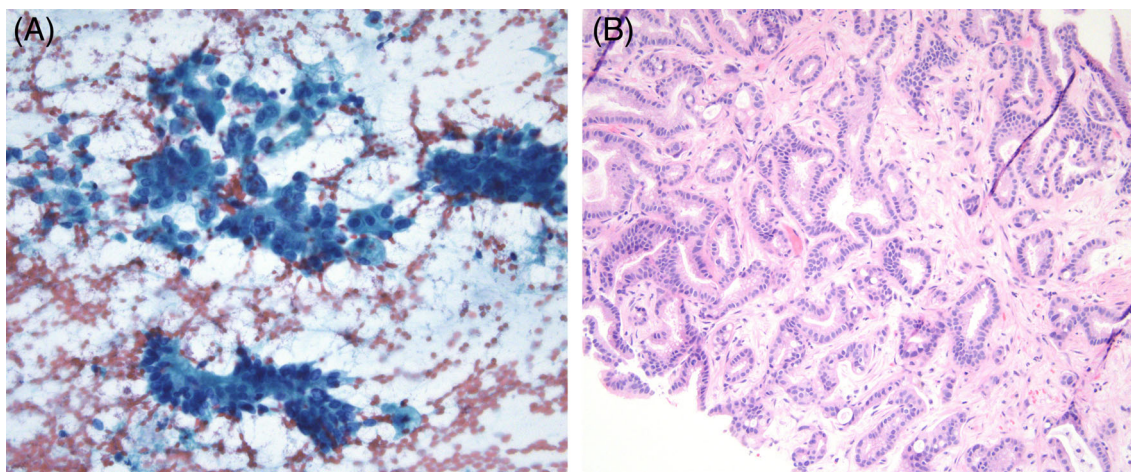

FIGURE 1 (A) Pancreatic FNA with clusters of adenocarcinoma cells (Papanicolaou stain, 40×). (B) Concurrent pancreatic needle core biopsy with sufficient malignant glands for ancillary studies (hematoxylin–eosin, 20×) [Color figure can be viewed at wileyonlinelibrary.com]

If the nondiagnostic FNAs are included, the sensitivity was 89% and the specificity was 100%. The sensitivity was 100% if the nondiagnostic cases were not included. The needle core biopsy showed 91% sensitivity and 100% specificity. The sensitivity and specificity for combined FNA/needle core biopsy were 90% and 100%, respectively; x^2 test, $p < .025$. Table 2 shows the gold standard follow-up for each diagnostic category.

6 | DISCUSSION

EUS-FNA is a safe, accurate and minimally invasive procedure with high sensitivity and specificity for diagnosing pancreatic lesions.[6] So too, EUS-guided needle core biopsy is an effective diagnostic tool for sampling pancreatic lesions. EUS-needle core biopsy offers the additional benefit of obtaining a large enough volume of lesional tissue (Figure 1) for not only histologic assessment but also ancillary studies including immunohistochemistry and molecular analysis; a limiting factor of FNA.[4,7]

At our institution EUS-guided FNAs and needle core biopsies are performed concurrently to increase the diagnostic yield and to obtain sufficient material for ancillary tests. In the age of precision medicine multiple recuts of either cell block or histologic slide material are needed for molecular analysis.

The results of the current study demonstrate that EUS-FNAs and needle core biopsies are equally specific for diagnosing pancreatic neoplasms including pancreatic adenocarcinoma, pancreatic neuroendocrine tumor, mucinous neoplasm and intraductal papillary mucinous neoplasm. Both techniques showed similar sensitivity if nondiagnostic FNAs were included in the calculation, as neoplastic cells were found in 28/87 (32%) needle core biopsies from nondiagnostic FNAs. The routine use of rapid on site evaluation for EUS-FNAs enables the gastroenterologist to proceed directly to needle core biopsy if three to four non-diagnostic passes are performed and assessed. Discordant diagnoses are attributed primarily to sampling as the fibrotic nature of the tumor may hinder procurement of an FNA sample. For comparison, Fitzpatrick and colleagues[7] reported a greater nondiagnostic rate of 6% for needle core biopsies compared to 3% for concurrent FNA smears; findings attributed to lower tissue quality/scanty cellularity on tissue samples. There is controversy in the literature as to the diagnostic accuracy of FNAs versus needle core biopsies. In a series of 52 EUS-guided pancreatic FNAs with concurrent core biopsies, the sensitivities for FNAs and core biopsies were 97% and 68%, respectively and the specificity for both was 100%.[8] Other studies reported similar sensitivities for detecting solid pancreatic neoplasms by both methods.[9,10] The results of the current study showed high sensitivity and specificity for both methods in the diagnosis of pancreatic neoplasms and concurrent needle core biopsies provided diagnostic material for nondiagnostic FNAs.

Although some studies[7] have reported that simultaneous review of FNA smears and needle core biopsies by cytopathologists could optimize EUS-FNA performance, all biopsies at our institution are interpreted by fellowship-trained gastrointestinal pathologists. Routine cyto-histologic correlation is subsequently performed by cytopathologists to compare both the EUS-FNA and EUS-needle core biopsy findings. In addition, the majority of ancillary tests at our institution are performed on biopsy material as (1) cell blocks are not made on FNAs with limited cellular material or (2) the cellular material in the cell block is limited, hampering further testing.

In conclusion, both FNA and needle core biopsy show high sensitivity and specificity in the detection of pancreatic neoplasms. However, utilization of both techniques enhances cellular yields; in particular unsatisfactory FNAs, and often provides sufficient material for ancillary tests in this era of precision medicine.

CONFLICT OF INTEREST

No conflict of interest declared.

DATA AVAILABILITY STATEMENT

Research data are not shared.

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