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The Final Cytopathologic Diagnosis of Initially “Indeterminate” Pancreatic Mass Lesions

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To the Editor

Endoscopic Ultrasound (EUS)-guided Fine Needle Aspiration (FNA) often provides confirmatory histologic diagnoses on patients found to have evidence of a pancreatic mass on prior imaging. EUS-FNA has grown in favor as a diagnostic test since histologic classification has important implications for treatment.^{1,2} Results are most often indicated as malignant, suspicious for malignancy, atypical cells, benign, or insufficient material. The “indeterminate” results, *suspicious* or *atypical*, often lead to repeat procedures, which can lead to patient and provider uneasiness.^{3,4} We aimed to determine the final pathologic diagnosis in patients with pancreatic masses undergoing EUS-FNA whose initial cytology report was characterized as *atypical* or *suspicious*.

This study used a retrospective cohort design and evaluated patients at a single academic center. All patients were referred for EUS-FNA of a pancreatic mass, without known pathologic diagnosis, at our medical center from 2000–2011. Initial cytology results were characterized as *benign*, *atypical*, *suspicious*, *malignant*, or *insufficient material*. Patients were divided into two groups: those with malignant final pathology and those without malignant final pathology. The primary study outcome was to determine the probability of malignancy by final pathology if the initial EUS-FNA cytology sample was *atypical* or *suspicious*.

From 2000 to 2011, 619 patients underwent EUS-FNA of a solid pancreatic mass. Of the original 619 patients, 28 had insufficient material to make cytopathologic diagnosis but were included in the total count given the final pathology was known. The 619 patients were divided into two groups based solely on final pathology: malignant and non-malignant. The malignant group (529 patients) included the following pathologic diagnoses: lymphoma,

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adenocarcinoma, neuroendocrine tumor, and metastatic disease. The non-malignant group (90 patients) included the following diagnoses: benign mass, lymphoid tissue, and lipoma.

Of the cytology results on initial EUS-FNA, seen in Table 1, 459 had a *malignant* cytology, 26 had *suspicious* cytology, 29 were *atypical*, and 75 were *benign*. Of the 26 patients with *suspicious* cytology results, 92.3% were eventually found to have a malignant diagnosis. In the 29 patients with *atypical* cytology, 65.5% were eventually deemed malignant on final pathology. For comparison, in the 459 patients with an initial *malignant* report, 99.6% had the malignancy subsequently confirmed. The probability of an initial *suspicious* diagnosis being negative and an initial *malignant* diagnosis being negative were equivalent ($p=0.23$).

Data on each patient was expanded to size of mass (in cm) and location in the pancreas. *Suspicious* and *atypical* lesions were independently compared to the *malignant* lesions. Linear regression demonstrated that a *suspicious* cytology was most likely in lesions from the neck (OR = 2.01, 95% CI 1.23–2.79) and body (OR = 2.23, 95% CI 1.78–2.67). The same analysis revealed that *atypical* cytology was more likely to originate from the uncinate (OR = 3.05, 95% CI 2.47–3.64). Comparison of mass size did not reveal any significant difference in those that were *suspicious*. Patients with *atypical* cytology did have a higher likelihood of being 1–2cm (OR = 3.79, 95% CI 3.29–4.29) and 4–5cm (OR = 2.07, 95% CI 1.64–2.50).

This study found that in solid pancreatic masses, EUS-FNA results with an initial *suspicious* cytology are almost always found to be malignant. These findings suggest that it may be more appropriate for such patients with *suspicious* cytology to be treated as if the result was malignant. Considering the lesions malignant would serve to minimize repeated procedures and associated complications. Further studies on this topic may look specifically at patients receiving *suspicious* or *atypical* cytology results and following them prospectively for differences in clinical management.

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Table 1

Probability that a pancreatic mass was malignant given the EUS-guided FNA cytology results

Cytology Results	Malignant Pathology* (12,14,30,42,50)	Non-Malignant Pathology (1,20,21)	Total Count
Malignant	459 (99.6%)	2 (0.4%)	461
Suspicious	24 (92.3%)	2 (7.7%)	26
Atypical	19 (65.5%)	10 (34.5%)	29
Benign	18 (24.0%)	57 (76.0%)	75
Insufficient	9 (32.1%)	19 (67.9%)	28
Total Count	529 (85.5%)	90 (14.5%)	619

* Malignant pathologies include – lymphoma (12), pancreatic malignant neoplasm (14), metastatic melanoma (30), neuroendocrine tumor (42), and carcinoma of uncertain primary (50). Non-malignant pathologies include - pancreatic benign mass (1), lymphoid tissue (20), and lipoma (21)