ORIGINAL ARTICLE

Feasibility and safety of microforceps biopsy in the diagnosis of pancreatic cysts

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Background and Aims: The tissue acquisition and diagnostic yield of cyst fluid cytology is low-to-moderate and rarely provides a specific diagnosis. The aim of this study was to compare the tissue acquisition and diagnostic tissue yield of microforceps biopsy (MFB) with cyst fluid cytology.

Methods: In this multicenter study, data of 42 patients who had cysts both aspirated by EUS-guided FNA (EUS-FNA) and biopsy specimens were then obtained with an MFB device, were collected. Cytology analysis of cyst fluid and histologic analysis of biopsy specimens were done. Acquisition yield was defined as percentage of patients with tissue present in the aspirate or biopsy. Diagnostic tissue yield was evaluated at 3 levels: the ability of differentiation between mucinous and/or nonmucinous cysts, detection of high risk for malignancy, and specific cyst type diagnosis.

Results: The mean patient age was 69 years. Sixteen pancreatic cysts (38.1%) were located in the head, 17 (40.5%) in the body, and 9 (21.4%) in the tail. The mean cyst size was 28.2 mm (12-60 mm); 25 of 42 (60%) were septated. The EUS-FNA tissue (fluid) acquisition yield was 88.1% (37/42). The MFB tissue acquisition yield was 90.4% (38/42). The diagnostic cytology yield to differentiate between mucinous and/or nonmucinous cysts was 47.6% (20/42), and the MFB histologic yield to differentiate between mucinous and/or nonmucinous cysts was 61.9% (26/42) ($P = .188$). The percentage of cysts at high risk for malignancy by cytology was 54.7% (23/42), and MFB was 71.5% (30/42) ($P = .113$). However, the ability of MFB to provide a specific cyst type diagnosis was 35.7% (15/42), and that for cytology was 4.8% (2/42) ($P = .001$). Surgical histology was concordant with that of MFB in 6 of 7 patients (85%), and with that of cytology in 1 of 7 patients (15%).

Conclusion: The cyst tissue acquisition yield for MFBs was 90%. Although cytology of cyst fluid and MFB were comparable in distinguishing mucinous and nonmucinous cysts and detecting cysts at high risk for malignancy, MFB was far superior to cytology for providing a specific cyst diagnosis. (Gastrointest Endosc 2018;■:1-8.)

Abbreviations: CEA, carcinoembryonic antigen; cPNET, cystic pancreatic neuroendocrine tumor; EUS-FNA, EUS-guided FNA; IPMN, intraductal papillary neoplasm; MCN, mucinous cystic neoplasm; MFB, microforceps biopsy.

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Primary pancreatic cysts are broadly divided into non-neoplastic and neoplastic, the latter termed pancreatic cystic neoplasms. Pancreatic cystic neoplasms are further classified into nonmucinous neoplasms (serous cystadenomas), mucinous neoplasms (intraductal papillary neoplasms [IPMN]), and mucinous cystic neoplasms [MCN]). In addition to primary pancreatic cysts, solid tumors can become cystic secondarily from degeneration, including pancreatic ductal adenocarcinoma and cystic pancreatic neuroendocrine tumors (cPNETs). The risk of malignancy in pancreatic cysts usually dictates the need for surgical resection.[1,2]

The most commonly used tools for both the diagnosis and differentiation of pancreatic cysts are cross-sectional imaging and EUS.[3,4] Because imaging alone has some limitations, cyst fluid analysis obtained by EUS-guided FNA (EUS-FNA) aids in further evaluation.[4-6] Cytology is limited because of scant cellularity and difficulty in detecting thin, watery, extracellular mucin, but cytology has been shown to be highly accurate for the diagnosis of a cyst at high risk for malignancy.[7-10] However, cytology is dependent on cells being shed into the cyst fluid for analysis. Interpretation challenges arise from GI contamination, degenerative changes of the cells, heterogeneity of the cyst lining epithelium, and lack of experience and interpretive expertise.[11]

Recently, a U.S. Food and Drug Administration–approved single-use Moray microforceps biopsy device (U.S. Endoscopy, Mentor, Ohio) (Fig. 1) has been designed for use in EUS procedures to enable sampling from cysts that can be accessed with a 19-gauge EUS-FNA needle. The aim of this study was to compare the tissue acquisition and diagnostic yield of the microforceps biopsy (MFB) with cyst fluid cytology.

PATIENTS AND METHODS

This study is a retrospective, controlled, open label, and multicenter investigation including Massachusetts General Hospital, University of Florida Health, University of California at Irvine, Mount Sinai Hospital, and University of Colorado. The patients gave their consent for EUS-FNA, cyst fluid analysis, and for use of the MFB device in the evaluation of pancreatic cysts. The institutional review boards of each center approved the study. The data of all patients (initial and subsequent) undergoing MFBs between 2015 and 2016 were collected, without a predefined study protocol. Exclusion criteria included patients with a bleeding diathesis, women with known pregnancy, patients with a history of pancreatic cancer, patients with acute pancreatitis or a high clinical suspicion of a pseudocyst or abscess, patients with a solid pancreatic mass or a clinically suspected pancreatic adenocarcinoma with cystic degeneration, and patients with cysts of extra-pancreatic origin.

Figure 1. Moray microforceps. Permission granted by US Endoscopy.

EUS-FNA and pancreatic cyst biopsy

In this multicenter study, data of 42 patients who had cysts aspirated by EUS-FNA were collected, and biopsy specimens were then obtained with an MFB device. Before the start of the procedure, all patients were given broad-spectrum antibiotics. The number, location, size of the cyst, presence or absence of septations, mural nodule and an adjacent mass on EUS were recorded. After evaluating the cyst with EUS, a 19-gauge Flex EUS needle (Boston Scientific, Marlborough, Mass) was placed into the cyst cavity, and the cyst fluid was aspirated first. Without removing the needle, an MFB device was introduced through the needle (Fig. 2), and pinch biopsy specimens were obtained from the cyst wall, septations, nodules, or adjacent masses if present (Fig. 3). The standardized order of obtaining biopsy specimens was the adjacent mass, mural nodule, cyst wall, and septations, respectively. If the biopsy specimen seemed insufficient in size for histology, additional passes were made. Aspirated cyst fluid was sent for CEA evaluation and for cytology analysis by using a cytospin preparation stained with routine Papanicolaou stain. The MFB specimens were sent in formalin and processed as a routine histology specimen. Adverse events including intra-cystic bleeding, pain, or pancreatitis related to the procedure were assessed during the procedure and for 2 hours after the procedure before discharge.

Cytology and histology evaluation

Failure to obtain fluid by EUS-FNA or tissue by MFB were considered acquisition failures and were classified as non-diagnostic. The term *tissue acquisition yield* referred to the ability to collect fluid or tissue for analysis and was calculated as the number of patients with fluid or tissue obtained by aspiration or MFB, which was either diagnostic or non-diagnostic, divided by the total number of patients.

The diagnostic tissue yield was evaluated at 3 levels (defined below) and calculated as the number of cases