Thieme

# Histologic analysis of pancreatic cystic lesions: Is tissue the issue?

OPEN ACCESS

Authors
Jad P AbiMansour[1], Ryan Law[1]

Institutions
1 Division of Gastroenterology, Mayo Clinic, Rochester, United States

Keywords
Pancreatobiliary (ERCP/PTCD), Tissue diagnosis, Pancreas, Endoscopic ultrasonography, Fine-needle aspiration/biopsy, GI Pathology

received 19.12.2023
accepted after revision 3.1.2024

Bibliography
Endosc Int Open 2024; 12: E341–E343

DOI 10.1055/a-2241-8038
ISSN 2364-3722



Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

Corresponding author
Dr. Ryan Law, Mayo Clinic, Division of Gastroenterology, 200 1st Street SW, 55905-0002 Rochester, United States
dr.ryanlaw@gmail.com

Pancreatic cystic lesions (PCL) are common with a prevalence ranging from 24% to 57% in population studies [1, 2]. Due to the widespread use of cross-sectional imaging, these lesions are often identified incidentally [3]. PCLs represent a broad spectrum of pathology which includes inflammatory, non-neoplastic, and neoplastic cysts. In one operative cohort of 851 patients, the most common diagnoses included intraductal papillary mucinous neoplasms (IPMNs) (38%), mucinous cystic neoplasms (23%), serous cystic neoplasms (16%), and cystic neuroendocrine neoplasms (7%) [4].

Accurately classifying a PCL helps inform surveillance and management, including the need for surgical resection. While clinical context and cross-sectional imaging findings can be suggestive, endoscopic ultrasound (EUS) provides additional diagnostic and prognostic information. In many cases, endosonographic characteristics alone are insufficient to differentiate between mucinous (MN) and non-mucinous lesions (n-MN) or to exclude the presence of malignancy, thus prompting EUS-guided sampling of PCLs [5, 6, 7]. There is significant interest in optimizing tissue acquisition and accurate histologic diagnosis, as up to 22% of patients inappropriately undergo major pancreatic resections for benign disease [8].

In the current issue of Endoscopy International Open, Castro et al. report the retrospective outcomes of a cohort of 145 patients with a PCL who underwent EUS-guided tissue acquisition (EUS-TA) using a 20-gauge EUS-guided fine needle biopsy (FNB) needle to aid in the differentiation of MN and n-MN lesions as well as evaluate for the presence of malignancy [9]. Ultimately, 81 patients were diagnosed with MNs (67 benign, 14 malignant) and 64 patients with n-MNs (53 benign, 11 malignant) with the final diagnosis largely defined by histologic findings from the FNB itself (81, 55.9%) and surgery (58, 40%). The calculated sensitivity was 92.6% and 92% for the diagnosis of MN and malignancy from FNB, respectively. In the cohort of patients who underwent surgery, sensitivity was 88% for differentiating malignant from non-malignant lesions. An overall adverse event rate of 2.7% was noted with three cases of bleeding and one case of pancreatitis.

The concept of sampling the wall of PCLs for histology has been well described including an early report in 2005 which used a relatively-novel “trucut” needle to enhance histologic analysis [10]. Several EUS-compatible “cutting” needles are now available, but most devices maintain similar design principles to allow for core tissue acquisition. The authors utilized a 20-gauge needle iterated with lateral pores on the needle shaft aimed to optimize the ability to obtain cyst fluid and histology. While needle design certainly can impact how a needle behaves during a procedure (e. g. traversing tissue or use in angulated scope positions), it is unlikely that small tip variations translate to significant improvements in clinical outcome. The majority of studies show equivalent tissue adequacy regardless of needle-tip design [11, 12]. Furthermore, data from solid pancreatic neoplasms suggest that FNB is not necessarily superior to fine needle aspiration (FNA) in regard to cost-effectiveness, tissue

acquisition, and diagnosis [13], and the incremental benefit it may provide in PCLs is similarly not well established [7].

Current guidelines suggest the use of FNA as the gold standard for PCL fluid acquisition and cytologic analysis [7]. It is notable that only 40% of the patients in the current study had cyst fluid available for biochemical analysis, which is lower than one might expect with the use of a 20-gauge needle. FNA with a 22-gauge needle remains the standard of care in our practice and is preferentially performed in PCLs. Certain technical considerations are worth highlighting which can maximize the yield of cyst fluid aspiration including the use of a stylet to clear the needle tip before aspirating and adapting a pneumatic insufflator to apply negative pressure to collect viscous fluid. Numerous studies have been published on FNA with one meta-analysis suggesting a specificity of 88%, sensitivity of 63%, and area under the curve of 0.89 for differentiating MNs from n-MNs [14]. Sensitivity for the presence of malignancy is generally lower, ranging from 27% to 55% [15, 16]. A hybrid technique of obtaining biopsies of the cyst wall using microscopic forceps (Moray Micro Forceps; Steris, Mentor, Ohio, United States) after needle access is obtained seems to improve the diagnostic performance of FNA but is more technically challenging, associated with a higher risk of adverse events, and it has not seen widespread adoption [17].

The diagnostic performance of FNB with histology in the current study appears quite robust when compared with FNA data, with seemingly adequate tissue in all samples and a sensitivity for malignancy of 92%. However, this must be evaluated in the context of the study which may have been confounded by selection bias of the retrospective cohort. For the majority of patients, it is also important to note that the reference gold standard was a diagnosis obtained by the sampling methodology being investigated, and the duration of clinical follow up (12 months) is likely insufficient to clinically exclude occult malignancy. External validity is also impaired by a population that likely differs from the PCLs seen by endoscopists in everyday practice, including 52 patients (36%) presenting with symptomatic cysts and a surgical intervention rate of 40%. Previous work has been more equivocal than what is reported here, with studies showing a specimen adequacy ranging from 46% to 87% [18, 19]. Even in cases in which FNB might be theoretically advantageous (e. g. presence of solid components), tissue adequacy was less than 50% using a 22-gauge biopsy needle [18]. There is inadequate comparative data to truly assess diagnostic performance of the technique, and therefore, it is our practice to reserve FNB for select cases. Generally, FNA can be performed and the same needle may be used to sample a thickened cyst wall or solid components after partial or complete decompression of the lesion, a technique which has been described as “targeted cyst wall puncture” [20].

While the techniques discussed in this article all have high specificity if malignancy is detected, they are limited by relatively poor sensitivity, requiring clinicians to interpret negative pathology in the context of each individual patient. This is driven by inherent limitations of sampling techniques as well as the diversity and pathophysiology of PCLs which, for example, may be associated with field defects and the development of carcinoma outside the reference lesion [21]. No sampling approach is a panacea and none can replace a thorough clinical history, risk factor evaluation, and review of characteristic imaging features, which must be performed in parallel with EUS-TA.

The recently available data on EUS-FNB are certainly intriguing and at the very least highlight the technical feasibility, applicability, and safety of its use in the evaluation of PCLs; however, there are no high-quality data suggesting that a particular combination of needle type, size, or technique is superior to another. There are likely multiple ways to obtain an adequate specimen to supplement clinical, radiographic, and endosonographic evaluation of PCLs. The specific technique should be driven by lesion morphology, endoscopist preference and comfort with specific devices, and locally available pathology expertise. Continued investigation with prospective, randomized trials and ongoing innovation in this area are essential to continue to refine the ability of clinicians to detect pre-neoplastic and neoplastic lesions and provide patients with appropriate, timely care.

## Conflict of Interest

Ryan Law: Consultant: Medtronic, Olympus, Boston Scientific, ConMed; Research Support: Olympus, Boston Scientific; Royalties: UpToDate

## References


[1] Kromrey ML, Bülow R, Hübner J et al. Prospective study on the incidence, prevalence and 5-year pancreatic-related mortality of pancreatic cysts in a population-based study. Gut 2018; 67: 138–145 doi:10.1136/gutjnl-2016-313127

[2] Ikeda M, Sato T, Morozumi A et al. Morphologic changes in the pancreas detected by screening ultrasonography in a mass survey, with special reference to main duct dilatation, cyst formation, and calcification. Pancreas 1994; 9: 508–512

[3] Laffan TA, Horton KM, Klein AP et al. Prevalence of unsuspected pancreatic cysts on MDCT. AJR Am J Roentgenol 2008; 191: 802 doi:10.2214/AJR.07.3340

[4] Valsangkar NP, Morales-Oyarvide V, Thayer SP et al. 851 resected cystic tumors of the pancreas: A 33-year experience at the Massachusetts General Hospital. Surgery 2012; 152: S4–S12 doi:10.1016/j.surg.2012.05.033

[5] Brugge WR, Lewandrowski K, Lee-Lewandrowski E et al. Diagnosis of pancreatic cystic neoplasms: a report of the cooperative pancreatic cyst study. Gastroenterology 2004; 126: 1330–1336 doi:10.1053/j.gastro.2004.02.013

[6] Cellier C, Cuillerier E, Palazzo L et al. Intraductal papillary and mucinous tumors of the pancreas: accuracy of preoperative computed tomography, endoscopic retrograde pancreatography and endoscopic ultrasonography, and long-term outcome in a large surgical series. Gastrointest Endosc 1998; 47: 42–49 doi:10.1016/s0016-5107(98)70297-4

[7] Muthusamy VR, Chandrasekhara V, Acosta RD et al. The role of endoscopy in the diagnosis and treatment of cystic pancreatic neoplasms. Gastrointest Endosc 2016; 84: 1–9 doi:10.1016/j.gie.2016.04.014

[8] Giannone F, Crippa S, Aleotti F et al. Improving diagnostic accuracy and appropriate indications for surgery in pancreatic cystic neoplasms: the role of EUS. Gastrointest Endosc 2022; 96: 648–656.e2

[9] Castro J, Taglieri E, Neto O et al. Clinical usefulness of tissue acquisition of pancreatic cystic lesions using an endoscopic ultrasound-guided needle for histological analysis. Endosc Int Open 2024; 12: E155–E163

[10] Levy MJ, Smyrk TC, Reddy RP et al. Endoscopic ultrasound–guided trucut biopsy of the cyst wall for diagnosing cystic pancreatic tumors. Clin Gastroenterol Hepatol 2005; 3: 974–979 doi:10.1016/s1542-3565(05)00408-8

[11] Nayar MK, Paranandi B, Dawwas MF et al. Comparison of the diagnostic performance of 2 core biopsy needles for EUS-guided tissue acquisition from solid pancreatic lesions. Gastrointest Endosc 2017; 85: 1017–1024

[12] Bang JY, Hebert-Magee S, Navaneethan U et al. Randomized trial comparing the Franseen and Fork-tip needles for EUS-guided fine-needle biopsy sampling of solid pancreatic mass lesions. Gastrointest Endosc 2018; 87: 1432–1438 doi:10.1016/j.gie.2017.11.036

[13] Eloubeidi MA, Decker GA, Chandrasekhara V et al. The role of endoscopy in the evaluation and management of patients with solid pancreatic neoplasia. Gastrointest Endosc 2016; 83: 17–28

[14] Thosani N, Thosani S, Qiao W et al. Role of EUS-FNA-based cytology in the diagnosis of mucinous pancreatic cystic lesions: a systematic review and meta-analysis. Dig Dis Sci 2010; 55: 2756–2766 doi:10.1007/s10620-010-1361-8

[15] Sedlack R, Affi A, Vazquez-Sequeiros E et al. Utility of EUS in the evaluation of cystic pancreatic lesions. Gastrointest Endosc 2002; 56: 543–547 doi:10.1067/mge.2002.128106

[16] Frossard JL, Amouyal P, Amouyal G et al. Performance of endosonography-guided fine needle aspiration and biopsy in the diagnosis of pancreatic cystic lesions. Am J Gastroenterol 2003; 98: 1516–1524 doi:10.1111/j.1572-0241.2003.07530.x

[17] Westerveld DR, Ponniah SA, Draganov PV et al. Diagnostic yield of EUS-guided through-the-needle microforceps biopsy versus EUS-FNA of pancreatic cystic lesions: a systematic review and meta-analysis. Endosc Int Open 2020; 8: E656–E667 doi:10.1055/a-1119-6543

[18] Barresi L, Tarantino I, Traina M et al. Endoscopic ultrasound-guided fine needle aspiration and biopsy using a 22-gauge needle with side fenestration in pancreatic cystic lesions. Dig Liver Dis 2014; 46: 45–50

[19] Phan J, Dawson D, Sedarat A et al. Clinical utility of obtaining endoscopic ultrasound-guided fine-needle biopsies for histologic analyses of pancreatic cystic lesions. Gastroenterology 2020; 158: 475–477.e1

[20] Hong SKS, Loren DE, Rogart JN et al. Targeted cyst wall puncture and aspiration during EUS-FNA increases the diagnostic yield of premalignant and malignant pancreatic cysts. Gastrointest Endosc 2012; 75: 775–782

[21] Patra KC, Bardeesy N, Mizukami Y. Diversity of precursor lesions for pancreatic cancer: the genetics and biology of intraductal papillary mucinous neoplasm. Clin Transl Gastroenterol 2017; 8: e86 doi:10.1038/ctg.2017.3