Preoperative Histological Diagnosis of Pancreatic Cystic Neoplasms: Is Through the Needle Forceps Sampling the Answer?

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Abstract

Accurate preoperative diagnosis of pancreatic cystic lesions (PCLs) is a challenge as image-guided cytology has a very low sensitivity for its diagnosis. The recent advances in endoscopic ultrasound (EUS) such as needle confocal laser endomicroscopy and through the needle biopsy forceps has led to better characterization and diagnosis of the PCL. In this news and views, we discuss a prospective study that has evaluated the efficacy and safety of EUS-guided throughtheneedle biopsy sampling (EUS-TTNB) for diagnosis of PCLs.

Keywords
- endosonography
- pancreas
- cyst
- cytology

Introduction

The frequency of diagnosis of pancreatic cystic lesions (PCLs) is on the rise due to widespread availability and increased use of cross-sectional imaging in various intra-abdominal diseases. Accurate characterization of these lesions is important as the management and further surveillance of these cystic lesions depend upon the type and malignant potential of the cyst. The diagnostic imaging of choice to initially evaluate the PCL is magnetic resonance imaging (MRI) with magnetic resonance cholangiopancreatography (MRCP). However, it has low accuracy in characterizing these lesions, which warrant further evaluation by endoscopic ultrasound (EUS).[1] EUS allows detailed examination of cyst wall, septations, and mural nodules.[2] EUS-guided aspiration of the cyst fluid for cytology, amylase, sugar and tumor markers has improved our diagnostic capability.[3] Fluid analysis helps in differentiating mucinous cysts from non-mucinous but does not help in accurate characterization of cysts as well as in accurate determination of their malignant potential. Also, the fluid cytology has very low sensitivity, which often need the combination of methods to support the diagnosis.[1,4] The recent advances in EUS-like needle confocal laser endomicroscopy and through the needle biopsy (TTNB) sampling has led to an increase in appropriate characterization and diagnosis of the PCL. The ability to obtain tissue from the cystic wall or mural nodule by TTNB forceps can provide a histologic diagnosis for PCLs.[5] However, the exact role of TTNB sampling in routine clinical practice is unclear and also its diagnostic ability has not been compared with the conventional modalities including EUS morphology, cross-sectional imaging, and cystic fluid analysis. In this news and views, we discuss a prospective study from South Korea that has evaluated the efficacy and safety of EUS-TTNB in PCLs. This study has also compared the diagnostic accuracy of EUS-TTNB with the presumptive diagnosis made by combinations of conventional diagnostic modalities (i.e., EUS morphology, cross-sectional imaging, and cystic fluid analysis) for diagnosis of PCLs.[6]

In this study, authors reviewed the prospectively collected data of 45 patients enrolled between January 2019 and January 2021. They included patients with PCL in whom

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the malignant potential of the lesion was not excluded after routine imaging and EUS evaluation. Thus EUS-TTNB was expected to change the management and surveillance strategy of these patients. The morphology of cysts on EUS, growth rate, and serum CA 19-9 levels were considered before performing the EUS-TTNB. PCLs with diameter of less than 2 cm and lesions with high suspicion for adenocarcinoma were excluded.

EUS was done by two experienced endosonographers using a curvilinear array echoendoscope (GF-UCT 260; Olympus Optical, Tokyo, Japan). PCLs were punctured by a 19-gauge needle (EUSN-19-T; Cook Endoscopy, Winston-Salem, NC, USA). After the removal of the stylet, a microforcep (Moray microforceps; Steris endoscopy, Ohio, USA) was passed into the cyst through the needle. The lesions sampled with microforceps were cyst wall, septations, solid components, or mural nodules with mural nodules, thickened walls, or thickened septations being preferred targets for sampling. The sampled tissue was deposited in formalin jar and processed as routine histological samples and three to four visible fragments of tissue were obtained per patient. After completion of biopsy sampling, the cyst fluid was aspirated and sent for cytology and analysis of the CEA and amylase/lipase levels.

The primary outcome measures evaluated were technical success (ability to obtain gross specimens), diagnostic yield (ability to obtain adequate specimen for pathologic examination), and adverse events. They also evaluated the factors contributing to diagnostic failure (not sufficient for pathologic examination) and the discrepancies in the diagnosis between EUS-TTNB and the presumptive diagnosis made by the combination of conventional diagnostic modalities including EUS morphology, cross-sectional imaging, and cyst fluid analysis.

EUS-TTNB was successfully performed in all 45 patients with a mean PCL size of 45.08 ± 1.97 mm. The PCLs were located in the head of the pancreas in 10 (22%), uncinate process in 4 (9%), body in 6 (13%), and tail in 25 (56%) patients and 11(24%) cysts had mural nodules and 28 (62.2%) had septations. Tent sign was observed in all patients and passed with EUS needle per patient ranged from 1 to 6 and the number of biopsy specimens per patients ranged from 1 to 7 (median: 4). Histological diagnosis of PCL could be made in 82% of patients and this was IPMN (49%), mucinous cystic neoplasm (27%), serous cystadenoma (11%), lymphoepithelial cyst (8%), solid pseudopapillary neoplasm (3%), and lymphangioma (3%). Adverse events were reported in three patients (7%), and these were self-limited intra-cystic bleeding in one patient and mild acute pancreatitis in two patients.

Of 45 studied patients, 10 patients underwent surgical resection and one of these had diagnostic failure. The presumptive diagnosis in this patients was branch duct IPMN, TTNB specimen was inadequate and the final histological diagnosis of surgical specimen high-grade dysplasia of IPMN. The histological diagnosis obtained via EUS-TTNB was concordant with that of the surgical specimens in remaining nine patients. One of these,nine patients had a discrepancy in the diagnosis between EUS-TTNB (MCN) and the presumptive diagnosis (IPMN). However, histopathological diagnosis of resected specimen was concordant with that of EUS-TTNB.

The results obtained via TTNB (37/45 patients) were compared with the presumptive diagnosis made by the combination of EUS morphology, cross-sectional imaging, and cyst fluid analysis. Ten patients (27%) showed a discrepancy between EUS-TTNB and presumptive diagnosis. Of these 10 patients, 1 patient underwent surgical resection (described earlier in previous paragraph where in the histological diagnosis of EUS-TTNB was concordant with the diagnosis obtained on histopathological examination of the resected specimen). Diagnostic failure occurred in eight (18%) patients and there were no significant differences in the diagnostic yield according to either the presence of septations, size of PCL, targeted lesion of sampling, or the location of PCL. The mean number of microforcep biopsy samples obtained per session was significantly different between the success and failure group (3.9 vs. 2.6 respectively; $p = 0.011$).

Commentary

Accurate non-surgical diagnosis of PCLs is a frontier in diagnostic gastroenterology that still needs to be conquered. EUS and cyst fluid analysis by enabling the differentiation between mucinous and non-mucinous PCLs has significantly improved the ability to better characterize these lesions. However, accurate characterization of the malignant potential of PCLs and identification of dysplastic lesions is still a challenge. Newer innovations such as needle confocal endomicroscopy and TTNB has helped in improving the accuracy of characterization of PCL.

The significant advantage of EUS-TTNB compared to other tests is giving a confirmatory diagnosis regarding the type of cysts and risk of malignancy. However, experience with TTNB is limited to mainly retrospective case series and a recent systematic review reported that it has acceptable technical and clinical success rates with an excellent safety profile along with a high rate of tissue acquisition.[5] However, prospective data on the role of TTNB are limited and its impact on clinical management is not known. The currently discussed retrospective study by Cho et al has demonstrated that EUS-TTNB has high technical success rates as well as diagnostic yield, with good safety profile and improves the categorization of types of PCLs. The possibility of obtaining histological sample via TTNB is a significant advancement in accurate preoperative diagnosis of PCL as it helps in subclassification of IPMNs as well as finding the grade of dysplasia.

Currently, the TTNB has not been integrated in the diagnostic algorithm for evaluation of PCLs.For determining its exact role in the management algorithm, one need to study the causes of diagnostic failures. Crino et al had shown that for adequate histological diagnosis only two micro-biopsy samples from the PCL are enough and adding a third biopsy sample did not significantly improve the diagnosis.[7]

However, in the current study, the authors found that the diagnostic yield was significantly better when ≥4 biopsy samples were taken as compared to <four biopsy samples (93% vs. 67% respectively; $P = 0.045$). This issue of optimum number of biopsy samples per patient needs to be looked by future prospective studies. A recent prospective study has demonstrated that EUS-guided TTNB modified clinical management in about one-tenth of patients with PCLs.[8] Both EUS-TTNB and nCLE are newer promising modalities for evaluation of PCLs. A recent single retrospective study compared the EUS-TTNB and nCLE with standard tests and reported their diagnostic yield of 75% and 84.1%, respectively. Combining the EUS-TTNB and nCLE with standard tests had a diagnostic yield of 93.2%.[9]

The accurate diagnosis and characterization of the PCL poses a significant challenge to the clinicians. Often,a combination of various tests is needed to establish an accurate diagnosis and the EUS-TTNB has been proven to be more useful than the routinely performed tests. Although the initial studies on the role of TTNB in PCLs including the study by Cho et al are promising, future multicenter, prospective comparative studies are needed to assess the benefits and cost-effectiveness of these promising newer modalities.

Conflict of Interest
None declared.

References

1 Elta GH, Enestvedt BK, Sauer BG, Lennon AM. ACG clinical guideline: diagnosis and management of pancreatic cysts. Am J Gastroenterol 2018;113(04):464–479
2 Rana SS, Gupta R. Contrast enhanced EUS for evaluation of mural nodule in pancreatic cystic neoplasm (with video). Endosc Ultrasound 2021;10(03):216–218
3 Ge N, Brugge WR, Saxena P, et al. An international, multi-institution survey of the use of EUS in the diagnosis of pancreatic cystic lesions. Endosc Ultrasound 2019;8(06):418–427
4 Canakis A, Lee SL. State of the art update of pancreatic cysts. Dis Dig Sci 2021; Aug 12. Doi: 10.1007/s10620-021-07084-1. Epub ahead of print
5 Guzmán-Calderón E, Martinez-Moreno B, Casellas JA, de Madaria E, Aparicio JR. Endoscopic ultrasound-guided, through-the-needle forceps biopsy for diagnosis of pancreatic cystic lesions: a systematic review. Endosc Int Open 2020;8(09):E1123–E1133
6 Cho SH, Song TJ, Seo DW, et al. Efficacy and safety of EUS-guided through-the-needle microforceps biopsy sampling in categorizing the type of pancreatic cystic lesions. Gastrointest Endosc 2022;95(02):299–309
7 Crinò SF, Bernardoni L, Brozzi L, et al. Association between macroscopically visible tissue samples and diagnostic accuracy of EUS-guided through-the-needle microforceps biopsy sampling of pancreatic cystic lesions. Gastrointest Endosc 2019;90(06):933–943
8 Kovacevic B, Klausen P, Rift CV, et al. Clinical impact of endoscopic ultrasound-guided through-the-needle microbiopsy in patients with pancreatic cysts. Endoscopy 2021;53(01):44–52
9 Cheesman AR, Zhu H, Liao X, et al. Impact of EUS-guided microforceps biopsy sampling and needle-based confocal laser endomicroscopy on the diagnostic yield and clinical management of pancreatic cystic lesions. Gastrointest Endosc 2020;91(05):1095–1104

