Article published online: 2022-12-15

EUS-guided treatments of pancreatic cystic neoplasms – a call for methodological improvements

OPEN ACCESS

Authors

Andrea Lisotti*,1, Ryan Law*,2

Institutions

1 Gastroenterology Unit, Hospital of Imola, University of Bologna, Imola, Italy.

2 Mayo Clinic, Department of Gastroenterology and Hepatology, Rochester, Minnesota, United States

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

Bibliography

Endosc Int Open 2022; 10: E1526–E1527

DOI 10.1055/a-1965-3191

ISSN 2364-3722

Corresponding author

Dott. Andrea Lisotti, UOC di Gastroenterologia, Hospital of Imola, University of Bologna, Via Montericco 4, 40026 Imola (BO), Italy

lisotti.andrea@gmail.com

Pancreatic cystic neoplasms (PCN) affect up to 5 % of the general population, with a relative prevalence increase in recent decades, mostly due to increased life-expectancy and the improvements in the diagnostic potential and widespread availability of cross-sectional imaging [1, 2].

The clinical management of patients affected by PCNs should take into account the estimation of the underlying malignant potential balanced with the risks associated with pancreatic surgery. In fact, while some PCNs bear a negligible malignant risk (i. e. serous cystadenoma), mucinous cystic neoplasms (such as IPMNs and mucinous cystic neoplasms), cystic neuroendocrine neoplasms and solid pseudopapillary tumors demonstrate malignant potential in a significant number of cases. Therefore, the differential diagnosis of PCNs (i. e., mucinous vs. non-mucinous, or other neoplasms), together with accurate estimates of high-risk stigmata for malignancy is crucial for a correct treatment strategy [3]. The differential diagnosis of PCNs nature is usually based on cross-sectional imaging, and EUS with cyst fluid analysis in most patients; however, the diagnostic performance of conventional imaging, B-mode EUS, and cytology lacks accuracy (50–80 %) [1, 2].

Several clinical guidelines have been published to guide clinicians in identifying the best strategy for patients with PCNs. In order to reduce the great burden related to long-term follow-up and the potentially severe adverse events of pancreatic surgery, EUS-guided interventions have been proposed to ablate pancreatic cystic epithelium to decrease, or even abolish, the risk of malignant evolution of PCNs.

In the current issue of Endoscopy International Open, Othman et al. presented the outcomes of a pilot study designed to assess safety of EUS-fine needle injection (EUS-FNI) of a novel compound specifically designed for injection into solid tumors, namely large surface area microparticle paclitaxel (LSAM-PTX) [4]. The authors prospectively enrolled 19 patients with mucinous PCNs and observed optimal safety, with no procedure or drug-related adverse events. Moreover, there was no evidence of systemic absorption of injected paclitaxel observed in the study with nearly 70 % of treated PCNs showing a volume reduction after EUS-FNI of LSAM-PTX.

Othman et al. reported enthusiastic results; however, EUS-guided ablation of PCNs cannot be considered an effective treatment option at present, due to the limitations of available evidence. The available literature includes several cases of patients with pancreatic cysts undergoing EUS-guided ablation with no cyst characterization and no clear treatment indication. In particular, a meta-analysis of studies reporting the efficacy of paclitaxel-based EUS-FNI included up to 50 % of patients with serous cystic neoplasms, pseudocysts or undetermined cysts [6]. *Patients' selection*, *cyst characterization* and *treatment indication a priori* are paramount in the development of this technique and its future role. Since it seems impossible to assess the clinical benefit of any intervention without a reliable estimation of the potential burden of the underlying disease, the correct pre-procedural assessment of PCNs represents Columbus' Egg in patients undergoing EUS-FNI.

* Ryan Law and Andrea Lisotti contributed equally to this manuscript, writing the paper. All Authors approved the final version of the manuscript.

Recently, an international group of experts published a position statement on EUS-FNI for PCNs. The manuscript by Teoh et al. included *treatment indications* which were clearly defined and should be adopted in all subsequent studies, including the present study [5]. Teoh et al. identified patients with unilocular or oligolocular mucinous cysts, larger than 3 cm or with proven increase in size over time as the ideal candidates for EUS-FNI; the international panel contraindicated EUS-FNI in cysts with low malignant potential. In the present study, Othman et al. adopted cyst fluid analysis for the definition of mucinous nature of the PCNs, as the authors included 2 patients with MCNs and 17 with branch duct IPMNs with no mural nodules and no main pancreatic duct dilation. According to current guidelines, most such PCNs should be referred for clinical and radiological follow-up, since no high-risk stigmata or even worrisome features were present.

Local treatment response should be assessed according to proposed criteria [5]. Data interpretation of the effectiveness of EUS-FNI using LSAM-PTX in the current study could be misinterpreted according to different points of view. The authors stated that "by week 24 a cyst volume reduction (10–78 %) was seen in 70.6 % of subjects" [4]; however, according to the proposed criteria [5], 11 out of 17 (65 %) patients who completed the 24-month follow-up showed a null response (5 volume increase, 6 decrease < 30 %), and the remaining patients showed only partial responses (volume reduction between 30–78 %). No patient showed a complete response.

To date, no randomized controlled trials with adequate follow-up have been conducted comparing surgery and EUS-guided ablation or clinical/radiological surveillance and EUS-guided ablation, thus the *clinical impact* of EUS ablation for PCNs is still unknown. Indeed, studies on EUS-radiofrequency ablation of mural nodules within IPMNs recently reported inspiring results with 100 % effectiveness [7]. However, long-term follow-up (3 years) of these patients resulted in up to 12 % incidence of pancreatic cancer [8].

In conclusion, EUS-guided interventions seem to be an effective strategy for the management of patients with PCNs bearing high-risk potential for malignancy. Moving forward future rigorous studies on safety and dose-response of novel compounds for EUS-FNI are desperately needed. Such rigorous studies will be mandatory to ensure an evidence-based comparison of EUS-guided approaches.

Competing interests

Andrea Lisotti declares no conflict of interests. Ryan Law is a consultant for Boston Scientific, ConMed, and Medtronic.

References

[1] Tanaka M, Fernandez-del Castillo C, Kamisawa T et al. Revisions of international consensus Fukuoka guidelines for the management of IPMN of the pancreas. Pancreatology 2017; 17: 738–753

[2] The European Study Group on Cystic Tumours of the Pancreas. European evidence-based guidelines on pancreatic cystic neoplasms. Gut 2018; 67: 789–804

[3] Lisotti A, Napoleon B, Facciorusso A et al. Contrast-enhanced EUS for the characterization of mural nodules within pancreatic cystic neoplasms: systematic review and meta-analysis. Gastrointest Endosc 2021; 94: 881–889

[4] Othman MO et al. Early phase trial of intracystic injection of large-surface-area microparticle paclitaxel for the treatment of mucinous pancreatic cysts. Endoscopy Int Open 2022; 10: E1517–E1525

[5] Teoh AY, Seo DW, Brugge W et al. Position statement on EUS-guided ablation of pancreatic cystic neoplasms from an international expert panel. Endosc Int Open 2019; 7: E1064–E1077

[6] Attila T, Adsay V, Faigel DO. The efficacy and safety of endoscopic ultrasound-guided ablation of pancreatic cysts with alcohol and paclitaxel: a systematic review. Eur J Gastroenterol Hepatol 2019; 31: 1–9

[7] Barthet M, Giovannini M, Lesavre N et al. Endoscopic ultrasound-guided radiofrequency ablation for pancreatic neuroendocrine tumors and pancreatic cystic neoplasms: a prospective multicenter study. Endoscopy 2019; 51: 836–842

[8] Barthet M, Giovannini M, Gasmi M et al. Long-term outcome after EUS-guided radiofrequency ablation: Prospective results in pancreatic neuroendocrine tumors and pancreatic cystic neoplasms. Endosc Int Open 2021; 9: E1178–E1185