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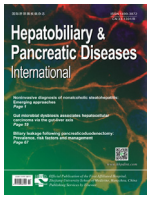

Editorial

Endosonography guided ethanol ablation for pancreatic cystic lesions: Current status

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During the last 30 years, endoscopic ultrasound (EUS) has evolved from a diagnostic tool to an interventional instrument with impressive and rapidly evolving applications that range from tissue acquisition to biliary tree drainage or creation of anastomosis [1]. Pancreatic lesion ablation using thermal energy or through the injection of substances under EUS guidance is one of the more promising applications [2,3].

In 1999, Brugge et al. [4] reported the first experimental EUS-guided radiofrequency ablation (RFA) in a pig model. Later on, other devices have become available. A bipolar hybrid cryotherm probe has been used for experimental protocols in animal models and patients [5,6]. In 2015 a monopolar "trough the needle" electrode for treatment of cystic and solid lesions was used [7]. In the same year, a water-cooled monopolar RFA needle with an active tip with different lengths (5–30 mm, diameter 18–19 G) was made commercially available, after preliminary experiences on animal models [8]. Early experiences offered satisfactory results in different fields of application, pancreatic adenocarcinoma [9], pancreatic neuroendocrine tumors (pNETS), and extra-pancreatic solid lesions [2,10–12]. Ongoing trials will better clarify the possible fields of application of EUS-guided RFA [13].

EUS-guided ethanol ablation (EUS-EA) has been used to treat cystic lesions of the pancreas, pNETS and for the palliative treatment of pancreatic ductal adenocarcinoma, in combination with celiac plexus neurolysis [14]. In 2016, ethanol injection was recommended by the European Federation of Societies for Ultrasound in Medicine and Biology guidelines in nonsurgical candidates for treatment of pNETS [15].

In fact, the treatment of pancreatic cystic lesions (PCL) appears to be a complex question. This ensues from the high prevalence of PCL in the general population combined with the problem of neoplastic precursors arising among them. Incidentally discovered pancreatic cysts offer a wide variety of pathologies, ranging from completely benign to premalignant or malignant lesions, and may be a diagnostic dilemma. Surgical resection is considered the optimal treatment for premalignant and malignant conditions, but it carries a relevant morbidity rate and a non-negligible mortality rate [16]. Moreover, a retrospective study conducted by Salvia et al. of 476 patients who underwent resection for a suspected pancreatic cystic neoplasm showed that the rate of inaccurate preoperative diagnosis was of 21.6%, even in expert hands [17]. For this reason, many different guidelines have been published in recent years aiming to optimize the selection of surgical candidates, accompanying a growing understanding of the etiology and differential diagnosis. This has led to a more conservative policy favoring follow-up instead of aggressive surgical options.

While RFA has been more enthusiastically applied to solid lesions, several groups especially in Eastern countries have reported EUS-EA of PCLs, with or without paclitaxel [18,19], aiming to destroy the cystic epithelium. Long-term outcomes after EUS-EA were reported in 2017 [19]. In this single-center, prospective study [19], 164 patients underwent ablation using ethanol and paclitaxel, including unilocular or oligolocular cysts, clinically indeterminate cysts requiring EUS-guided fine needle aspiration, or cysts that grew during the observation period. EUS-EA was performed using a 22-G needle by a single puncture. The mean cyst diameter was 32 mm and the median volume was 17.1 mL. The study achieved complete resolution in 72.2% of treated lesions, with partial resolution in 19.6%, and persistent cyst in 8.2%. Twelve out of 13 patients with persistent cysts underwent surgery reporting complete denudation of the cystic epithelium in 58.3% of cases. Interestingly, at a 6-year follow-up after complete ablation, 98.3% of cases showed complete remission and no malignancy was discovered during follow-up. There were sixteen adverse events (AEs), of which only one was severe. Follow-up was conducted by computed tomography scan 3 months after EUS-ablation, every six months up until resolution, and yearly thereafter.

The article by Choi et al., published recently, reported a large single-center experience at the Seoul National University Hospital with the aim of evaluating the safety of EUS-EA [20]. They included 214 patients for treatment of pancreatic cysts with low probability of malignancy or unfit for surgical treatment between 2006 and 2018. Overall AEs occurred in 71 patients (33.2%). The predictive factors of AE, especially acute pancreatitis and abdominal pain, were intraductal papillary mucinous neoplasm (IPMN), multilocular cysts, suspected ethanol leakage during procedure, sticky cystic fluid, and exophytic cyst. The response rate of the pancreatic cysts to the procedure of endoscopic ultrasound-guided ethanol ablation was 69.0%.

Comparing these studies, some technical aspects can be highlighted: differences in needle caliber, number of punctures, addition of paclitaxel, follow-up, which might explain slightly

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different rates of AE and of complete response. A recent article by Choi et al. [21] showed EUS-EA for PCL with low risk of malignancy might not provide a survival benefit, but improve quality of life, avoiding unnecessary surgery. Further doubts raise from the observation that the incidence of PCL is 2600/100 000 persons/year, but the incidence of pancreatic adenocarcinoma, mucinous type, is only 1/100 000 persons/year in the USA [22]. That is, we are dealing with a large number of patients, but with a fairly uncommon malignant transformation [23]. Therefore, a mini-invasive procedure instead of high-risk surgery looks adequate. The long-term results and low rate of complications seem to favor EUS-EA; nonetheless, the retrospective nature of the studies and the inclusion criteria not reflecting a strict surgical indication leave some doubts.

In the end, can we support EUS-EA in properly selected surgical patients and report this approach in common practice? Significant experiences, like the article by Choi [20], together with the recent position statement of an international panel of experts addressing the indications and modalities of EUS-EA for PCL on the base of available evidence, may mark the route for a more extensive application of the procedure [24]. However, further prospective studies are needed to improve the technique and to confirm the positive results obtained in retrospective studies.

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Competing interest

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