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Review Article

Endoscopic ultrasound-guided ablation of pancreatic cystic lesions

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A B S T R A C T

Endoscopic ultrasound (EUS)-guided ablation procedures are emerging as minimally invasive therapeutic methods that address unmet needs in treatment methods for pancreatic cystic lesions (PCLs). Several studies have been published on the feasibility and efficacy of EUS-guided chemical ablation for PCLs, but further research on the actual treatment effects and real clinical benefits is needed. EUS-guided radiofrequency ablation for PCLs has recently been introduced. This review aimed to describe the broad framework of EUS-guided ablation treatments for PCLs and to present a blueprint for the future of these treatment methods.

Keywords: Antineoplastic agents; Endosonography; Ethanol; Pancreatic cyst; Radiofrequency ablation

Introduction

Pancreatic cystic lesions (PCLs) consist of a heterogeneous group of lesions, including intraductal papillary mucinous neoplasm (IPMN), mucinous cystic neoplasm (MCN), serous cystic neoplasm, and pancreatic solid pseudopapillary neoplasm.[1] Small PCLs discovered by chance show a natural course that generally does not substantially change during follow-up, but some lesions can undergo malignant transformation.[2,3] Therefore, surgery is recommended if there is a high risk of malignancy; otherwise, changes are observed through periodic follow-up.[4–6] However, surgical resection of the pancreas has been reported to involve a serious risk of complications, with a morbidity rate of 20% to 40% and a mortality rate of 1% to 2%.[7,8] The dichotomous decision-making of surgery or a wait-and-see strategy has caused quite a bit of concern, and endoscopic ultrasound (EUS)-guided treatments for PCLs have entered the limelight as a treatment option to address unmet needs in real-world settings.

In recent years, an increasingly conservative direction has been pursued for the management of incidentally found PCLs on the basis of several robust guidelines,[4–6] and EUS-guided treatment has shown promising results.[9,10] Previous studies reported that EUS-guided ablation was effective, with complete remission (CR) rates from 8.7% to 84.6%,[11–19] and the long-term effects of treatment have been well maintained.[16,17] Treatment with EUS-guided ablation rather than surgical resection or a wait-and-see strategy enabled patients to maintain their quality of life by obviating the need to worry about morbidity caused by unnecessary surgical resection, and it was possible to expect a certain level of CR.[20] In addition, in patients with CR, EUS-guided treatment might reduce resource-consuming, life-long surveillance with regular magnetic resonance imaging.

This article reviews the up-to-date results of studies on EUS-guided treatment for PCLs and discusses the proper indications and directions for future development of EUS-guided treatment based on recently published recommendations of an expert panel.

EUS-Guided Chemical Ablation for PCLs

EUS-guided ethanol ablation for PCLs

Ethanol has a low viscosity and can be easily injected through a small needle; it is commonly used as a treatment for other organ cysts or solid masses as a relatively inexpensive option that causes tissue necrosis and induces fibrosis, blood clots in small blood vessels, and granuloma tissue formation.[21] The protocol of EUS-guided ablation varies slightly across studies, but a common aspect is that nearly all the cystic fluid is removed after puncturing PCLs with an aspiration needle, and then ethanol (at a concentration of 80%–100%) is stored and removed after 3 to 5

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minutes. Usually, the volume of injected ethanol is equal to that of the aspirated cystic fluid. Table 1 shows the results of previous studies in patients who underwent EUS-guided ethanol ablation.

In the pilot study that first reported the results of this procedure in 2005, no significant difference in effect was found according to the concentration of ethanol used.[11] The authors also reported that five patients underwent surgical resection because of incomplete response to this treatment, and various degrees of cauterization of the epithelium were observed, including complete ablative cases. These reports suggest that complete epithelial ablation occurred after the procedure with ethanol, but the cystic form was still observed on imaging tests, leading to a misjudgment that CR had not been reached. However, there still were doubts about the actual effectiveness of using ethanol for ablation instead of simply washing and removing all fluids to reduce the size of PCLs. A well-designed, prospective, randomized double-blinded clinical trial was conducted to answer that question by comparing the effects of ethanol and normal saline.[18] That study found statistically significant differences between the two groups when comparing the initial assessment and the 3-month follow-up, with a 28.1% decrease in size in the EUS-guided ethanol ablation group and a 6.9% decrease in size in the normal saline group. In addition, when patients who first received saline were treated with ethanol, a significant decrease in size (48.2%) was observed, and there were no statistically significant differences from the group treated with ethanol twice in a row. Similarly, other small-scale studies have additionally reported the equivalent effect of ethanol ablation, but it seems difficult to guarantee the long-term effect due to the insufficient follow-up period or number of patients in those studies.[12,19]

Considering the slow growth of PCLs, long-term follow-up results must be analyzed in a larger number of patients than in previous studies in order to evaluate the definite clinical implications of this procedure. A retrospective study of 91 patients with long-term follow-up (median, 40 months) showed a 45% CR rate, confirming the long-term effect.[16] However, that study reported diagnoses made through cystic fluid analyses; in particular, only 21 cases were clearly suspected to be mucinous cysts, and among them, IPMN showed a very limited response with an 11% CR rate in response to ethanol ablation. A possible explanation for the poor effect on IPMN is that the mucus covers the epithelium, which is connected to the main pancreatic duct, making the ethanol more prone to be washed away than to be retained. In contrast, the CR rate of MCN was 50%, which was similar to that of serous cystic adenoma, suggesting that ablation therapy using ethanol is appropriate for MCN.

Meanwhile, data have also been released that raise doubts about the effectiveness of ethanol, especially in a study including 23 patients with IPMN or MCN who underwent EUS-guided ethanol ablation and were followed for a median of 40 months.[15] The authors were concerned about the low efficacy of ethanol ablation, with a CR rate of 9% and a decreased cystic size of 52.2%. Furthermore, they reported one patient who was diagnosed with pancreatic ductal adenocarcinoma 41 months after index EUS-guided ethanol ablation. According to this result, appropriate follow-up after ethanol ablation for PCLs seems necessary, and proper indications for this procedure are required.

EUS-guided ablation including chemotherapeutic agents for PCLs

After the effectiveness of ethanol ablation was reported, paclitaxel in sequential combination with ethanol (1 : 1) was used to increase the efficacy of EUS-guided ablation treatment, and a pilot study reported a CR rate of 78.6% after a median follow-up of 9 months.[22] Paclitaxel is a commonly used chemotherapeutic agent that alters microtubules; it has a hydrophobic nature with high viscosity, for which reason it is expected to be retained within PCLs, resulting in fewer adverse events due to the procedure. It was suggested that the sequential combination of these two chemicals was expected to have a synergistic effect, in which

Table 1 Previous Studies of EUS-Guided Ablation

Author (year)	Number	Ablative agent	Median follow-up (mo)	Mean size (mm)	CR (%)	CR (*n*)			Malignant transformation	Adverse event	
						MCN	IPMN	Others		Minor	Severe
EUS-guided ethanol ablation											
Gan et al[11] (2005)	23	E	6–12	19.4	34.8	14	3	6	0	0	0
DiMaio et al[12] (2011)	13	E	13.4	20.1	38.5	-	13	-	0	1	0
Caillol et al[19] (2012)	13	E	26	24	84.6	13		-	0	0	0
Park et al[16] (2016)	91	E	40	30	45.1	12	9	70	0	21	0
Gómez et al[15] (2016)	23	E	45.8	23	8.7	4	15	4	1*	1	1
EUS-guided ablation Including chemotherapeutic agents											
Oh et al[13] (2011)	47	E + P	21.7	31.8	61.7	9	-	38	0	5	0
DeWitt et al[14] (2014)‡	21	E + P	27	25	47.6	6	12	4	0	5	4
Choi et al[17] (2017)	164	E + P	69	32	72.2	71	11	82	0	15	1
Kim et al[23] (2017)	8	E	22.3	25.8	56	NA	NA	NA	0	5	4
	28	E + P									
Moyer et al[25] (2017)	18	E + G + P	12	25	61	4	19	2	0	4	1
	21	G + P	12	25	67				0	0	0

EUS, endoscopic ultrasound; CR, complete response; MCN, mucinous cystic neoplasm; IPMN, intraductal papillary mucinous neoplasm; E, ethanol; P, paclitaxel; G, gemcitabine; NA, not available.
*Pancreatic cancer arising from ablation branch-duct type IPMN (the patient refused surgery for remnant branch-duct type IPMN).
‡CR in 10 patients, 47.6.

ethanol is injected first to deform the epithelium of the cyst and paclitaxel then penetrates better through damaged epithelial cells to induce apoptosis. Table 1 shows the results of previous studies with patients who underwent EUS-guided ablation including chemotherapeutic agents for PCLs.

This combinatorial therapy showed a CR rate of 61.7% after a median follow-up of 21.7 months.[13] Other studies have reported similar efficacy of combinatorial treatment, with CR rates of 50% to 72%.[14,17,23] In the prospective cohort study with largest number of patients, the authors reported long-term follow-up results for 158 patients with a median follow-up of 72 months, and the rate of CR was 72%.[17] In that study, the volume of ethanol was equal to that of the cystic fluid that was aspirated; after lavage for 3–5 minutes, dosages of 1.5–24 mg in a diluted formulation of Taxol (Bristol-Myers Squibb Co., New York, NY, USA) or 12–30 mg in a non-diluted formulation (Genexol-PM; Samyang Biopharm, Seongnam, Korea) were injected into the cysts. The results of cystic fluid analysis showed promising results for the efficacy of EUS-guided ablation with ethanol and paclitaxel even for mucinous cysts, as CR was found in 76.1% of MCNs and 50% of IPMNs. In addition, the recurrence rate after CR was only 1.7%. A DNA mutation analysis showed the elimination of all *KRAS* mutations and loss of heterozygosity that presented in the pre-ablative cystic fluid analysis.[14] However, according to the cytological analysis in another study, no significant difference in the histopathological change of cellular atypia was observed between the CR and partial-response (PR) group, and the effect of this treatment on the molecular or cellular level remained inconclusive.[23] Although combinatorial therapy showed a better CR rate and it might have a mutation restoration effect, thereby inhibiting malignant transformation, it is almost unacceptable to use this chemotherapy agent other than for malignant tumors in real-world practice.

Regarding EUS-guided ablation including ethanol, some researchers suggested concerns that most adverse events were

Table 2 Adverse Events Reported in Previous Studies

Author (year)	Number	Ablative agent	Adverse event			
			Rate (%)	Details (*n*)	Mild to moderate	Severe
EUS-guided ethanol ablation						
Gan et al[11] (2005)	23	E	0		0	0
DiMaio et al[12] (2011)	13	E	8	Abdominal pain (1)	1	0
Caillol et al[19] (2012)	13	E	0		0	0
Park et al[16] (2016)	91	E	23.1	Abdominal pain (18) Acute pancreatitis (3)	21	0
Gómez et al[15] (2016)	23	E	8.7	Acute pancreatitis (1) Abdominal pain (1)	1	1
Choi et al[28] (2019)	214	E	33.2	Abdominal pain (70) Acute pancreatitis (21) Duodenal stricture (2) Bleeding (1) Cholangitis (1)	27	3
EUS-guided ablation Including chemotherapeutic agents						
Oh et al[13] (2011)	52	E + P	9	Fever (1) Acute pancreatitis (1) Abdominal pain (1) Pericystic spillage (1) Splenic vein obstruction (1)	5	0
DeWitt et al[14] (2014)	21	E + P	75	Abdominal pain (4) Acute pancreatitis (3) Peritonitis (1) Gastric wall cyst (1)	5	4
Choi et al[17] (2017)	164	E + P	9	Acute pancreatitis (6) Pseudocyst (2) Abscess (2) Portal vein thrombosis (1) Fever (1) Splenic vein obstruction (1) Pancreatic duct stricture (1) Pericystic spillage (1) Intracystic hemorrhage (1)	15	1
Kim et al[23] (2017)	8	E	25	Abdominal pain (4) Acute pancreatitis (4) Intracystic hemorrhage (1)	5	4
	28	E + P				
Moyer et al[25] (2017)	18	E + G + P	28	Abdominal pain (4) Acute pancreatitis (1)	4	1
	21	G + P	0		0	0

EUS, endoscopic ultrasound; E, ethanol; P, paclitaxel; G, gemcitabine.

induced by ethanol. A pilot study was conducted to evaluate the efficacy of alcohol-free ablation and it showed equivalent efficacy between ablation using chemotherapeutic agents with or without ethanol.[24] Consequently, the same group of authors reported the results of a randomized double-blinded clinical trial that compared the efficacy of gemcitabine and paclitaxel with or without ethanol for EUS-guided cystic ablation.[25] In that study, 80% ethanol or normal saline was used with an infusion of a chemotherapeutic mixture (3 mg/mL paclitaxel and 19 mg/mL gemcitabine, maximum of 8 mL) at an amount equal to the original amount aspirated to re-establish the original cyst size and volume. The CR rate was not significantly different between the two groups at 12 months after the procedure (61% in the alcohol-free group and 67% in the alcohol-containing group); a severe adverse event occurred in one patient who developed acute pancreatitis and mild adverse events occurred in 4 patients who experienced abdominal pain, in the alcohol-containing group only. The authors argued that ethanol is not necessary for inducing an ablative effect and suggested that ethanol instead causes adverse events in EUS-guided ablation treatment for PCLs. However, those findings should be interpreted conservatively insofar as that study compared the short-term treatment effects in relatively few patients with only a 12-month follow-up period after the procedure, and it seems that this study does not furnish enough evidence to conclude that ethanol is a problematic drug to a degree that would prevent it from being used in EUS-guided ablative therapy for PCLs.

EUS-guided lauromacrogol ablation for PCLs

Recently, lauromacrogol, which has been used as an sclerosant for esophageal variceal bleeding, showed good efficacy in EUS-guided ablation for PCLs.[26] A CR rate of 37.9% and a PR rate of 31% were observed at 9 months after EUS-guided ablation with lauromacrogol, as well as a CR rate of 51.4% and a PR rate of 25.7% at more than 1 year of follow-up, which included patients who underwent a second ablation.[27] Major adverse events occurred in 3.6% of patients, including two patients with acute pancreatitis and one patient with fever, and minor adverse events occurred in 35.7% of patients. All patients recovered without any special treatment.

Safety of EUS-guided ablation therapy for PCLs

The safety of EUS-guided ablation therapy is important because of its limited efficacy as an alternative treatment to surgical resection and the difficulty of predicting the long-term effects of this procedure. Furthermore, a thorough review of the adverse events of this procedure is necessary to establish its proper indications and to exclude cases where severe adverse events are expected to occur. Table 2 shows the adverse events that were reported as related to EUS-guided ablation therapy in previous studies.[11–17,19,23,25,28] In a total of 689 patients, the incidence rate of adverse events ranged from 0% to 75%, but only 14 (2.0%) patients experienced severe adverse events, of which acute pancreatitis was one of the most common. A recent retrospective study with 214 patients was conducted at a single tertiary center to identify predictive factors for adverse events.[28] According to this study, adverse events occurred in 33.2% of patients, and 1.4% of patients experienced severe adverse events. The authors suggested that branch duct-type IPMN, multilocular cysts, suspected ethanol leakage during the procedure, and sticky cystic fluid were predictors of post-procedural acute pancreatitis. In addition, PCLs of the uncinate process and PCLs with an exophytic portion were predictors of post-procedural abdominal pain.

EUS-guided ethanol ablation seems to be a safe procedure, but it causes quite cumbersome adverse events for patients. The two main mechanisms of adverse events during EUS-guided ablation are direct chemical damage to pancreatic or peri-pancreatic tissue by extravasated ethanol, and direct chemical injury caused by ethanol flow directly into the pancreatic duct. As these ethanol induced mechanisms have been recognized as a double-edged sword in this procedure, alcohol-free ablation with chemotherapeutic agents has been attempted and showed equivalent efficacy without adverse events in the CHARM (chemotherapy for ablation and resolution of mucinous pancreatic cysts) trial with durable efficacy after long-term follow-up (ClinicalTrials.gov ID : NCT01475331).[29] Large multicenter CHARM II trial will further solidify the evidence for this alcohol-free method of cystic ablation (https://clinicaltrials.gov/ct2/show/NCT03085004). Based on this result, recently published position statements have suggested that ethanol is not required when a chemotherapeutic agent is used for EUS-guided ablation for PCLs.[30] Nevertheless, ethanol is still seen as a good treatment because it has the advantage of being inexpensive and applicable to the procedure without the need for custom-made instruments, and the frequency of adverse events is not high. If ethanol is used when conducting EUS-guided ablation, patients need to receive a sufficient evaluation for risk factors for adverse events, and it is recommended to proceed with ablation with chemotherapeutic agents at institutions where those agents are available.

Review of the position statement on EUS-guided ablation of pancreatic cystic neoplasms from an international expert panel

Experts in EUS-guided procedures recently issued a consensus statement exploring the issues surrounding EUS-guided pancreatic cyst ablation by generating a list of clinical questions and providing answers based on the best scientific evidence available (Table 3).[30] One of the most notable aspects of this position statement is its presentation of the indications of this procedure. The authors recommended that pancreatic cyst ablation should be performed in patients who are not surgical candidates or refuse surgery with a reasonable life expectancy and suffer from either a unilocular or oligolocular mucinous cyst, or enlarging PCLs with a diameter of > 2 cm or PCLs with a diameter of > 3 cm. Furthermore, PCLs with six or fewer locules and measuring 2 to 6 cm in diameter are expected to show the best response to ablation therapy. The following relative contraindications were suggested: PCLs with enhancing mural nodules, cysts with no or low malignant potential, dilated main pancreatic duct > 5 mm, clear open communication with the main pancreatic duct, more than six locules comprising the cyst, thick walls or septations, main pancreatic ductal stricture with pancreatic tail atrophy, significant solid components, and a past medical history of acute pancreatitis. Therefore, the foremost step prior to ablation for PCLs is to conduct an accurate evaluation of the diagnosis of the PCLs and the risk-benefit balance of the procedure.

Other guidelines have similar but more conservative recommendations for EUS-guided ablation for PCLs, suggesting that the procedure might be considered in patients who refuse or are not suitable for surgery. Because EUS-guided ablation is still judged to have insufficient evidence for its effectiveness, guidelines say that it is considered as a salvage therapy rather than an equivalent treatment that can be suggested as an alternative to surgery.[5,31]

Table 3 Summary of the Position Statement on EUS–Guided Pancreatic Cyst Ablation

Question	Statement
Indications for the procedure	
When should we perform pancreatic cyst ablation?	Patients who are not surgical candidates or refuse surgery with a reasonable life expectancy and suffering from either: - Unilocular or oligolocular cyst with a presumed or confirmed diagnosis of a mucinous cyst - Enlarging PCLs with a diameter of > 2 cm or PCLs with diameter of > 3 cm
Which pancreatic cysts respond best to ablation?	- PCLs with ≤ 6 locules - PCLs 2 to 6 cm in diameter
What are the contraindications to the procedure?	Absolute contraindications - Pregnancy - Irreversible coagulopathy - Signs of pancreatic malignancy - Active pancreatitis or pancreatic necrosis - Short life expectancy Relative contraindications - PCLs with enhancing mural nodules - Cyst with no or low malignant potential - Dilated main pancreatic duct > 5 mm in size - Clear open communication with the main pancreatic duct - > 6 locules comprising the cyst - Thick walls or septations - Main pancreatic duct stricture with pancreatic tail atrophy - Significant solid components - Past medical history of acute pancreatitis
What level of certainty of diagnosis is required before the procedure?	The treating physician should be reasonably certain that the cyst is not a benign asymptomatic pancreatic cyst with no or low malignant potential
Procedural preparations	
What investigational modalities are required before EUS cyst ablation is performed?	CT (pancreatic protocol), MRI with MRCP (enhancement) ± EUS ± FNA
Are prophylactic antibiotics required?	Fluoroquinolones or beta-lactamase are recommended
How long do antibiotics need to be continued if given?	3 to 5 days
Procedural considerations	
Should the fluid be aspirated completely or not before ablation?	Leave a small rim of fluid around the tip of the needle within the cyst after the initial aspiration
What should be done if the cyst fluid is too viscous to be aspirated out during EUS-FNA?	- Use a 19-gauge needle under high suction pressure - Viscosity can then be lowered by injection of normal saline or alcohol that were aspirated out
What are the available agents for the procedure?	- Ethanol lavage only - Ethanol lavage followed by the infusion of paclitaxel - Alcohol-free saline lavage followed by an admixture of paclitaxel-gemcitabine - Lauromacrogol
Is ethanol required for effective pancreatic cyst ablation?	- Ethanol is the traditional agent used for ablation - Ethanol is not required when a chemotherapeutic agent is used
What is the difference between aspiration, lavage, and retention? Are there any differences between the practices?	- Aspiration: removal of cyst fluid by the aspiration needle - Lavage: repetitive aspiration and reinjection of the lavage agent for 3 to 5 minutes - Retention: retain the injected ethanol for 20 to 40 minutes while rotating the patient's position, and the injected ethanol is aspirated completely - Infusion: replacement of the cyst content with an ablation agent, which is then left in place
Outcomes of EUS-guided pancreatic cyst ablation	
How should response to therapy be defined after the procedure?	Completeness of response: defined by the amount of reduction in the volume of the cyst as measured by the radius of primary imaging modality at initial and 6-month follow-up - Complete response: 95% or greater reduction in volume - Partial response: 75% to 95% reduction in volume - Non-response: < 75% reduction in volume
What are the results of pancreatic cyst ablation?	- Ethanol alone: CR in 30% of treated PCLs - Ethanol + paclitaxel: CR in 60%–79% of treated PCLs
What are the effects of ablation on the cyst epithelium?	- Surgery is rarely performed after cyst ablation - Reported histologic epithelial ablation rates are generally 50%–100%
What are the cytological and genetic changes after the procedure?	- Limited data suggesting that genetic changes revert to normal after cyst ablation

Table 3 Continued

Question	Statement
Follow-up and monitoring	
How should these patients be followed up and monitored?	- Followed non-operatively - Cross-sectional imaging at 6-month intervals for the first year - Annually until no longer warranted due to patient age and medical conditions
Potential adverse events and management	
What are the potential adverse events of the procedure?	- The baseline risks of standard EUS-FNA procedures, which are considered safe and rarely associated with adverse events - Specific adverse events associated with the ablation itself include self-limiting abdominal pain, acute pancreatitis, and VTE
Are there systemic effects from the chemotherapeutic agent during and after the procedure?	- Paclitaxel in doses used for pancreatic cyst ablation has been shown without identifiable blood levels of the agent post-procedure

This table was revised from the position statement on EUS-guided ablation of pancreatic cystic neoplasms from an international expert panel.[30]
EUS, endoscopic ultrasound; PCL, pancreatic cystic lesion; CT, computed tomography; MRI, magnetic resonance imaging; MRCP, magnetic resonance cholangiopancreatography; FNA, fine-needle aspiration; VTE, venous thromboembolism.

Future directions of EUS-guided chemical ablation

The remaining key question for this procedure is, "does EUS-guided ablation therapy have the survival gain by prevention of pancreatic cancer in patients with PCLs?" This is a difficult question to answer conclusively based on various studies with different approaches. Instead, it seems possible that EUS-guided ablation therapy improves the quality of life in patients with PCLs by avoiding surgery. A retrospective comparative study compared several clinical outcomes in patients with EUS-guided ethanol ablation and patients under a wait-and-see strategy, and there were no differences in overall survival between the two groups, but patients treated with EUS-guided ethanol ablation less frequently underwent surgical resection, and a CR rate of 32.1% was reported when only using the endoscopic procedure.[20] It can be inferred that performing EUS-guided ablation could reduce unnecessary surgery and the consequent morbidity or mortality, but long-term, large-scale, prospective, randomized comparative studies are needed in the future to conclusively answer this question.

EUS-Guided Radiofrequency Ablation for PCLs

Radiofrequency ablation (RFA) damages cells by causing local thermal injuries through a high-frequency (460–500 kHz) alternating current, which results in apoptosis and necrosis of tissue, and consequently activates the immune system with an altered level of cytokines.[32,33] EUS-guided RFA for PCLs has recently been attempted based on the results of animal tests, and the efficacy was reported in a small study, with a CR rate of 25% and size reduction in 50% of cases without any major adverse events at 3 to 6 months after the procedure.[32,34] In a prospective multicenter study including 17 patients with PCLs, the significant response rate was 71%, including 11 CR cases, and all mural nodules disappeared with a complication rate of only 10%.[35] Despite these promising results, it seems too early to confirm the effectiveness of this procedure, and it is worth anticipating the results of a phase II multicenter trial of EUS-guided RFA of PCLs (RADIOCYST01) that is currently recruiting up to 97 patients to evaluate at 12 months post-procedure (https://clinicaltrials.gov/ct2/show/study/NCT02343692).

Conclusions

EUS-guided ablation of PCLs using ethanol or chemotherapeutic agents is used as a minimally invasive treatment method with proven safety that addresses unmet needs in the dichotomous treatment options of surgery or a wait-and-see strategy for PCLs. Better efficacy was achieved when using a combinatorial treatment of ethanol and chemotherapeutic agents, with fewer adverse events, although it remains reasonable to perform the procedure using the agents at a specific institution. A high level of evidence that clearly proves the effects of this modality in terms of prolonged survival, cancer prevention, or clinical benefits is needed in the future. In addition, EUS-guided RFA is a new promising treatment for PCLs. It is necessary to use these EUS-guided ablative treatments in accordance with the suggested proper indications and to promote further development by fine-tuning the indications in the future. Furthermore, it seems necessary to address unmet needs through minimally invasive treatments using EUS, as we further explore and develop various new technologies and materials that can be used for EUS-guided ablation with comparable efficacy and greater safety.

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Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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