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Review Article

Recent developments in endoscopic ultrasound-guided ablation treatment

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ABSTRACT

Endoscopic ultrasound (EUS)-guided fine-needle aspiration was introduced in the early 1990s. EUS has evolved from a diagnostic modality to a therapeutic tool for patients with various pancreatic neoplasms. Recent advances in EUS-guided interventions include drainage and ablation. EUS-guided treatment provides a minimally invasive option for patients with pancreatic neoplasms instead of surgery or the percutaneous approach. This review aimed to provide an overview of the current EUS-guided ablation treatments, such as ethanol ablation and radiofrequency ablation, for treating various pancreatic tumors.

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Keywords: Ablation; Endoscopic ultrasound; Pancreatic neoplasms

Introduction

Pancreatic neoplasms have a wide spectrum of biological behaviors from benign to malignant. Pancreatic cancer has a poor prognosis, with a 5-year overall survival rate of < 5% and a median survival of < 6 months.¹ Surgical resection can provide the only chance of a cure, with 5-year overall survival rates of 18%–24%; however, only one-fifth of patients have a resectable disease status.² The outcomes of chemotherapy or radiation therapy are unsatisfactory, with most patients with pancreatic cancer experiencing only a small benefit. Benign pancreatic neoplasms, such as pancreatic cystic lesions (PCLs) and neuroendocrine tumors (NETs), are increasingly encountered in clinical practice owing to the widespread use of cross-sectional imaging.³ As surgical resection is associated with substantial morbidity (20%–40%) and a mortality rate of 2%, the management of these tumors is challenging.^{4,5} Therefore, new advances in the treatment of pancreatic neoplasms are required.

Over the past two decades, endoscopic ultrasound (EUS)-guided intervention has evolved from a diagnostic method to a therapeutic modality. As EUS-guided treatment is effective and safe,

it can be an alternative for patients with pancreatic neoplasms, especially for those who are poor surgical candidates. This review aimed to provide an overview of the latest published evidence and innovations in EUS-guided ablation treatment of pancreatic neoplasms.

EUS-Guided Ethanol Ablation

EUS has enabled injecting an ablative agent directly into the pancreas. Ethanol is a commonly used an ablating agent because it is cheap and widely available. With its low viscosity, it can be easily injected and reaspirated using a 22-gauge fine-needle aspiration (FNA) needle. Direct injection of ethanol induces coagulation necrosis through cellular dehydration, protein denaturation, and vascular occlusion. The typical indications for EUS-guided ethanol ablation are pancreatic NETs and pancreatic cystic neoplasms. EUS-guided celiac plexus neurolysis (CPN) with ethanol will not be discussed here.

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Pancreatic NETs

Pancreatic NETs are rare, accounting < 2% of all pancreatic tumors.⁶ These tumors are being increasingly diagnosed; however, the management of tumors measuring < 2 cm and low-grade, incidentally discovered tumors is debated.^{7,8} The treatment for pancreatic NETs should be tailored according to the patient's age, performance, and symptoms; location of the disease; and experience of the center as surgical resection of the pancreas could lead to serious adverse events. Considering that these tumors are diagnosed before the age of 60 years in many patients, the risk of surgical adverse events should be minimized. Long surveillance can also cause considerable anxiety, leading to deterioration of quality of life. Therefore, EUS-guided ethanol ablation can be a good option.

Technical aspects of EUS-guided ethanol ablation for NETs

Careful examination with diagnostic contrast-enhanced harmonic EUS (CE-EUS) helps in evaluating the extent of the mass. After calculating the tumor volume with computed tomography (CT) and EUS, the maximal targeting ethanol volume is decided. If the tumor is located close to a vessel or the main pancreatic duct, the volume could be reduced to one-third of the calculated volume based on the endosonographer's discretion. Thereafter, the tumor is punctured with a 22-gauge FNA needle without a side hole. For ablation, 95%–99% ethanol is most commonly used. During the injection, the endosonographer can observe a hyperechoic cloud under EUS in real time. The injection is terminated when the hyperechoic cloud reaches the tumor border. Additional puncture can be performed if there are inadequately ablated areas. Mixing lipiodol can help evaluate complete response on CT after the procedure. CE-EUS can also help evaluate residual viable tumors.

Literature review

Although most studies had a small sample size, they demonstrated safety and efficacy (Table 1).^{9–16} Park et al¹⁵ conducted the largest case series with 11 patients with 14 tumors (10 nonfunctional tumors and 4 insulinomas). The tumor size ranged from 8 to 19 mm. After a single treatment session, 7 patients (7/13,

53.8%) showed complete response and 2 patients with insulinomas became asymptomatic. Levy et al¹³ and Qin et al¹⁴ treated 5 and 4 insulinomas with EUS-guided ethanol injection, respectively, and reported symptomatic improvement in all cases. All other cases of insulinoma showed improved symptoms and/or no recurrence.^{9–12,16} EUS-guided ethanol therapy seems to be highly valuable for functional NETs, such as insulinoma, especially for small tumors measuring < 2 cm. The greatest concerns are the risk of progression after incomplete ablation during follow-up and the risk of pancreatitis. As it is impossible to judge complete response through pathologic evaluation, there is always a risk of incomplete ablation even with a radiologic complete response. Furthermore, injected ethanol does not evenly distribute within the tumor capsule, and the endosonographer can only depend on hyperechoic blush during the procedure. Therefore, researchers believe that the ideal indication for ethanol injection would be a tumor with a capsule measuring ≤ 15 mm. Most studies have only reported mild pancreatitis as an adverse event. In a patient with a functional NET, ablation caused necrotizing pancreatitis, requiring laparoscopic necrosectomy.¹⁰ Direct injection of ethanol into the pancreatic parenchyma has a risk of causing severe pancreatitis. This may be related to a direct cytotoxic effect on the ductal epithelium, activation of zymogen, and/or pancreatic ductal hypertension. In the case series by Park et al,¹⁵ pancreatitis occurred after injection of > 2 mL ethanol in a single session. The endosonographer should keep the needle inside the tumor, should not inject too much ethanol, and should minimize ethanol leakage into the surrounding normal area.

Pancreatic cystic neoplasms

Many types of pancreatic cystic tumors are diagnosed yearly, and their types and clinical courses vary. Some have the potential for malignant transformation. Intraductal papillary mucinous neoplasms (IPMNs) and mucinous cystic neoplasms (MCNs) have a risk of malignant transformation, although the exact risk is unclear.¹⁷ Most cysts are small (< 1 cm), and only 0.8% cysts measure > 2 cm.¹⁸ Resected IPMNs can show malignancy in up to 25% cases; however, the risk of malignant transformation in unresected IPMNs is markedly low.¹⁹ Clinicians attempt to remove

Table 1 Summary of Representative Published Data on EUS-Guided Ethanol Ablation for Neuroendocrine Tumors

Study	No. of patients	Indication	Size (mm)*	Needle (gauge)	Ethanol (%)	Session	Result	Adverse events
Jürgensen et al ⁹ (2006)	1	Insulinoma	13	22	95	1	No recurrence at 34 mo	Mild pancreatitis
Muscattello et al ¹⁰ (2008)	1	2 nonfunctional NET	7, 11	NA	40	2	No recurrence at 18 mo	Necrotizing pancreatitis
Deprez et al ¹¹ (2008)	1	Insulinoma	NA	NA	98	1	No recurrence at 24 mo	Mild pancreatitis, duodenal wall hematoma and ulceration
Vleggaar et al ¹² (2011)	1	Insulinoma	9	25	96	1	Decreased size, asymptomatic at 6 mo	None
Levy et al ¹³ (2012)	5	Insulinoma	8, 16, 18, 20, 21	22, 25	95, 98, 99	2 (n = 4), 3 (n = 1)	3 asymptomatic, 2 improved symptoms	None
Qin et al ¹⁴ (2014)	4	Insulinoma	5.4, 10, 10, 11.8	25	95	1	4 asymptomatic	None
Park et al ¹⁵ (2015)	11	10 nonfunctional NET, 4 insulinoma	12.3 (8–19)	22	99	1 (n = 6), 2 (n = 3), 3 (n = 2)	9 complete response, 4 partial response, 1 excluded	Mild pancreatitis, pancreatic duct stricture
de Sousa Lages et al ¹⁶ (2017)	1	Insulinoma	12	NA	95	1	1 asymptomatic	None

EUS, endoscopic ultrasound; NET, neuroendocrine tumor; NA, not available.

*Number or mean (range).

risky cystic neoplasms before malignant transformation occurs by evaluating the lesion with respect to size, morphology, main pancreatic duct diameter, symptoms, etc.²⁰ However, it is true that there are not many things to do rather than doing regular image surveillance. Finally, EUS has brought therapeutic progress to this field by enabling ablation with ethanol and chemotherapy infusion.

Technical aspects of EUS-guided ethanol ablation for cystic neoplasms

Careful EUS examination before ablation is necessary to determine the anatomical and morphologic features of lesions. Especially, the suitable location for the procedure (stable scope position) and the cyst characteristics (size, septation, wall thickness, mural nodule, communication with the pancreatic duct) should be evaluated.²¹ CE-EUS may help avoid the overdiagnosis of branch duct IPMNs with mural nodules.²² Further, EUS-guided FNA is performed for cyst evacuation. We prefer a 22-gauge needle in most cases. A 19-gauge needle can be used if the mucin takes too much time to aspirate; however, it has a risk of leakage. A 25-gauge needle is not appropriate for aspiration and injection. The amount of aspirated fluid should be recorded, and the fluid should be sent for further examination (e.g., amylase and carcinoembryonic antigen examination). Ethanol or other ablative agent is injected into the cyst in a volume equal to that of the originally aspirated fluid. Clinicians should keep in mind that an approximately 0.8 mL of fluid is held inside the 22-gauge FNA needle itself (19-gauge needle: 1.1 mL), and this should also be considered when determining the injection volume.²³ Lavage of the cyst, which entails repeated injection and aspiration with an ablative agent into and from the cystic cavity, is performed 3–5 times depending on the situation. Instead of lavage, retention (a single injection and removal after 3–5 minutes) can be adopted when the cyst is too large for lavage. At the end of the session, the ablative agent should be completely evacuated.²¹

Literature review

The main purpose of EUS-guided pancreatic cyst ablation is preventing death from the malignant progression of pancreatic cysts. The mechanism of EUS-guided ablation is believed to be epithelial denudation with fibrosis and atrophy of the epithelium induced by contact with an ablative agent.^{24–26} However, there is no consensus regarding the risk of malignant transformation, and no randomized trial has compared intervention (ablation or surgery) and watchful waiting. Most published studies were not large enough to show a survival benefit (Table 2).^{3,25–33} A recent position statement on EUS-guided ablation of pancreatic cystic neoplasms was published to provide answers to the clinical questions.³⁴ It recommended EUS-guided ablation for patients who are unfit for surgery or who refuse surgery, but have a reasonable life expectancy. The cyst should be unilocular or oligolocular and should have a premalignant potential. The number of locules could be up to 6. It is reasonable to ablate an enlarging cyst measuring > 2 or 3 cm.³⁴ Oh et al²⁶ reported that lesions with a diameter of < 3.5 cm are more likely to show complete resolution. In this perspective, MCNs would be the most ideal candidate for ablation. However, in a recent study by Moyer et al,²⁷ no relationship between variables (initial diameter < 2.5 cm, locularity, carcinoembryonic antigen level, presumed diagnosis) was found in terms of complete resolution. Five studies used ethanol only^{25,28–31}; four studies used ethanol and paclitaxel^{3,26,32,33}; and one study used ethanol, paclitaxel, and gemcitabine injection.²⁷ The outcomes of the studies showed a complete resolution rate of 33%–79%. Hence, the effect

seems to be rather durable. DeWitt et al³³ reported a durable effect over a 27-month median follow-up in patients in whom complete ablation was achieved. In a study by Choi et al,³⁵ 98.3% patients in whom complete ablation was achieved showed a durable effect over a 6-year follow-up.

Abdominal pain is the most common adverse event. However, acute pancreatitis, peritonitis, and venous thrombosis have also been reported. Overall, adverse events occur in 2%–10% cases, and most are managed with conservative care.²³ Ethanol seems to be the culprit of adverse events. Therefore, Moyer et al²⁷ conducted a prospective, randomized, controlled trial to evaluate an alcohol-free pancreatic cyst ablation protocol for mucinous-type pancreatic cysts. A total 39 patients were managed with EUS-guided pancreatic cyst lavage with either 80% ethanol (control) or normal saline (alcohol-free group). Finally, an admixture of paclitaxel and gemcitabine was infused into the cyst in both groups. The complete ablation rate was 67% in the alcohol-free group and 61% in the saline group 1 year after the procedure. The rates of serious adverse events in the control and alcohol-free groups were 6% (1/18) and 0% (0/21), respectively, implying reduced procedure-related adverse events. Another study used lauromacrogol, a sclerosant with a mild anesthetic effect, as the sole ablative agent and reported a complete resolution rate of 37.9%.³⁶

The limitation of cyst ablation, similar to solid tumor ablation, is the risk of incomplete ablation. Even if the cyst shows complete resolution, sustained surveillance is needed as metachronous malignancy in the remaining pancreas is not uncommon.^{37,38}

EUS-Guided Radiofrequency Ablation

Radiofrequency ablation (RFA) uses high-frequency alternating current, which generates energy as heat, resulting in coagulative necrosis and cellular apoptosis in the target tissue.³⁹ RFA can be applied using monopolar or bipolar probes. The monopolar probe is used in a closed-loop system that includes an energy generator, an electrode, a dispersive electrode (ground pad), and the patient. High-current density energy heats the target tissue through the electrode. The ground pad closes the electric circuit and disperses the energy over a large area to reduce possible injury to the skin.³⁹ In a bipolar RFA system, a ground pad is not necessary because the current oscillates two interstitial electrodes. The bipolar probe confines the current flow to the area between the electrodes, reducing the heat-sink effect (perfusion-mediated cooling).⁴⁰ Therefore, heat injury of the lesion occurs more quickly with less damage to the surrounding normal tissue.^{39,41}

RFA has been used percutaneously and intraoperatively to treat various tumors, including hepatocellular carcinoma, renal cell carcinoma, and lung cancer.² However, percutaneous RFA could not be applied in lesions with interposition of organs and/or vessels. EUS-guided RFA (EUS-RFA) offers real-time imaging of the target lesion, in which RFA may enable safe tissue ablation. Recently, several reports have demonstrated that EUS-RFA is technically feasible, safe, and relatively effective for the treatment of pancreatic tumors such as unresectable pancreatic cancer and benign solid pancreatic tumors.^{2,42,43} EUS-RFA can also potentially be used for ablating PCLs.^{42,44} The application of EUS has an advantage in terms of minimal invasiveness and tolerability.

Technical aspects of EUS-RFA

Currently, several types of probes, including the 19-gauge EUS-FNA needle electrode (Radionics, Burlington, MA, USA), HabibTM EUS-RFA catheter (EMcision, London, UK), and EUSRA

Table 2 Summary of Representative Published Data on EUS-Guided Ethanol Ablation for Pancreatic Cystic Neoplasms

Study	No. of patients	Indication (%) [*]	Size (mm) [†]	Needle (gauge)	Ablative agent	Complete resolution rate	Session	Adverse events [‡]
Studies that used ethanol for ablation								
Gan et al ²⁸ (2005)	25	MCN (52), IPMN (16), SCN (12), pseudocyst (12), indeterminate cyst (8)	19.4	22	5%–80% ethanol	35%	1 (n = 25)	None
DeWitt et al ²⁵ (2009)	25	MCN (40), IPMN (40), SCN (12), PC (8)	10–41	22	80% ethanol	40.9%	1 (n = 6), 2 (n = 19)	Pancreatitis (n = 1)
DiMaio et al ²⁹ (2011)	13	IPMN (100)	10–32	22	80% ethanol	38%	2 (n = 13)	None
Caillol et al ³¹ (2012)	13	MCN (100)	10–50	NA	99% ethanol	85%	1 (n = 12), 2 (n = 1)	None
Gómez et al ³⁰ (2016)	23	IPMN (66), MCN (17), nonmucinous (17)	14.9–49.3	19, 22	0%–79% ethanol	9%	1 (n = 18), 2–3 (n = 5)	Pancreatitis (n = 1)
Studies that used ethanol and paclitaxel for ablation								
Oh et al ³ (2008)	14	MCN (14), SCN (21), lymphangioma (21), indeterminate cyst (44)	17–52	22	99% ethanol + paclitaxel (3 mg/mL)	79%	1 (n = 14)	Pancreatitis (n = 1)
Oh et al ³² (2009)	10	MCN (30), SNC (40), indeterminate cyst (30)	20–68	22	99% ethanol + paclitaxel (3 mg/mL)	60%	1 (n = 9), 2 (n = 1)	Pancreatitis (n = 1)
Oh et al ²⁶ (2011)	47	MCN (19), SCN/PC (32), indeterminate (49)	17–68	22	99% ethanol + paclitaxel (3 mg/mL)	62%	1 (n = 47)	Pancreatitis (n = 1), splenic vein obliteration (n = 1), pericystic spillage (n = 1)
DeWitt et al ³³ (2014)	22	IPMN (55), MCN (27), SCN (18)	15–43	22	100% ethanol + paclitaxel (2 mg/mL)	50%	1 (n = 13), 2 (n = 9)	Pancreatitis (n = 3), chemical peritonitis (n = 1), gastric wall cyst (n = 1)
Studies that used ethanol, paclitaxel, and gemcitabine for ablation								
Moyer et al ²⁷ (2017)	39	MCN (23), IPMN (69), indeterminate (8)	16–42	19, 22	3 mg/mL paclitaxel + 19 mg/mL gemcitabine with/without 80% ethanol	64%		Pancreatitis (n = 1)

EUS, endoscopic ultrasound; MCN, mucinous cystadenoma; IPMN, intraductal papillary neoplasm; SCN, serous cystadenoma; PC, pseudocyst; NA, not available.

^{*}Presumed diagnosis according to various modalities.

[†]Mean or range.

[‡]Abdominal pain was not considered an adverse event.

RF electrode (STARmed, Goyang, Korea), are available for EUS-RFA. Among these probes, EUSRA has an internal cooling system, which helps prevent charring of the electrode surface, thus enabling efficient transmission of heat.

Before EUS-RFA, administration of prophylactic antibiotics is usually required. After identifying the target lesion, the needle electrode is inserted into the target lesion under EUS guidance. The echogenic needle tip is positioned at the far end of the target lesion. RFA usually starts at the right distal part of the target lesion on the EUS image while the needle electrode is withdrawing, the needle electrode is subsequently reinserted, and ablation is repeated at the left side of the previous ablation site on the EUS view. After inserting the needle electrode, the radiofrequency generator is activated to deliver ablation power. Energy delivery is controlled automatically (owing to a change in tissue impedance) or manually, depending on the system. Energy is delivered after the location of the tip of the needle electrode has been confirmed to be within the margin of the lesion using EUS. The RFA is repeated until the hyperechoic zone around the electrode is sufficiently covering the entire tumor. For larger lesions, the fanning technique can be applied to further ablate different areas within the same lesion.

The potential adverse events of EUS-RFA are thermal injury (including burns of the gastric wall), bowel injury, and peritonitis. Procedural adverse events are closely related to the duration of RFA.² To prevent thermal injury to adjacent organs, some technical precautions, such as maintenance of a 5-mm minimum safety margin from surrounding vessels and use of a step-up approach in the case of larger lesions (> 2 cm in diameter), are required.⁴³

For treatment response evaluation, CE-EUS has several advantages over CT, including lack of radiation and real-time visualization and detection of residual viable tumors. A recommended follow-up protocol after ablation is to perform CE-EUS within a week to detect residual tumors. Immediately after ablation, hyperemia develops around the ablation zone owing to tissue damage and the resultant inflammatory response. This inflammatory reaction often demonstrates a uniform rim of enhancement, which, unlike residual viable tumors, persists throughout the different enhancement phases. Therefore, postprocedure CE-EUS is recommended after at least 5 to 7 days.

Literature review

EUS-RFA was first described in an animal model by Goldberg

et al⁴⁵ in 1999; they used this procedure to complete coagulation necrosis in a porcine pancreas. In 2009, Varadarajulu et al⁴⁶ reported successful coagulation necrosis of the targeted areas using EUS-RFA of the liver in a porcine model.

In 2015, Pai et al⁴⁴ reported the first human pilot study evaluating the feasibility and safety of EUS-RFA in patients with pancreatic neoplasms (PCL, $n = 6$; NET, $n = 2$). In this prospective study, a monopolar radiofrequency catheter (HabibTM) was used for ablation. EUS-RFA was successful in all patients. Among patients with pancreatic cystic neoplasms, complete response was achieved in 2 patients and a 48.4% volume reduction was achieved in 3 patients.⁴⁴ The remaining 2 NET cases showed a change in vascularity with a central necrotic area. No major adverse events occurred within 48 h of the procedure. In a recent study by Lakhtakia et al,⁴⁷ 3 patients with a symptomatic pancreatic insulinoma underwent EUS-RFA using an internally cooled prototype needle electrode (EUSRA; STARmed). All patients experienced rapid symptom relief with biochemical improvement and remained symptom free at the 11- to 12-month follow-up. Procedure-related adverse events were not observed in any patient. A summary of the studies is presented in Table 3.^{2,39,42–44,48}

In a recent preliminary study, 6 patients with unresectable pancreatic cancer underwent EUS-RFA.² The tumors were located in the pancreatic head ($n = 4$) and body ($n = 2$). EUS-RFA was technically feasible in all patients. Two patients experienced postprocedural mild abdominal pain; however, there were no serious adverse events. In a study by Scopelliti et al,⁴⁸ 10 patients with nonmetastatic unresectable pancreatic cancer underwent EUS-RFA. RFA was successful in all cases, and no major adverse events occurred. A delineated hypodense ablated area within the

tumor was identified on 30-day CT in all patients. Although the role of EUS-RFA in patients with pancreatic cancer is being investigated, RFA can be used as an adjuvant treatment combined with systemic chemotherapy. For the treatment of advanced pancreatic cancer, systemic control with chemotherapy is mandatory in addition to local control of the disease. As blood flow increases around the RFA site after ablation, it might enhance the effect of systemic chemotherapy.²

EUS-RFA has been proposed as a treatment option for benign pancreatic lesions such as PCLs and NETs. In a study by Choi et al,⁴³ 10 patients with benign solid pancreatic tumors (nonfunctional NET, $n = 7$; solid pseudopapillary neoplasm, $n = 2$; insulinoma, $n = 1$) underwent 16 EUS-RFA sessions. RFA was successful in all patients, and radiologic complete response was achieved in 7 patients during a median follow-up of 13 months. With respect to adverse events, 1 patient developed abdominal pain and 1 patient developed mild pancreatitis, both the adverse events resolved with conservative treatment. In a more recent study by Barthet et al,⁴² 29 patients with either NET or PCL (NET, $n = 12$; PCL, $n = 17$) were treated with EUS-RFA. At 1-year follow-up, 12 patients with 14 NETs showed complete disappearance or necrosis of the lesion (86%). In the remaining 17 patients with PCLs (branch duct IPMN, $n = 16$; MCN, $n = 1$), 47% and 65% of the lesions had resolved at the 6- and 12-month follow-up, respectively. Among these patients, 10% experienced procedure-related adverse events, including acute pancreatitis and jejunal perforation. Although several reports have demonstrated that EUS-RFA is a feasible and safe treatment option for benign pancreatic tumors, the selection of patients eligible for EUS-RFA is controversial. The indication of EUS-RFA should be balanced with the patients' comorbidity,

Table 3 Summary of Representative Published Data on EUS-RFA for Pancreatic Neoplasms

Study	No. of patients	Indication (n)	RF device	Mean tumor size (range)	Application power and time	Mean RF sessions (range)	Technical success (%)	Clinical outcome (n)	Adverse events (n)
Pai et al ⁴⁴ (2015)	6	Mucinous cyst (4), IPMN (1), microcystic adenoma (1), neuroendocrine tumor (2)	Habib EUS-RFA catheter	PCL: 36.5 (24–70), NET: 27.5 (15–40)	5–25 W, 90–120 sec	1.3 (1–2)	100	2 cyst resolution, 4 cyst reduction, 50% reduction in 2 NETs with vascular changes	Mild abdominal pain (2)
Song et al ² (2016)	6	Locally advanced pancreatic cancer (4), metastatic pancreatic cancer (2)	EUSRA	38 (30–90)	20–50 W, 10 sec	1.3 (1–2)	100	Necrosis at the ablation site	Mild abdominal pain (2)
Lakhtakia and Seo ³⁹ (2017)	3	Insulinoma	EUSRA	19 (14–22)	50 W, 10–15 sec	1	100	Complete resolution of hypoglycemia	None
Scopelliti et al ⁴⁸ (2018)	10	Locally advanced pancreatic cancer	EUSRA	49.2 (35–75)	20 or 30 W, 100–560 sec	1.4 (1–2)	100	Necrosis at the ablation site	Mild abdominal pain (2), ascites (2), peripancreatic effusion (2)
Choi et al ⁴³ (2018)	10	NET (10), solid pseudopapillary neoplasm (2), insulinoma (1)	EUSRA	20 (8–28)	50 W	1.6 (1–3)	100	Radiologic complete response (7)	Mild abdominal pain (1), acute pancreatitis (1)
Barthet et al ⁴² (2019)	29	IPMN (16), MCN (1), NET (14 lesions in 12)	EUSRA	PCL: 28 (9–60), NET: 13.1 (10–20)	50 W	NA	100	NET: radiologic complete response (12), PCL: complete response (11), > 50% reduction (1)	Acute pancreatitis (1), jejunal perforation (1), main pancreatic duct obstruction (1)

EUS, endoscopic ultrasound; RFA, radiofrequency ablation; RF, radiofrequency; PCL, pancreatic cystic lesion; IPMN, intraductal papillary neoplasm; NET, neuroendocrine tumor; NA, not available.

postoperative morbidity, mortality, tumor location, life expectancy, and risk of long-term outcomes (exocrine and endocrine insufficiency).

Recently, EUS-RFA has been attempted for pain alleviation in patients with pancreatic cancer. In a study by Zin et al,⁴⁹ EUS-RFA of the celiac ganglia provided better pain relief in a patient with pancreatic cancer in whom initial treatment with EUS-guided CPN had failed. In a recent randomized controlled trial, EUS-CPN and EUS-RFA were compared for palliation of pain in patients with pancreatic cancer.⁵⁰ A total of 26 patients underwent EUS-RFA ($n = 12$) and EUS-CPN ($n = 14$). At the 4-week follow-up, the pain scores were significantly lower in the RFA group than in the CPN group using the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire pancreatic cancer module (49.0 vs 57.0; $P < 0.001$) and the EORTC Quality of Life Questionnaire core questionnaire (51.9 vs 64.4; $P = 0.032$). Compared with pharmacologic treatment of the celiac plexus using alcohol, which has an unpredictable effect owing to varying diffusion of the injected agent within the anatomic compartment containing the nerve fibers, EUS-RFA has a predictable treatment effect because of the size of necrosis being induced. Furthermore, its effect is more immediate than that of EUS-CPN. This preliminary study proposed that EUS-RFA may be superior to EUS-CPN for the palliation of pain and improvement of quality of life in patients with pancreatic cancer.

Most adverse events after EUS-RFA are associated with thermal injury to the pancreatic parenchyma and surrounding structures, such as blood vessels, bile ducts, the stomach, and the duodenum. Although all recent preliminary experience demonstrates that EUS-RFA is relatively safe, there are concerns regarding postprocedural adverse events. The real-time visualization of the needle probe during EUS helps avoid puncturing of vital structures and imaging of the thermal effect localized within the tumor helps reduce major adverse events, unlike percutaneous and intraoperative RFA methods. Moreover, the lack of an internal cooling mechanism in percutaneous or intraoperative probes could result in unintended thermal injury to surrounding structures. EUS-RFA in pancreatic lesions has milder adverse events, even in the absence of internal cooling probes.

Although the available data are limited, published reports have demonstrated that EUS-RFA is a technically feasible, safe, and relatively effective modality for the treatment of different types of pancreatic tumors.

Conclusions

EUS-guided ablation is a promising, minimally invasive treatment that may provide targeted, individualized therapy for patients who are not candidates for surgical resection. Given the promising results of preliminary studies, EUS-guided ablation treatment can potentially change the clinical practice in the management of pancreatic neoplasms. Large-scale prospective randomized controlled trials are needed to verify the role of EUS-guided ablation in patients with pancreatic neoplasms.

Conflicts of Interest

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

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