Endoscopic ultrasound guided radiofrequency ablation, for pancreatic cystic neoplasms and neuroendocrine tumors

Madhava Pai, Nagy Habib, Hakan Senturk, Sundeep Lakhtakia, Nageshwar Reddy, Vito R Cicinnati, Iyad Kaba, Susanne Beckebaum, Panagiotis Drymousis, Michel Kahaleh, William Brugge

AIM: To outline the feasibility, safety, adverse events and early results of endoscopic ultrasound (EUS)-radiofrequency ablation (RFA) in pancreatic neoplasms using a novel probe.

METHODS: This is a multi-center, pilot safety feasibility study. The intervention described was radiofrequency ablation (RF) which was applied with an innovative monopolar RF probe (1.2 mm Habib EUS-RFA catheter) placed through a 19 or 22 gauge fine needle aspiration (FNA) needle once FNA was performed in patients with a tumor in the head of the pancreas. The Habib™ EUS-RFA is a 1 Fr wire (0.33 mm, 0.013") with a working length of 190 cm, which can be inserted through the biopsy channel of an echoendoscope. RF power was applied to the electrode at the end of the wire to coagulate tissue in the liver and pancreas.

RESULTS: Eight patients [median age of 65 (range 27-82) years; 7 female and 1 male] were recruited in a prospective multicenter trial. Six had a pancreatic cystic...
neoplasm (four a mucinous cyst, one had intraductal papillary mucinous neoplasm and one a microcystic adenoma) and two had a neuroendocrine tumors (NET) in the head of pancreas. The mean size of the cystic neoplasm and NET were 36.5 mm (SD ± 17.9 mm) and 27.5 mm (SD ± 17.7 mm) respectively. The EUS-RFA was successfully completed in all cases. Among the 6 patients with a cystic neoplasm, post procedure imaging in 3-6 mo showed complete resolution of the cysts in 2 cases, whilst in three more there was a 48.4% reduction [mean pre RF 38.8 mm (SD ± 21.7 mm) vs mean post RF 20 mm (SD ± 17.1 mm)] in size. In regards to the NET patients, there was a change in vascularity and central necrosis after EUS-RFA. No major complications were observed within 48 h of the procedure. Two patients had mild abdominal pain that resolved within 3 d.

CONCLUSION: EUS-RFA of pancreatic neoplasms with a novel monopolar RF probe was well tolerated in all cases. Our preliminary data suggest that the procedure is straightforward and safe. The response range from complete resolution to a 50% reduction in size.

Key words: Endoscopic ultrasound; Radiofrequency ablation; Pancreas; Cystic neoplasms; Neuroendocrine tumors

© The Author(s) 2015. Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: This manuscript presents a pilot, safety feasibility study with the results of the first in humans endoscopic ultrasound (EUS) guided radiofrequency ablation (RFA) for cystic neoplasms and neuroendocrine tumors of the pancreas with a novel EUS-RFA catheter. EUS-RFA is feasible and well tolerated. EUS-RFA with this novel catheter provides endoscopic treatment option other than surgical resection for pancreatic lesions.

Pai M, Habib N, Senturk H, Lakhtakia S, Reddy N, Cincinatti VR, Kaba I, Beckebaum S, Drymousis P, Kahaleh M, Brugge W. Endoscopic ultrasound guided radiofrequency ablation, for pancreatic cystic neoplasms and neuroendocrine tumors. World J Gastrointest Surg 2015; 7(4): 52-59. Available from: URL: http://www.wjgnet.com/1948-9366/vol/v7/i4/52.htm DOI: http://dx.doi.org/10.4240/wjgs.v7.i4.52

INTRODUCTION

Incidental pancreatic solid or cystic lesions are diagnosed with increased frequency due to the widespread use of abdominal cross-sectional imaging to investigate unrelated symptoms. In a large single-centre study, pancreatic cysts were diagnosed in 1.2% of 24000 individuals subjected to abdominal cross-sectional imaging[1]. As a result, the majority of these lesions are diagnosed at an earlier stage, before they become invasive and present with jaundice, pancreatitis or abdominal pain[2]. Lesions such as neuroendocrine tumors (NET), mucinous cystadenomas and intraductal papillary mucinous neoplasms have the potential of malignant transformation. This risk is lower with NET, but significantly higher with mucinous lesions[3].

The standard treatment of solid or cystic pancreatic lesions with malignant potential has been surgical resection, with lesions in the pancreatic head requiring a Whipple resection whereas pancreatic tail lesions are treated with distal pancreatotomy. Both types of resection carry significant morbidity and mortality, resulting in unacceptably high risk/benefit ratios for many elderly patients with co-morbidities[4-6]. Currently, patients deemed unfit for major pancreatic surgery are offered cross-sectional imaging surveillance at regular intervals according to the International Association of Pancreatology Guidelines[7-10]; these guidelines recommend annual imaging for lesions < 10 mm, 6-monthly imaging for cysts 10-20 mm and 3-monthly imaging for lesions larger than 20 mm. However, controversy exists regarding the optimal follow up of patients with primary pancreatic cancers, underlying the need for minimally invasive ablative techniques as an alternative to surgical resection.

Radiofrequency ablation (RFA) has been used percutaneously and intraoperatively to treat primary and secondary liver cancers by achieving localized tumor necrosis[11-13]. Endo-biliary application of radiofrequency (RF) has been developed in our unit and used in patients with inoperable bile duct and pancreatic head adenocarcinomas presenting with biliary obstruction[14]. Many alternative techniques of endoscopic ultrasound (EUS)-guided tumor ablation have been described, including RF ablation, photodynamic therapy, laser ablation, and ethanol injection[12].

EUS-RFA could achieve complete ablation of pancreatic cysts with malignant potential in patients unfit for surgery, thus eliminating the requirement for long-term surveillance in this group of individuals. Gaidhane et al[13] showed that EUS-RFA of the pancreatic head using Habib EUS-RFA catheter (Emcision Ltd., United Kingdom) through a 19 gauge needle was well tolerated in 5 Yucatan pigs with minimum amount of pancreatitis. The aim of this study is to outline the safety, feasibility, adverse events and early results of EUS-RFA in patients with pancreatic neoplasms using a novel probe.

MATERIALS AND METHODS

Patients

Eight patients were subjected to EUS-RFA of a neoplastic lesion in the head of the pancreas. A novel monopolar RF catheter [Habib™ EUS-RFA catheter, Emcision Ltd., London (CE Marked)] (Figure 1) was placed through a 19 or 22 gauge fine needle aspiration (FNA) needle.
introduced into the target lesion. In pancreatic cystic lesions, effort was made to completely aspirate the cyst before applying RFA. The tip of the needle was positioned near the far end of the lesion. In case of pancreatic NET also, the FNA needle was positioned at the deepest part of the tumor. The stylet is removed from the biopsy needle and Habib™ EUS RFA catheter is gently pushed inside the hollow of the biopsy needle until it cannot be pushed any further. Carefully maintaining this position of the Habib™ EUS RFA probe, the FNA needle is gradually withdrawn by 3 cm in order to disengage contact between the active part of the RF catheter located at the tip and the metallic FNA needle. Fluoroscopy assists in visualization of the RFA probe protruding beyond the tip of the needle (Figure 2). The tip of the probe is floppy, and may take a curved shape in emptied cystic lesions.

RF energy is applied for 90-120 s at the set wattage. In larger lesions, the Habib™ EUS RFA probe and needle is pulled back as one unit and repositioned to ablate near end of the lesion (Figures 3-5). This process can be repeated as many times, as needed to ensure complete ablation of the lesion. In larger pancreatic lesions, repeat puncture with the FNA needle is done in a different axis (after withdrawing the RFA probe, with or without replacing with stylet). The patients were managed post procedure as per standard hospital practice for EUS interventional procedures.

RESULTS

Eight patients [median age of 65 (range 27-82) years; 7 female and 1 male] were recruited in a prospective multicentre trial. Six had a pancreatic cystic neoplasm (four a mucinous cyst, one had IPMN and one a microcystic adenoma). In all six cases, diagnosis was based on imaging reviewed by an expert radiologist. The remaining two cases, had a NET in the head of pancreas (previously documented with diagnostic FNA cytology and not suitable for surgical intervention). The mean size of the cystic neoplasms and NETs were...
36.5 mm (SD ± 17.9 mm) and 27.5 mm (SD ± 17.7 mm) respectively. RF [Rita (Model 1500X) or ERBE

(Model ICC 200) was applied at 5 watts, 15 watts, 20 watts and finally 25 watts in 3, 2, 2 and one patients respectively over 90 s for each watt setting (Table 1). The median number of applications was 4.5 (range 2-7). Patients with cystic neoplasm and one patient with NET had one session of RFA each, whilst a second patient with NET had two sessions of RFA.

The EUS-RFA was completed in all cases. Amongst the 6 patients with pancreatic cystic neoplasm, the post procedure imaging in 3-6 mo showed complete resolution of the cysts in 2 patients, whilst in 3 patients there was 48.4% reduction [mean pre RF 38.8 mm (SD ± 21.7 mm) vs mean post RF 20 mm (SD ± 17.1 mm)] in size (Table 2). Using cross sectional imaging in 2 patients with NET, a change in vascularity and central necrosis after EUS-RFA was demonstrated. There were no episodes of post-procedural pancreatitis, perforation or bleeding within 48 h. Two patients had mild abdominal pain that resolved in 3 d.

**DISCUSSION**

RFA is a well-recognized, safe and effective modality for the treatment of focal malignant diseases\[14,15\]. RFA uses high-frequency alternating current to generate thermal energy and thus coagulative necrosis to the tissue\[16\]. The technique is minimally invasive and has very good tolerability which are the major advantages\[17\]. RFA is increasingly applied in pancreatic lesions\[18\], including unresectable pancreatic carcinoma where RFA has an acceptable mortality but high morbidity\[16,17,19-21\]. In general, adverse events are associated with the duration of ablation. Pancreas is very thermo-sensitive, and when heat is applied on normal pancreas it produces an inflammatory response causing edema and later fibrosis and occasionally cystic transformation\[18\]. Massive necrosis of the pancreas following RFA have been reported, probably due to sequential ablations done in close proximity at the same session\[17,20\].

In recent years there have been reports of prospective studies using RFA in locally advanced pancreatic adenocarcinoma. In 2010, Girelli et al\[22\] reported ultrasound-guided RFA during laparotomy in fifty patients with locally advanced pancreatic cancer. In this prospective study the main outcome measures were short-term morbidity and mortality. In thirty four patients the tumor was located in the pancreatic head or the uncinate process and in 16 in the body or tail; median diameter was 40 (inter-quartile range 30-50) mm. Abdominal adverse events occurred in 24% of patients. Half of those were directly associated with RFA (two pancreatic fistulas and four cases of portal vein thrombosis) and were managed conservatively. When the applied heat was reduced from 105 degrees C to 90 degrees C there was a significant reduction in adverse events (ten vs two of 25 patients; \(P = 0.028\)). Median postoperative hospital stay was 10 (range 7-31) d. The authors concluded that RFA of locally advanced pancreatic cancer is feasible and relatively well tolerated. In another observational study, the same group compared patients with locally advanced pancreatic carcinoma treated with either primary RFA (group 1) or RFA following any other primary treatment (group 2)\[23\]. In total, 107 consecutive patients were treated with RFA of which 47 patients in group 1 and 60 in group 2. Median overall survival was 25.6 mo and it was significantly shorter in group 1 than in group 2 (14.7 mo vs 25.6 mo; \(P = 0.004\)). In this study the authors reported that RFA after alternative primary treatment was associated with prolonged survival.

RFA has been proposed by many groups as a strong adjuvant for antitumor response as it induces an immune response targeting tumor antigens\[24-26\]. \textit{In situ} tumor destruction by RFA provides the immune system with an antigen for the induction of antitumor immunity. Antigen-presenting cells take up antigens in the periphery after which they induce specific

---

**Table 1  Patient characteristics and procedure specifications**

| Age | Sex | Diagnosis                  | No. of RF applications/session | No. of sessions | Dead/ alive |
|-----|-----|---------------------------|--------------------------------|-----------------|-------------|
| 5 Watts |     |                           |                                |                 |             |
| 82  | F   | Mucinous cyst             | 3                              | 1               | Alive       |
| 73  | F   | Mucinous cyst             | 5                              | 1               | Alive       |
| 46  | F   | Microcystic adenoma       | 5                              | 1               | Alive       |
| 15 Watts |   |                           |                                |                 |             |
| 40  | F   | Mucinous cyst             | 3                              | 1               | Alive       |
| 27  | F   | Mucinous cyst             | 2                              | 1               | Alive       |
| 20 Watts |   |                           |                                |                 |             |
| 57  | F   | NET                       | 6                              | 1               | Alive       |
| 82  | F   | NET                       | 4                              | 2               | Alive       |
| 25 Watts |   |                           |                                | 7               | 1            | Alive       |
| 78  | M   | IPMN                      |                                |                 |             |

**Table 2  Outcome after endoscopic ultrasound radiofrequency ablation of pancreatic cystic neoplasm and neuroendocrine tumors**

| No. | Diagnosis                  | Pre ablation size (mm) | Post ablation size (mm) | Adverse events |
|-----|---------------------------|------------------------|-------------------------|---------------|
| 1   | Mucinous cyst             | 30                     | 10                      | No            |
| 2   | Mucinous cyst             | 40                     | Cyst not seen           | No            |
| 3   | Microcystic adenoma       | 20                     | 8                       | No            |
| 4   | Mucinous cyst             | 70                     | 45                      | Mild pain     |
| 5   | Mucinous cyst             | 24                     | Cyst not seen           | Mild pain     |
| 6   | IPMN                      | 35                     | 17                      | No            |
| 7   | NET                       | 15                     | Change in vascularity   | No            |
| 8   | NET                       | 40                     | Central area of necrosis 15 mm | No     |

IPMN: Intraductal papillary mucinous neoplasm; NET: Neuroendocrine tumors; RF: Radiofrequency; F: Female; M: Male.

---
immune responses\cite{25}. Wissniowski et al\cite{24} reported that RFA can induce a tumor-specific T-cell reaction in the non-reactive neoplasm-bearing host, probably by overcoming immune tolerance and leading to the presentation of otherwise cryptic neoplastic antigens. In another study, ablation of hepatocellular carcinoma (HCC) was found to induce a functional transient activation of myeloid dendritic cells associated with increased serum levels of TNF-α and IL-1β with a sustained antitumoral immune response\cite{26}. Moreover, animals treated with subtotal RF ablation showed significant increases in tumor-specific class I and II responses to male minor histocompatibility (HY) antigens and tumor regression\cite{27}. Subtotal RF ablation produces an enhanced systemic antitumor immune response and tumor regression which is related to increased dendritic cell infiltration. RFA can also induce a tumor-specific proliferative T cell response and even transplantable protective immunity\cite{28}.

Intraoperative RFA uses a larger device with higher energy and is associated with significant morbidity and mortality. However, EUS guided RFA is a more conservative approach and avoids surgical intervention. Goldberg et al\cite{18} applied EUS guided RFA to the pancreas of 13 Yorkshire pigs at 285 ± 120 mA for 6 min resulting in discrete zones of coagulation necrosis in the porcine pancreas. Only one of the 13 animals had increased lipase levels and mild focal pancreatitis. No other significant adverse events were observed. A more recent study in 2008 demonstrated the feasibility and efficacy of EUS RFA using a newly developed bipolar ablation probe combining RFA and cryotechnology in 14 pigs. The size of the ablation achieved was related to the duration of ablation; when applied for 900 s there was a high complication rate in the healthy pancreas. Adverse events were less common compared to conventional RFA needles\cite{29}. In a recent study by Kim et al\cite{30}, EUS-RFA of the pancreas was applied on 10 adult mini pigs. An 18 gauge endoscopic RFA probe was used to ablate the body and tail of the pancreas, with an output power of 50 W for 5 min. On histology, there was a spherical necrotic lesion surrounded by fibrous tissue localized in the pancreatic parenchyma. The mean diameter of the ablated tissue was 23.0 ± 6.9 mm. No major procedure-related adverse events were observed, and all pigs survived without any distressed behavioural pattern for 7 d until autopsy. Another minimally invasive technique for treatment of pancreatic cystic lesions with moderate success is the EUS-guided injection of ethanol into the cyst, with reported efficacy of 33.5%-62% in achieving cyst resolution\cite{31,32}. The adverse events associated with this technique are significant, with a reported risk of severe post-procedural pain and pancreatitis of 4%-20%. Also, the presence of multiple septations within the cyst reduces the efficacy of ethanol injection. Another limitation of ethanol ablation is that this method would not be suitable for treatment of solid pancreatic lesions. A major potential advantage of EUS-RFA of cystic tumors is that it could be done in a minimally invasive way, with the likelihood of fewer adverse events than the alcohol injection because the area of ablation can be assessed and monitored in real-time by EUS.

EUS-RFA using Habib EUS-RFA catheter (Emcision Ltd., United Kingdom) through a 19 gauge needle for ablation of lymphatic and pancreatic tissue, was reported in two animal studies. In the former study\cite{33}, EUS-guided RFA ablation of mediastinal lymph nodes was successfully attempted in six pigs. RFA was performed with the ERBE Vaio generator (ERBE, Tuttingen, Germany) with bipolar settings of 10 watts, effect 2 for 2 min. During the procedure, the probe was visible in all cases. No evidence of ablation effect in the surrounding tissue or at the needle puncture site was seen on gross examination. There was a direct correlation between the probe length and the size of necrosis. In the pancreatic study using the same catheter, five Yucatan pigs underwent EUS-guided RFA of the head of the pancreas\cite{34}. RFA was applied with 6 mm of the probe exposed at 4 watts for 5 min, 5 watts for 0.9 min, and 6 watts for 0.2 min. Then, with 10 mm of the probe exposed in the pancreas, RFA was performed at 4 watts for 4.3 min, 5 watts for 1.4 min, and 6 watts for 0.8 min. Autopsy showed moderate level of pancreatitis, with involvement of 20% of the proximal pancreatic tissue in only one pig. There was minimal tissue damage in the other animals. In this study EUS-guided RFA of the pancreatic head with the monopolar probe through a 19 gauge needle was well tolerated with a minimal amount of pancreatitis.

We have reported in this prospective study the application of RFA via the novel Habib EUS-RFA catheter (Emcision Ltd., United Kingdom) for pancreatic cystic neoplasms and NET. The concept of treating pre-malignant asymptomatic pancreatic lesions by means other than surgical resection is appealing, as the latter is associated with major morbidity and some mortality. This study shows that such an approach is feasible and safe. Our patients were discharged hours without any major adverse events. However, it is conceivable that the application of RF energy in the pancreatic parenchyma may be associated with some adverse events. Such adverse events may include (but not necessarily limited to) acute pancreatitis, pancreatic leaks, infection of necrotic pancreatic tissue post treatment and bleeding. Using lower energy also allows for repeating the ablation with low morbidity as per clinical indication. EUS-RFA of pancreatic neoplasms with a novel monopolar RF probe was well tolerated in all patients. These preliminary data results suggest that the procedure is technically easy and safe. The response ranged from complete resolution to a 50% reduction in diameter. Further multicenter experience is required before widespread use of this novel procedure.

**ACKNOWLEDGMENTS**

Nagy Habib is shareholder and director of EMcision.
Radiofrequency ablation for pancreatic cystic neoplasms

which designed and developed the device. None of the other authors have a conflict of interest or a financial disclosure to declare.

REFERENCES

1 Spinelli KS, Fromwiller TE, Daniel RA, Kiely JM, Nakeeb A, Komorowski RA, Wilson SD, Pitt HA. Cystic pancreatic neoplasms: observe or operate. Ann Surg 2004; 239: 651-657; discussion 657-659 [PMID: 15092960 DOI: 10.1097/00000658-199908000-00004]

2 Le Borgne J, de Calan L, Partensky C. Cystadenomas and cystadenocarcinomas of the pancreas: a multiinstitutional retrospective study of 398 cases. French Surgical Association. Ann Surg 1999; 230: 152-161 [PMID: 10450728 DOI: 10.1097:0.0000658 -199908000-00004]

3 Kitagawa Y, Unger TA, Taylor S, Kozarek RA, Traverso LW. Mucus is a predictor of better prognosis and survival in patients with intraductal papillary mucinous tumor of the pancreas. J Gastrointest Surg 2003; 7: 12-18; discussion 18-19 [PMID: 12559180 DOI: 10.1016/S1091-255X(02)00152-X]

4 Cameron JL, Riall TS, Coleman J, Belcher KA. One thousand consecutive pancreaticcreaticoduodenectomies. Ann Surg 2006; 244: 10-15 [PMID: 16794383 DOI: 10.1097:0.0.S00216736.04165.ea]

5 Birkmeyer JD, Sun Y, Wong SL, Stukel TA. Hospital volume and late survival after cancer surgery. Ann Surg 2007; 245: 777-783 [PMID: 17457171 DOI: 10.1097:0.0.S00254202.33814.d]

6 Tanaka M, Chari S, Adsay V, Fernandez-del Castillo C, Falconi M, Shimizu M, Yamaguchi K, Yamao K, Matsuno S. International consensus guidelines for management of intraductal papillary mucinous neoplasms and mucinous cystic neoplasms of the pancreas. Pancreatology 2006; 6: 17-32 [PMID: 16327281 DOI: 10.1159/000090023]

7 Jiao LR, Hansen PD, Haviik R, Mitry RR, Pignatelli M, Habib N. Clinical short-term results of radiofrequency ablation in primary and secondary liver tumors. Am J Surg 1999; 177: 303-306 [PMID: 10326484 DOI: 10.1016/S0002-9610(99)00434-3]

8 Weber JC, Navarra G, Jiao LR, Nicholls JP, Jensen SL, Habib NA. New technique for liver resection using heat coagulative necrosis. Ann Surg 2002; 236: 560-563 [PMID: 12409660 DOI: 10.1097:0.0000658-200211000-00004]

9 Pai M, Frampton AE, Mikhaili S, Resende V, Kornasiewicz O, Spalding DR, Jiao LR, Habib NA. Radiofrequency assisted liver resection: analysis of 604 consecutive cases. Eur J Surg Oncol 2012; 38: 274-280 [PMID: 22209064 DOI: 10.1016/j.ejso.2011.12.006]

10 Pai M, Spalding D, Jiao L, Habib N. Use of bipolar radiofrequency in parenchymal transection of the liver, pancreas and kidney. Dig Surg 2012; 29: 43-47 [PMID: 22441619 DOI: 10.1159/000353752]

11 Steel AW, Postgate AJ, Khorsandi S, Nicholls J, Jiao L, Vlavianos P, Habib N, Westaby D. Endoscopically applied radiofrequency ablation appears to be safe in the treatment of malignant biliary obstruction. Gastrointest Endosc 2011; 73: 149-153 [PMID: 21184881 DOI: 10.1016/j.gie.2010.09.031]

12 Yoon WJ, Brugge WR. Endoscopic ultrasound-guided tumor ablation. Gastrointest Endosc Clin N Am 2012; 22: 359-369, xi [PMID: 22629527 DOI: 10.1016/j.gec.2012.04.017]

13 Gaidhane M, Smith I, Ellen K, Gatesman J, Habib N, Foley P, Moskaluk C, Kahaleh M. Endoscopic Ultrasound-Guided Radiofrequency Ablation (EUS-RFA) of the Pancreas in a Porcine Model. Gastrointest Res Pract 2012; 2012: 431451 [PMID: 23049547 DOI: 10.1155/2012/431451]

14 Chen MH, Yang W, Yan K, Gao W, Dai Y, Wang YB, Zhang XP, Yin SS. Treatment efficacy of radiofrequency ablation of 338 patients with hepatic malignant tumor and the relevant complications. World J Gastroenterol 2005; 11: 6395-6401 [PMID: 16419172]

15 Toyota M, Kakizaki S, Horiuichi K, Takai K, Saito K, Takagi H, Mori M, Nakajima T. Computed tomography-guided transpulmonary radiofrequency ablation for hepatocellular carcinoma located in hepatic dome. World J Gastroenterol 2006; 12: 608-611 [PMID: 16489676]

16 Matsui Y, Nakagawa A, Kamiyama Y, Yamamoto K, Kubo N, Nakase Y. Selective thermocoumlation of unresectable pancreatic cancers by using radiofrequency capacitive heating. Pancreas 2000; 20: 14-20 [PMID: 10630378 DOI: 10.1097:0.00006676-200010000-00002]

17 Elias D, Baton O, Sideris L, Lasser P, Poccard M. Necrotizing pancreatitis after radiofrequency destruction of pancreatic tumours. Eur J Surg Oncol 2004; 30: 85-87 [PMID: 14736529 DOI: 10.1016/j.ejso.2003.10.013]

18 Carrara S, Arcidiacono PG, Albarello L, Addis A, Enderle MD, Boemo C, Campagnol M, Ambrosi A, Doglioni C, Testoni PA. Endoscopic ultrasound-guided application of a new hybrid cryoetherm probe in porcine pancreas: a preliminary study. Endoscopy 2008; 40: 321-326 [PMID: 18394449 DOI: 10.1055/s-2007-959595]

19 Sirlinavena AK. Radiofrequency ablation for locally advanced cancer of the pancreas. JOP 2006; 7: 1-4 [PMID: 16407612]

20 Wu Y, Tang Z, Fang H, Gao S, Chen J, Wang Y, Yan H. High operative risk of cool-tip radiofrequency ablation for unresectable pancreatic head cancer. J Surg Oncol 2006; 94: 392-395 [PMID: 16967436 DOI: 10.1002/jso.20580]

21 Spiliotis JD, Datsis AC, Michalopoulos NV, Keklos SP, Vazevanidou A, Rogakis AG, Christopoulos AN. High operative risk of cool-tip radiofrequency ablation for unresectable pancreatic head cancer. J Surg Oncol 2007; 96: 89-90 [PMID: 17345594 DOI: 10.1002/jso.20764]

22 Girelli R, Frigerio I, Salvia R, Barbi E, Tinazzi Martini P, Bassi C. Feasibility and safety of radiofrequency ablation for locally advanced pancreatic cancer. Br J Surg 2010; 97: 220-225 [PMID: 20069610 DOI: 10.1002/bjs.6001]

23 Cantore M, Girelli R, Mambrini A, Frigerio I, Boz G, Salvia R, Giardino A, Orlandi M, Aurienma A, Bassi C. Combined modality treatment for patients with locally advanced pancreatic adenocarcinoma. Br J Surg 2012; 99: 1083-1088 [PMID: 22648697]
Pai M et al. Radiofrequency ablation for pancreatic cystic neoplasms

DOI: 10.1002/bjs.8789

24 Wissniowski TT, Hänßler J, Neureiter D, Frieser M, Schaber S, Esslinger B, Voll R, Strobel D, Hahn EG, Schuppan D. Activation of tumor-specific T lymphocytes by radio-frequency ablation of the VX2 hepatoma in rabbits. Cancer Res 2003; 63: 6496-6500 [PMID: 14559842]

25 den Brok MH, Sutmüller RP, van der Voort R, Bennink EJ, Figdor CG, Ruers TJ, Adema GJ. In situ tumor ablation creates an antigen source for the generation of antitumor immunity. Cancer Res 2004; 64: 4024-4029 [PMID: 15173017 DOI: 10.1188/04-061]

26 Ali MY, Grimm CF, Ritter M, Mohr L, Allgaier HP, Weth R, Bocher WO, Endrulat K, Blum HE, Geissler M. Activation of dendritic cells by local ablation of hepatocellular carcinoma. J Hepatol 2005; 43: 817-822 [PMID: 16087270 DOI: 10.1016/j.jhep.2005.04.016]

27 Dromi SA, Walsh MP, Herby S, Traughber B, Xie J, Sharma KV, Sekhar KP, Luk A, Liewehr DJ, Dreher MR, Fry TJ, Wood BJ. Radiofrequency ablation induces antigen-presenting cell infiltration and amplification of weak tumor-induced immunity. Radiology 2009; 251: 58-66 [PMID: 19251937 DOI: 10.1148/radiol.2511072175]

28 Zerbini A, Pili M, Penna A, Pelosi G, Schianchi C, Molinari A, Schivazappa S, Zibera C, Fagnoni FF, Ferrari C, Missale G. Radiofrequency thermal ablation of hepatocellular carcinoma liver nodules can activate and enhance tumor-specific T-cell responses. Cancer Res 2006; 66: 1139-1146 [PMID: 16424051 DOI: 10.1158/0008-5472.CAN-05-2244]

29 Goldberg SN, Mallery S, Gazelle GS, Brugge WR. EUS-guided radiofrequency ablation in the pancreas: results in a porcine model. Gastroint Endosc 1999; 50: 392-401 [PMID: 10462663 DOI: 10.1053/ge.1999.v50.98847]

30 Kim HJ, Seo DW, Hassanuddin A, Kim SH, Chae HJ, Jang JW, Park do H, Lee SS, Lee SK, Kim MH. EUS-guided radiofrequency ablation of the porcine pancreas. Gastroint Endosc 2012; 76: 1039-1043 [PMID: 23078928 DOI: 10.1016/j.gie.2012.07.015]

31 DeWitt J, DiMaio CJ, Brugge WR. Long-term follow-up of pancreatic cysts that resolve radiologically after EUS-guided ethanol ablation. Gastroint Endosc 2010; 72: 862-866 [PMID: 20883866 DOI: 10.1016/j.gie.2010.02.039]

32 DiMaio CJ, DeWitt JM, Brugge WR. Ablation of pancreatic cystic lesions: the use of multiple endoscopic ultrasound-guided ethanol lavage sessions. Pancreas 2011; 40: 664-668 [PMID: 21562447 DOI: 10.1097/MPA.0b013e3182128d06]

33 Sethi A, Ellrichmann M, Dhar S, Hadeler K-GERD, Kahle E, Sechusen F, Klapper W, Habib N, Fritscher-Ravens A. S03 EUS-Guided Lymph Node Ablation With Novel Radiofrequency Ablation Probe: A Feasibility Study. Gastroint Endosc 2012; 75 (Suppl 4): ABI47 [DOI: 10.1016/j.gie.2012.04.079]

P- Reviewer: Cidon EU, Chiu KW, Ogura T, Tepes B, Watanabe M S- Editor: Ji FF L- Editor: A E- Editor: Lu YJ
