EUS-guided radiofrequency ablation of the porcine pancreas

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Background: EUS-guided radiofrequency ablation (EUS-RFA) could be used as an adjunct and effective alternative mode of treatment for unresectable locally advanced and nonmetastatic pancreatic adenocarcinoma. However, its translation into clinical practice has been restricted because of limited data and high procedure-related risk.

Objective: To evaluate the feasibility, efficacy, and safety of EUS-RFA in the normal porcine pancreas.

Design: Prospective, endoscopic, experimental study in a porcine model.

Setting: Tertiary-care referral center animal laboratory.

Patients: Animal study.

Intervention: EUS-RFA of the pancreas was attempted on 10 adult mini pigs. An 18-gauge endoscopic RFA electrode was used to puncture the body and tail of the pancreas, with an output power of 50 W for 5 minutes.

Main Outcome Measurements: The feasibility, efficacy, and safety of EUS-RFA.

Results: A spherical necrotic lesion surrounded by fibrous tissue localized in the pancreatic parenchyma was observed on histopathologic examination. The mean diameter of the ablated tissue was 23.0 ± 6.9 mm. No major procedure-related complications were noted, and all pigs survived without any distress behavioral pattern for 7 days until autopsy.

Limitations: Small sample size with short-term observation and the lack of evaluation of the head of the pancreas.

Conclusion: EUS-RFA of the pancreatic body and tail was feasible, effective, and relatively safe in a porcine model. More animal studies to assess damage to adjacent organs are required before human trials can be conducted.

Pancreatic cancer, albeit being one of the most aggressive cancers, could potentially be cured by radical surgery. However, it is most often quiescent and remains so until its clinical presentation at the later stages. Thus, only 15% to 20% of patients have cancers that are confined to the pancreas, whereas the majority, 30% to 40%, are locally advanced, and approximately another 40% have distant metastasis at the time of diagnosis.1,2

Radiofrequency catheter ablation (RFA) is a well-established technique to ablate neoplastic tissue via local thermal-induced coagulative necrosis of the tumor. In clinical practice, it has been used extensively for tumors of the liver, kidney, and prostate gland.3 RFA has been used during laparotomy for locally advanced and nonmetastatic pancreatic adenocarcinoma. Although feasible intraoperatively, the procedure is invasive with debatable benefits and safety outcomes.2,3 Meanwhile, percutaneous RFA guided by transabdominal US has been restricted because of poor visualization of the retroperitoneal pancreas. This approach may result in erroneous cytoreductive ablation and subsequently inadvertent damage to adjacent organs.
With the development of linear-array EUS, a less-invasive RFA treatment modality could be used.\(^5,6\) The advantage of EUS-guided RFA (EUS-RFA) is to better delineate the deep-seated pancreas by real-time imaging, thus allowing selective ablation of the tumor. This would minimize and avoid possible injury to the surrounding structures. However, its application in human trials has been hampered by limited data, discouraging complications, and ineffective ablative results.\(^7\) Therefore, we designed an in vivo study to evaluate the feasibility, efficacy, and safety of EUS-RFA on the porcine pancreas with an 18-gauge endoscopic RFA electrode.

**MATERIALS AND METHODS**

**Animals**

Ten mini pigs (mean weight 40 kg, weight range 38-42 kg) were used. Approval of the Institutional Animal Care and Use Committee was obtained before initiation of the study. All pigs were fasted for 6 hours before EUS-RFA and 3 hours after the procedure. The pigs were sedated for general anesthesia, and induction was achieved by using a drug combination of tiletamine and zolazepam (7.5 mg/kg) (Zoletil 50; Virbac, Korea) and xylazine hydrochloride (2 mg/kg) (Rompun; Bayer, Korea). The animals were then intubated and administered 1.5% isoflurane (Forane; JW Pharmaceutical, Korea). Cardiopulmonary parameters were monitored throughout the procedure.

**RFA system**

An 18-gauge RFA electrode and a VIVA RF generator (STARmed, Korea) were used for the procedure (Fig. 1). Total length of the electrode including the delivery system was 150 cm. The exposed distal end of the electrode was needle-shaped and echogenic. The active electrode tips were manufactured with various fixed length of 0.5 cm, 1 cm, 1.5 cm, or 2 cm. We chose the 1-cm active electrode length for this study. During ablation, the RF electrode was...

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**Take-home Message**

- EUS-guided radiofrequency ablation of the pancreas is a technically feasible and relatively safe procedure in a porcine model. It has the potential to be used as a local treatment modality for advanced pancreatic cancer in humans.
cooled and perfused internally with circulating chilled saline solution (0°C) delivered via a pump.

**Two-step RFA approach**

**Ex vivo test.** In the ex vivo test, 6 samples of bovine liver were used to determine the optimal ablation power. The energy with different powers of 30 W, 50 W, and 80 W, respectively, were applied for 6 minutes. The ablation power of 50 W showed the most effective depth and size of the ablation zone, compared with those of 30 W or 80 W. The size of ablated lesions with the powers of 30 W and 80 W were smaller compared with those at 50 W. The 80-W power resulted in a higher surface electrode tip temperature that produced tissue charring. This resulted in an impedance rise with subsequent reduction in coagulative necrosis effect.

**In vivo RFA method.** A linear array EUS (EU-C2000; Olympus Optical Co Ltd, Tokyo, Japan) and an 18-gauge endoscopic RFA electrode were used for the procedure. All procedures were directed toward the body and tail of the porcine pancreas via an EUS-guided transgastric approach. RFA was performed with a 1-cm active electrode tip at 50 W of power for 5 minutes.

**Postprocedure assessment**

The 10 pigs were kept alive for 7 days. Although the vital signs, body weight, and performance were checked daily, the pigs’ liver profiles, serum amylase, and serum lipase were taken before the procedure, on day 3, and on day 3.
7 of the experiment. Laparotomy was performed to macroscopically evaluate the ablated lesion of the pancreas and to examine gross anatomical injuries to adjacent organs on day 7 in all pigs. After that, histopathologic examination of the porcine pancreas was performed on 4 pigs.

Statistical analysis
The comparisons of the laboratory parameters related to complications were calculated by using a nonparametric, 2-tailed Wilcoxon signed rank test. The continuous variables were expressed as the mean ± standard deviation. P values of < .05 were considered statistically significant. All statistical analyses were performed by using the SPSS 18.0 statistical package (Chicago, Ill).

RESULTS
Feasibility
EUS-RFA of the body and tail of the pancreas were technically successful in all 10 pigs. The RFA electrode was clearly visualized extruding out of the working channel of the echoendoscope and was inserted directly into the pancreatic parenchyma under real-time EUS imaging (Fig. 2A). During ablation, an echogenic cloud formed around the tip of the RFA electrode, resulting in the creation of a round, hyperechoic lesion at the end of the procedure. Under endosonographic view, the measured mean diameters of the ablated lesions were 14.5 ± 1.5 mm (Fig. 2B).

Efficacy
The gross pathology specimens showed a well-demarcated ablated lesion distinguished from surrounding pancreatic parenchyma by a whitish peripheral rim (Fig. 3). The mean diameters of the ablated lesions were 23.0 ± 6.9 mm. The ablated lesions were spherical.

Microscopic view revealed the whitish wall to be fibrous tissue sandwiched between normal pancreatic parenchyma and necrotic tissue (Fig. 4).

Safety
There were no significant changes in the laboratory test results, including serum levels of aspartate transaminase, alanine transaminase, amylase, and lipase, before and after the procedures (Table 1). All pigs showed satisfactory behavioral performance and had no change in body weight during the 7-day observation period.

Necropsy findings revealed normal surrounding pancreatic parenchyma around the ablated lesion, devoid of any evidence of parenchymal necrosis or pancreatic duct injury. In addition, there were no signs of major vessel injuries or adjacent organ damage.

Fibrosis and adhesions were found in 3 pigs, none of which showed any behavioral distress. One exhibited retroperitoneal fibrosis, and two had adhesions of the pan-
creas to the stomach wall and bowel wall, respectively (Fig. 5).

**DISCUSSION**

This study revealed that EUS-RFA of the normal porcine pancreas was technically feasible, effective, and relatively safe. EUS-RFA was conducted with an ablative power of 50 W for a period of 5 minutes with an 18-gauge 1-cm needle electrode length. A well-demarcated discrete ablation zone was created within the body and tail of the pancreas, and there were no significant complications except for intestinal wall adhesions and retroperitoneal fibrosis located at the adjacent organs.

Goldberg et al previously evaluated the role of EUS-RFA of the pancreas in an animal model. Although the procedure was technically successful, the size of the coagulative focus was limited to <10 mm. In this study, we were able to produce an ablation zone of about 2 cm in diameter. The size of this discrete spherical ablation core might be sufficient to ablate a specific span of pancreatic tumors successfully.

There were several limitations in this study. First, the number of pigs used was relatively small, with a short-term follow-up period. Although the sample size was comparable to that of other studies, a further larger-sample-size study is required. Second, the effect of ablation achieved on different tissues used in this study might not be truly representative of the expected ablation focus produced in human pancreatic ductal adenocarcinoma in view of differing blood supply and a diverse cytologic milieu. Furthermore, as a result of the anatomic characteristics of the porcine stomach and the inflexibility and rigidity of the 18-gauge RFA needle within the proximal small intestine, EUS-RFA was performed on the pancreatic body and the tail, excluding evaluation of its outcome on the head of the pancreas. This represents an added drawback in this study.

This experimental study suggests that EUS-RFA is feasible and has the potential to be an effective treatment modality. Its clinical application requires further evaluation in future studies.

**REFERENCES**


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