Initial experience of EUS-guided radiofrequency ablation of unresectable pancreatic cancer

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Background and Aims: Radiofrequency ablation (RFA) has been used as a valuable treatment modality for various unresectable malignancies. EUS-guided radiofrequency ablation (EUS-RFA) of the porcine pancreas was reported to be feasible and safe in our previous study, suggesting that EUS-RFA may be applicable as an adjunct and effective alternative treatment method for unresectable pancreatic cancer. This study aimed to assess the technical feasibility and safety of EUS-RFA for unresectable pancreatic cancer.

Methods: An 18-gauge endoscopic RFA electrode and a radiofrequency generator were used for the procedure. The length of the exposed tip of the RFA electrode was 10 mm. After insertion of the RFA electrode into the mass, the radiofrequency generator was activated to deliver 20 to 50 W ablation power for 10 seconds. Depending on tumor size, the procedure was repeated to sufficiently cover the tumor.

Results: EUS-RFA was performed successfully in all 6 patients (median age 62 years, range 43-73 years). Pancreatic cancer was located in the head (n = 4) or body (n = 2) of the pancreas. The median diameter of masses was 3.8 cm (range 3cm-9cm). Four patients had stage 3 disease, and 2 patients had stage 4 disease. After the procedure, 2 patients experienced mild abdominal pain, but there were no other adverse events such as pancreatitis or bleeding.

Conclusions: EUS-RFA could be a technically feasible and safe option for patients with unresectable pancreatic cancer.

Pancreatic cancer carries a poor prognosis, with a 5-year overall survival rate of <5% and a median survival of <6 months.1 Resection provides the only chance of a cure, with 5-year overall survival rates of 18% to 24%; unfortunately, however, only one fifth of patients present with resectable disease. The outcomes of chemotherapy or chemoradiation therapy are not satisfactory,2 with most pancreatic cancer patients experiencing only a small benefit. Therefore, new advances for the treatment of pancreatic cancer are needed.

Radiofrequency ablation (RFA) works by emitting energy resulting in coagulative necrosis of the surrounding tissue.2,3 RFA is considered a safe and potentially curative method and has been used widely for the treatment of tumors of the liver, lung, and kidney, but not of the pancreas. The reluctance of clinicians to use RFA for pancreatic cancer may be related to the fear of adverse events, such as thermal injury-induced pancreatitis, thermal damage to structures around the pancreas, and technical limitations.4 Recent studies have shown that RFA is feasible in patients with unresectable pancreatic cancer in an open, laparoscopic, or percutaneous setting.5 Particularly, EUS-guided RFA (EUS-RFA) allows real-time imaging of the pancreatic mass, where RFA may result in safe tissue ablation.

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According to our previous study, EUS-RFA was feasible and safe for the porcine pancreas.6

The aim of this study was to assess the feasibility and safety of EUS-RFA for unresectable pancreatic cancer.

PATIENTS AND METHODS

We obtained permission from the Institutional Review Board of each center and performed prospective data collection. A total of 6 consecutive patients were included in the study between February 2013 and March 2014. The inclusion criteria were (1) histologically confirmed pancreatic cancer, (2) unresectable stage due to locally advanced or metastasis disease, and (3) resistance to a previous treatment modality. The exclusion criteria were (1) advanced heart or lung disease precluding adequate sedation, (2) poor performance status, and (3) a lack of informed consent.

The procedure was performed by 2 experienced endosonographers (D.W.S. and S.L.), experienced in both ERCP and EUS and who perform >500 EUS procedures for pancreaticobiliary diseases annually.

EUS-RFA was performed by using an 18-gauge RFA needle and a VIVA RF generator (STARmed, Koyang, Korea). The total length of the electrode, including the delivery system, was 150 cm. The exposed distal end of the electrode was needle-shaped and echogenic, and the length of the exposed tip of the electrode was 10 mm.

We administered broad-spectrum prophylactic antibiotics before the procedure. During the procedure, patients received intravenous midazolam and meperidine. The procedure was performed by using a linear-array echoendoscope (GF-UCT 260-AL 10; Olympus Medical Systems, Tokyo, Japan) or a forward-viewing echoendoscope (GF-UCT 160J-AL 10; Olympus Medical Systems). To avoid major vessel injury, real-time Doppler imaging was used during the procedure. After insertion of the RFA electrode into the mass, the radiofrequency generator was activated to deliver 20 to 50 W ablation power. The ablation was performed for 10 seconds at one site and was repeated until the hyperechoic zone around the electrode tip sufficiently covered the tumor. Initially, ablation began at the right distal portion of the mass on the EUS image while the RFA electrode was withdrawn, and then the RFA electrode was reinserted, and ablation was repeated at the left side of the previous site.

A simple abdominal radiograph and blood tests for complete blood count, liver function tests, and serum amylase

![A radiofrequency ablation (RFA) electrode. An 18-gauge RFA electrode is composed of an electrode covered with protective tubing, a handle, and catheters for the cooling system. B, The exposed distal end of the electrode was needle-shaped and echogenic, and the length of the exposed tip of the electrode was 10 mm.](image)

Figure 1. A, A radiofrequency ablation (RFA) electrode. An 18-gauge RFA electrode is composed of an electrode covered with protective tubing, a handle, and catheters for the cooling system. B, The exposed distal end of the electrode was needle-shaped and echogenic, and the length of the exposed tip of the electrode was 10 mm.

<table>
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<tr>
<th>No.</th>
<th>Age</th>
<th>Sex</th>
<th>Tumor size, cm</th>
<th>Tumor location</th>
<th>Primary symptom</th>
<th>Session of RFA</th>
<th>Duration of follow-up, mo</th>
<th>Adjuvant chemotherapy</th>
<th>Procedure-related adverse events</th>
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<td>Abdominal pain</td>
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<td>4</td>
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</tbody>
</table>

RFA, Radiofrequency ablation.
and/or lipase were checked for adverse events on the next day. Other studies were performed depending on the clinical signs and symptoms. Adverse events were defined as major if they threatened the patients’ life, produced substantial morbidity, or prolonged the hospital stay.4

RESULTS

EUS-RFA was performed successfully on all 6 patients. The median age of the patients was 62 years (range 43-73 years), and the male to female ratio was 1:5 (Table 1).

Figure 2. Imaging of EUS-guided radiofrequency and follow-up contrast-enhanced EUS. A, EUS-guided radiofrequency ablation (RFA) was performed from the duodenal bulb with 50 W of ablation power for 10 seconds and was repeated 6 times. B, After RFA, contrast-enhanced EUS showed a nonenhanced central necrotic portion (arrowhead) and increased blood flow at the peripheral site (arrow).

Figure 3. Imaging findings of patients with cancer of the pancreatic head. A, CT shows a low-density mass at the pancreas head, which did not respond to second-line chemotherapy. B, EUS-guided radiofrequency ablation (RFA) was performed by using forward-viewing EUS with 50 W of ablation power for 10 seconds and was repeated 8 times. C, One month after RFA, follow-up CT showed necrosis and air bubbles in the mass (arrow). D, Two months after RFA, CT showed a decrease of the low density mass.
Pancreatic cancer was located in the pancreas head in 4 patients and in the pancreas body in 2 patients. The median diameter of the tumor was 3.8 cm (range 3-9 cm). All of the pancreatic cancers were unresectable; 4 patients had locally advanced disease and 2 had metastasis. After the procedure, 2 patients experienced mild abdominal pain, but this improved with analgesics. There were no major adverse events such as pancreatitis, bleeding, duodenal injury, or portal vein and/or splenic vein thrombosis. There was no procedure-related mortality.

On contrast-enhanced EUS after RFA, thermal necrosis at the ablation sites appeared as nonenhancing areas surrounding areas with increased blood flow (Fig. 2). Gemcitabine-based systemic chemotherapy was performed on the same day in 3 patients to enhance the effect of chemotherapy. In 1 patient, follow-up CT after RFA showed necrosis with air bubbles in the tumor (Fig. 3). There were no infections or perforations.

**DISCUSSION**

Until now, the feasibility and safety of EUS-RFA for the treatment of advanced pancreatic cancer has not been addressed. EUS can be used to target the area of ablation, and it ensures safety by avoiding damage to the surrounding structure. Our preliminary experience demonstrated that EUS-RFA for pancreatic cancer was well-tolerated and had no significant adverse events.

The pancreas is a highly thermosensitive organ, and the thermal ablation of normal pancreatic tissue may lead to inflammation with edema and fibrotic and cystic transformation. Potential adverse events of pancreatic RFA include pancreatitis, peripancreatic fluid collection, burns of the gastric wall, bowel injury, and peritonitis. These adverse events appear to be related to the duration of the ablation. In our previous study, the size of the ablation area was 2.5 cm when EUS-RFA was delivered with 50 W ablation power for a duration of 5 minutes. Based on these results, we determined the optimal duration and the number of repeated needle punctures required for the ablation of pancreatic tumors.

RFA for advanced pancreatic cancer is a type of cytoreductive therapy that does not aim to eradicate the tumor. Combined multiple-treatment followed by RFA can prolong survival. For the treatment of advanced pancreatic cancer, systemic control with chemotherapy is needed in addition to local control of the disease. In this study, post-RFA contrast-enhanced-EUS revealed increased blood flow around the RFA site, and, therefore, it might enhance the effect of systemic chemotherapy. Based on this finding, we performed post-RFA systemic chemotherapy with gemcitabine on the same day as we performed EUS-RFA.

Large tumors required multiple needle punctures and radiofrequency applications, but RFA could not result in complete ablation of tumors. However, several studies reported that thermal ablation therapy can stimulate and modulate the systemic immune response against the tumor. Therefore, even a suboptimal RFA treatment may result in a systemic antitumor immune response.

Because this preliminary study aimed to assess the technical feasibility and safety of EUS-guided RFA, and the follow-up duration was limited, we could not evaluate long-term survival. A further prospective study is necessary to demonstrate the overall survival benefit of EUS-RFA for pancreatic cancer.

In conclusion, EUS-RFA can be a technically feasible and safe option for patients with unresectable pancreatic cancer. EUS-RFA may be used as an adjunct and effective alternative treatment method for unresectable pancreatic cancer.

**REFERENCES**