



# Endoscopic therapy: a promising treatment for pancreatic cancer

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## Introduction

Pancreatic cancer remains one of the most malignant tumors all over the world (1,2). Most of the patients were diagnosed as advanced pancreatic cancer, which was unresectable. Although great progress has been made to elucidate the molecular pathogenesis and explore novel treatments for pancreatic cancer, the 5-year mortality and morbidity of pancreatic cancer is still high, and the survival is poor (3).

For such patients who lose the opportunity of surgical resection, palliative treatments could be administrated, including endoscopic therapy (4). Initially, endoscopic palliative interventions have been mainly introduced to treat obstructive jaundice caused by malignant biliary stricture in patients with advanced pancreatic cancer. With the development of new endoscopic device and procedures, celiac plexus neurolysis under the guidance of endoscopic ultrasound (EUS) or by natural orifice transluminal endoscopic surgery (NOTES) has been applied to alleviate the cancer related pain. Besides, radioactive stent was designed, which can achieve the goals of both drainage and local radiotherapy. Several studies have proved these endoscopic therapies for pancreatic cancer were effective in easing the symptoms of the patients in a relatively short-term and thus improving their life quality (5-7), which could bring benefits to the patients in both short- and long-term.

## Endoscopic therapeutic treatments for pancreatic cancer

### *Endoscopic stent placement*

Malignant biliary obstruction is very common in patients

with advanced pancreatic cancer. Biliary stent implantation during endoscopic retrograde cholangiopancreatography (ERCP) can alleviate the biliary stricture and maintain normal biliary drainage, which can be repeated. It was reported that the usage of metal stent, especially self-expanding metal stents (SEMS), was associated with less complication, longer patency and better prognosis compared with plastic stent (8). Radioactive stent was developed, which have the function of brachytherapy (5,9). We ever placed radioactive stent and SEMS or plastic stent in the common bile duct to treat 11 patients with unresectable malignant cholangiopancreatic tumors (5). The success rate of radioactive stent placement was 100%, and the severe complication rate was 0%. However, radioactive had shorter duration than plastic stent, which needs special attention (10). Furthermore, stent relocation and occlusion after placement should be closely monitored.

### *Biliary drainage via EUS or ERCP*

For such patient with obstructive jaundice, biliary drainage should be performed. During ERCP, biliary drainage can be achieved by endoscopic nasobiliary drainage (ENBD), endoscopic sphincterotomy (EST) and other modalities, but the biliary cannulation was technically difficult due to the inaccessibility of the papilla. Thus, EUS guided biliary drainage was another option, which was X-ray fluoroscopy free and minimally invasive. The effectiveness of EUS guided biliary drainage was comparable to percutaneous biliary drainage, but had a relatively lower complication rate and a rapid recovery. Several randomized clinical trials have already validated the clinical success of EUS guided biliary drainage (7,11).

### ***Endoscopic ablation***

The current endoscopic ablation available mainly included radiofrequency ablation, laser (Nd:YAG) ablation, photodynamic therapy (PDT) and ethanol ablation using EUS as a guide (12-14). It was easy to conduct and can be performed directly targeting the lesions in pancreas during the operation (15). Ablation can also destroy pancreatic tissue, which can cause pancreatitis and pancreatic fistula (16). A retrospective study conducted by Hua *et al.* (17), investigated the clinical efficacy and safety of EUS guided radiofrequency ablation in treating 102 patients diagnosed with pancreatic cancer and synchronous liver oligometastasis. The 1-year survival rate was 47.1% and the median overall survival time was 11.40 months. Ninety-six point one percent (244/254) of the tumors achieved complete ablation in 137 of 145 RFA sessions (94.5%).

### ***Anti-pain procedures***

Pain is often a troubling symptom in patients with pancreatic cancer. Celiac plexus neurolysis is recommended, but the anti-pain effect is short-lived (18,19). EUS guided or NOTES radiofrequency ablation has been utilized for ablating celiac ganglia in such patients (20). A special poly (lactic acid-co-glycolic acid)-poly (ethylene glycol)-poly (lactic acid-co-glycolic acid) (PLGA-PEG-PLGA) Thermogel has been designed for tunnel creation in NOTES, and the feasibility and safety has been validated to be good in a porcine model. This gel is sensitive to temperature, which is a fluid at room temperature but a gel at body temperature. Pavlov *et al.* ever reported the clinical experience of treating 10 patients with pain associated with pancreatic cancer by celiac plexus blockade under EUS navigation, and the data proved that it was simple, safe and highly effective (19). Celiac ganglia were first located by EUS and injections of local anesthetic bupivacaine and ethanol were made in celiac ganglia or surrounding celiac trunk by standard 22G fine needle. Ninety percent of the patients had an obvious pain reduction after 1–3 days after the procedure, including the frequency and dosage of analgesics, and there were no complications during the study period.

### ***EUS guided interstitial brachytherapy***

EUS guided interstitial brachytherapy could be used to treat unresectable pancreatic cancer growing surrounding

the gastrointestinal tract (21). We have ever established a novel EUS guided interstitial brachytherapy based special treatment planning system (TPS) for patients with unresectable pancreatic cancer, and the results indicated that this new TPS was feasible and effective in guiding the interstitial brachytherapy for advanced pancreatic cancer patients (22).

### ***Novel endoscopic therapies for pancreatic cancer***

EUS examinations can determine the location of the tumor much accurately based on the detection of ultrasound. Comprehensive therapy for pancreatic cancer is the main focus at present. The combination of endoscopic therapy with chemotherapy, radiotherapy and immunotherapy will be deepened. Anti-tumor agents into the tumor delivered under EUS is expected to kill tumor cells more directly and efficient (23). Placement of fiducial markers under endoscopy has been used for image-guided radiotherapy (24-26). A retrospective study of 514 patients who underwent EUS-guided fiducial marker placement showed that EUS guided fiducial marker placement without X-ray fluoroscopy was technically feasible and safe (24). A total of 1,093 gold fiducial markers were placed under EUS, and 510 fiducials were placed in 188 patients with pancreatic cancer. Only minimal intra-/post-procedure complications were recorded.

### **Conclusions and perspectives**

Endoscopic interventional therapy is an alternative treatment for patients with unresectable pancreatic cancer. Although the endotherapy for pancreatic cancer is not curative, it can help ease the symptoms and minimize the tumor size. Minimally invasive therapeutic procedures have several advantages over surgery in terms of rapid recovery, minimal trauma and less complication, and will be accepted as a promising treatment for advanced pancreatic cancer. In order to deal with the technical difficulty under endoscopy, the exploration of new device and equipment should be further carried on.

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