

Endoscopic Ultrasound-Guided Celiac Plexus Neurolysis for Pancreatic Cancer Pain: A Single-Institution Experience and Review of the Literature

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Abstract Pancreatic cancer is a common gastrointestinal malignancy with a poor prognosis. The primary goal for caregivers is effective palliative care, especially pain control, which is routinely managed by administration of narcotic analgesics. An alternative or adjunctive modality is celiac plexus neurolysis (CPN), a safe and effective procedure. Recent advances in the use of endoscopic ultrasonography (EUS) have made it an attractive guidance technique for CPN while allowing for a simultaneous tissue diagnosis. We report our experience using EUS-guided CPN and review the available literature regarding this modality.

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Pancreatic cancer is the second-most common gastrointestinal (GI) malignancy and fourth-leading cause of cancer deaths in the United States, with an estimated 32,180 new cases and 31,800 deaths in 2005.¹ The majority of these cases are unresectable as well as highly resistant to conventional chemoradiation therapies, leading to poor prognoses; less than 20% of patients survive their first year and only 4% survive for 5 years.^{2,3} Consequently, palliative care is often considered a primary goal of management. Narcotic analgesics are effective and serve as the mainstay of pain management for most patients. However, due to the severity of this pain, opioids may be effective at pain control only in dosages that induce significant side effects, such as constipation, nausea, vomiting, and delirium.

The abdominal pain of pancreatic cancer is usually secondary to cancer progression that causes neural invasion or nerve compression.⁴ Affected nerves from the abdominal viscera transmit signals via nociceptive pathways toward the central nervous system. The celiac plexus, which contains these autonomic fibers, is located in the retroperitoneal space posterior to the stomach and pancreas near the takeoff of the celiac artery.

The neuropathic pain of pancreatic carcinoma is a target for effective palliation.

Celiac plexus neurolysis (CPN) involves the injection of a neurolytic agent (absolute alcohol, most commonly) into or around the celiac plexus to disrupt these impulses and effectively control pain without the noted side effects typical of opioids. CPN has been performed percutaneously under guidance from fluoroscopy or computed tomography (CT) or at the time of laparotomy by isolating the celiac artery and injecting an agent into the surrounding area. Common side effects may include back or abdominal pain (96%), diarrhea (44%), and postural hypotension (38%).⁵ Rare complications such as paraplegia, bleeding, intestinal ischemia, pneumothorax, and lumbar puncture have been reported depending on various approaches; these causes are potentially secondary to imprecise identification of the celiac plexus with radiologic or anatomic landmarks, in addition to procedure-related structural injury or extravasations of the neurolytic agent.⁵

More recently, CPN performed under guidance with endoscopic ultrasound (EUS) has been explored. EUS was first developed to assist in detecting and staging GI malignancies, providing high-resolution images of GI and adjacent structures.⁶ With the advent of curvilinear echoendoscope and its fine-needle aspiration capability, retrieval of tissue and confirmation of diagnosis have become

Manuscript submitted January 10, 2006; accepted February 2, 2006.

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J Support Oncol 2006;4:460-462 © 2006 Elsevier Inc. All rights reserved.

a routine part of the examination. The vascular structures are readily identified with ultrasonography, and since the celiac artery takeoff is located within 1–2 cm of the proximal gastric wall, a short needle puncture and injection can be performed safely. As with other GI endoscopies, EUS may be performed on an outpatient basis using conscious sedation and can offer simultaneous tissue diagnosis and pain palliation. We report our experiences on pain management using EUS-guided CPN in patients with pancreatic cancer.

A Presenting Case

A 42-year-old man was admitted to the University of California at Davis Medical Center with a complaint of abdominal pain in the mid-epigastrium for several months. Four months prior to this admission, he suffered a perforated appendix complicated by postoperative venous thromboembolism. One month prior to admission, he presented to his primary care physician for similar symptoms. At that time, a CT scan showed inflammation and stranding of the pancreas consistent with pancreatitis. An upper GI endoscopy revealed only a hiatal hernia. He was placed on a proton pump inhibitor, advised to consume a low-fat diet, and given oral narcotics for pain control. However, the pain persisted, and he was referred to our institution.

The patient described progressive worsening of the mid-epigastric pain radiating to the back over several months. He rated the pain at 8 on a 0–10 rating scale (0 = no pain and 10 = the worst pain). He used hydrocodone on an as-needed basis but did not receive adequate analgesia. The physical examination was normal except for mild tenderness to palpation at the epigastrium and right-upper quadrant. Laboratory evaluation was normal.

An abdominal CT scan showed a 4 × 3 cm soft-tissue mass posterior to the body of the pancreas with adjacent lymphadenopathy. The patient was referred for EUS-guided fine-needle aspiration for tissue diagnosis. During a pre-procedure discussion, the physician and patient agreed that if the mass were adenocarcinoma with an advanced stage, palliative pain control with CPN would be performed. EUS showed the mass in the pancreatic body with encasement of the celiac artery and adjacent lymphadenopathy. Fine-needle aspiration and immediate cytopathology revealed adenocarcinoma. Given the progressive nature of the patient's abdominal pain, EUS-guided CPN was completed.

A curvilinear scanning echoendoscope (GF-UCT140, Olympus Corp., Melville, NY) was passed transorally through the pharynx and esophagus and into the stomach. The descending aorta was followed from the distal esophagus through the gastroesophageal junction to the point where the celiac artery takeoff was identified (Figure 1). A 22-gauge EUS needle (EchoTip, Wilson-Cook, Winston-Salem, NC) was introduced transgastrically under ultrasound guidance. Once the needle was in the anterocephalad position to the celiac artery takeoff, suction was applied to confirm no blood return. Sterile normal saline (3 mL) was injected to flush the channel, which was followed by 20 mL

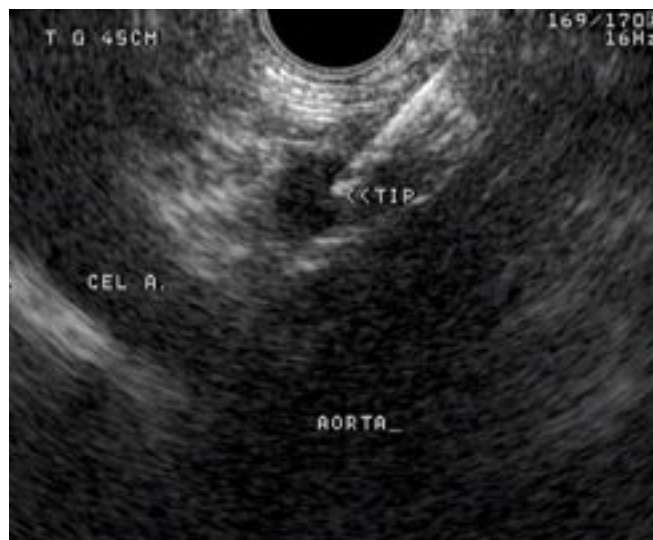


Figure 1 Endoscopic Ultrasound View of the Aorta and Celiac Artery

The needle tip is positioned at the celiac artery takeoff at approximately the location of the celiac plexus.

of 0.25% bupivacaine. Lastly, 20 mL of dehydrated alcohol was injected at the site. An echogenic cloud seen at the target site after alcohol injection confirmed that the substance was injected in the region of the celiac artery takeoff. The needle apparatus was withdrawn, and there was no evidence of immediate complications. Within 72 hours of the procedure, the patient reported significant relief of his abdominal pain and rated his pain as 2 on the 10-point scale. After 7 months, his abdominal pain returned, and he had a repeat CPN. The patient had adequate pain relief until he died 2 months later.

Case Series

A retrospective review of EUS-guided CPN performed at the University of California at Davis Medical Center between February 2003 and June 2005 revealed 10 EUS-guided CPN completed on 8 patients. There were 5 males and 3 females who underwent the procedure at a mean age of 54 years (range, 43–83 years). Six patients had stage IV disease and 2 patients had stage III disease. All were considered nonsurgical patients. All EUS-guided CPN procedures were performed similarly to the example case and were performed by one physician.

Pain relief was defined as a reduction in the numerical rating system for pain or a decrease in narcotic usage. Of the 10 procedures performed, 7 resulted in immediate pain relief, 4 of which were in patients who died within 7 months of diagnosis. Two procedures did not result in immediate alleviation of the abdominal pain, and both patients required hospital admission for pain control. One of those patients required multiple stents to alleviate symptoms of obstructive jaundice due to the malignancy; she required increasing amounts of narcotics until her death 3 months after diagno-

sis. One patient was lost to follow-up, and no outcome of the procedure was obtained.

Discussion

Since its initial description in 1914,⁷ CPN has been performed with techniques of progressive sophistication, each striving to increase efficacy and decrease complications. In the early 1990s, reviews of the efficacy of CPN produced conflicting conclusions. However, in 1995, Eisenberg et al⁵ published a meta-analysis that consisted of 24 papers reporting on 1,145 patients with cancer pain, 63% of whom had pancreatic malignancies. CPN was performed on all patients, although only 68% had radiographic guidance. Good-to-excellent control was reported in 89% of patients during the first 2 weeks after CPN, whereas 70%–90% maintained partial-to-complete control 3 months after CPN. Adverse effects such as increased pain, diarrhea, and postural hypotension were noted but were mostly mild and transient; adverse effects were rare.

In most studies, regardless of how CPN was performed, pain alleviation was achieved to a significant degree. In a prospective, randomized, double-blind study of 137 patients with unresectable pancreatic cancer,⁸ 65 underwent intraoperative chemical splanchnicectomy with alcohol. There were no differences in hospital mortality or complications between splanchnicectomy versus placebo, but the experimental group had significantly lower mean pain scores at 2, 4, and 6 months after the procedure. In another randomized controlled trial, all 61 patients underwent CPN through three different percutaneous techniques, and 70%–80% of all patients had complete pancreatic pain relief.⁹ The pain relief lasted beyond 3 months in 60%–75% of patients.

It has also been demonstrated that CPN significantly reduces opioid usage. In trials comparing CPN with or without narcotics, CPN has been shown to be an effective modality in treating pain. In a prospective, randomized, double-blind study of 24 patients with pancreatic cancer,¹⁰ 12 patients underwent CPN under fluoroscopic guidance and 12 patients were treated pharmacologically. All patients in the CPN group had significant reduction in visceral pain 24 and 48 hours after the procedure. These patients also had significantly less opioid use than the group treated with only pharmacologic means. Of these 12 patients, 10 had adequate pain relief until death, with 1 patient having complete relief with CPN alone.

In another trial with 20 patients with pancreatic cancer, 10 patients had CPN and achieved at least partial pain relief in 2 weeks.¹¹ All 10 patients had a significant reduction of opioid usage and 7 patients had long-term partial relief (> 3 weeks). In addition, CPN resulted in consistent quality of life for pancreatic cancer patients when added to pharmacologic therapy as compared with morphine or nonsteroidal anti-inflammatory drugs alone.¹²

More recently, EUS-guided CPN was reported as a safe and effective pain management modality in pancreatic cancer patients.¹³ In the initial series of 25 patients with pancreatic cancer who underwent EUS-guided CPN, pain relief was obtained in 88% of patients, for a median duration of 10 weeks. In a larger prospective study¹⁴ of 58 patients with painful and inoperable pancreatic cancer, mean pain scores were significantly lower at 2 weeks after EUS-guided CPN, and the effect was sustained at 24 weeks when adjusted for morphine use and adjuvant therapy. Of the 58 patients, 45 were noted to have reduced pain scores. Five patients had transient abdominal pain, 12 patients had hypotension that responded to fluids, and 9 patients had transient diarrhea that was treated with antidiarrheals.

We consider EUS-guided CPN an effective way to relieve pain from pancreatic cancer and believe that it offers advantages over other techniques. Both surgery and EUS provide direct access to the celiac plexus, but since EUS is less invasive, there are fewer complications. Preoperative detection and tissue diagnosis of pancreatic cancer are a routine part of the index EUS examination. If tissue diagnosis can be obtained during the procedure, CPN can be completed at the same time. The proximity of the celiac ganglia to the gastric wall ensures accurate placement of neurolytic agents while minimizing potential sequelae. With its anterior approach, the EUS method avoids traversing posterior structures, reducing the chance of their injury. Because of the inherent costs of conscious sedation and the endoscopic procedure itself, the cost-effectiveness is most enhanced when the procedure is performed at the time of diagnostic EUS-guided fine-needle aspiration; the added benefit is a reduced number of procedures for patients.¹⁵ The morbidity of EUS-guided CPN is low, and there has been no reported mortality. Thus, use of EUS-guided CPN should be considered and performed relatively early in the course of disease to offer optimal pain relief and increase the patient's quality of life.

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