Endosc Ultrasound. 2014 Oct-Dec; 3(4): 213–220.
doi: 10.4103/2303-9027.144515
PMCID: PMC4247528

EUS-guided celiac plexus interventions in pancreatic cancer pain: An update and controversies for the endosonographer

Leticia Perondi Luz,[1,2] Mohammad Ali Al-Haddad,[1] and John A. DeWitt[1]

[1]Department of Medicine, Division of Gastroenterology and Hepatology, Indiana University School of Medicine, United States

[2]Gastroenterology Section, Richard L. Roudebush VA Medical Center, Indianapolis, Indiana, United States

Address for correspondence Dr. Leticia Perondi Luz, E-mail: moc.liamtoh@zulaicitel

Received 2014 Feb 26; Accepted 2014 Jun 22.

Abstract

Patients with pancreatic cancer (pancreatic ductal adenocarcinoma [PDAC]) can develop abdominal pain that can be debilitating. Celiac plexus neurolysis (CPN) is a chemical ablation of the celiac plexus that can be used to treat pain caused by pancreatic malignancy. It can be performed by an anterior or posterior approach, and also can be done percutaneously or under guidance of transabdominal ultrasound, computed tomography, intra-operatively or most recently under linear endoscopic ultrasound (EUS) guidance (EUS-CPN). EUS is well-suited for identification of the celiac plexus due to the close proximity of the gastric wall to the origin of the celiac artery. EUS-CPN is now widely practiced, and different EUS approaches have been developed in order to improve the efficacy of this technique. Our objective is to review the use of EUS-CPN in PDAC, including a description of different techniques, review of its efficacy, predictors of pain response, and describe its limitations and safety, as well as new developments.

Keywords: Celiac plexus neurolysis, endoscopic ultrasound, pancreatic cancer

INTRODUCTION

Patients with pancreatic cancer (pancreatic ductal adenocarcinoma [PDAC]) commonly develop abdominal pain that can be debilitating. Celiac plexus neurolysis (CPN) is a chemical ablation of the celiac plexus that can be used to treat pain caused by PDAC.

Celiac plexus intervention for pancreatic pain was first described by Kappis in 1914.[1] The initial approach utilized for injection was posterior and percutaneous, which can nowadays also be performed under fluoroscopic or computed tomography (CT) guidance. A modified anterior approach can be performed under guidance of transabdominal ultrasound, CT, intra-operatively or most recently under linear endoscopic ultrasound (EUS) guidance (EUS-CPN). EUS is well-suited for identification of the celiac plexus due to the close approximation of the gastric wall with the origin of the celiac artery [Figure 1].

Endoscopic ultrasound-CPN was first described by Wiersema and Wiersema.[2] in 1996, in a series of 30 patients with

intra-abdominal malignancy treated with injection of bupivacaine and 98% absolute alcohol. Patients in this study reported significant improved pain scores at 12 weeks after the procedure. Since its first description, different EUS approaches have been developed in order to improve the efficacy of EUS-CPN. EUS-CPN is now widely practiced and current National Comprehensive Cancer Network guidelines (version 1.2014) for pancreatic adenocarcinoma, recommend EUS-CPN for the treatment of a severe tumor-associated pain.[3] In this review, we discuss EUS-CPN in PDAC from endosonographers perspective, focusing on efficacy, complications, different EUS approaches, as well as novel techniques.

OVERVIEW AND DEFINITIONS

Although the terms “celiac plexus” and “splanchnic nerves” are often used interchangeably, they are anatomically distinct structures. The splanchnic nerves are located above and posterior to the diaphragm and anterior most often to the T12 vertebra. The celiac plexus is located below and anterior to the diaphragm and surrounds the origin of the celiac trunk. This is usually located at the level of L1 vertebra, but may vary from T12 to L2. The celiac plexus is comprised of a dense network of ganglia and interconnecting fibers. In most patients, two to five ganglia are present. The right ganglia are, on average, 0.6 cm inferior to the celiac artery, while the left are 0.9 cm inferior to the celiac artery. The majority of pancreatic pain is mediated by sympathetic visceral afferent fibers relaying via the celiac plexus to the splanchnic nerves and entering the spinal cord at the 5^{th} to 9^{th} thoracic segments.[4,5,6,7]

Celiac plexus neurolysis refers to permanent ablation of the celiac plexus. It is usually performed by injection of phenol or alcohol in a patient with malignant disease such as PDAC. Celiac plexus block, on the other hand, denotes temporal inhibition of pain transmission via the celiac plexus. It is most commonly performed with injection of corticosteroid and long acting local anesthetic in a patient with chronic pancreatitis.

TECHNIQUE

The initial description of EUS-CPN by Wiersema and Wiersema involved placement of the linear EUS scope at the level of the celiac artery. It is then rotated toward the patient's left (clockwise rotation along axis of the endoscope) until the celiac artery origin is no longer visualized. A longitudinal view of the aorta however can still be seen. A fine-needle aspiration (FNA) needle is prepared by flushing the device with 0.9% saline solution. After removal of the stylet, a syringe with 5 ml of saline solution is attached to the hub of the needle. The needle assembly is placed through the biopsy channel and advanced immediately adjacent and anterior to the lateral aspect of the aorta under direct EUS visualization. Aspiration is performed, and if no blood is obtained, 3 ml of bupivacaine, followed by 10 ml of dehydrated 98% absolute alcohol are injected on each side of the celiac artery. This is called the bilateral technique. Alternatively, the entire mixture can be injected at one single location at the base of the celiac trunk (central injection). With this technique, the preloaded EUS needle is advanced in the angle between the base of the celiac artery and the aorta. With either technique, the alcohol injection creates an echogenic cloud adjacent to the aorta.[2]

Recent reports have documented accurate identification of celiac ganglia in 62-88% of patients with pancreatic cancer and 81-88% of unselected patients.[8,9,10,11] Therefore, researchers have evaluated whether efficacy of CPN can be improved by direct ganglia injection[12] (celiac ganglia neurolysis [CGN]). During EUS-CGN, direct ganglia injection is performed into as many visualized ganglia as possible. For a ganglion smaller than 1 cm, the needle tip is positioned within the central point of ganglia. For ganglia 1 cm or larger, the needle tip is typically advanced to the deepest point within the ganglia relative to the echoendoscope and the injectate is slowly administered while the needle is withdrawn within the ganglion.

Endosonographers with competency with EUS and EUS-FNA technique should be allowed to perform EUS-CPN. We do not believe this technique should be limited to referral centers.

CONTRAINDICATION

The principal contraindications to celiac plexus interventions include coagulopathy (international normalized ratio

>1.5), thrombocytopenia (platelets <50,000/L) and hemodynamic or respiratory instability prohibiting adequate sedation. Rarely, inability to visualize anatomical landmarks to ensure correct needle-tip placement may occur due to of altered anatomy secondary to previous surgery, large tumor mass or lymphadenopathy, or eccentric origin of the celiac artery or ectatic aorta.[6,12]

EFFICACY OF ENDOSCOPIC ULTRASOUND-CELIAC PLEXUS NEUROLYSIS

Endoscopic ultrasound guided neurolysis was first described in 1996 by Wiersema and Wiersema in 30 patients with intra-abdominal malignancy (25 with PDAC) treated with injection of bupivacaine and 98% absolute alcohol. Pain scores were assessed using a standardized 11-point continuous visual analog scale (VAS), with "0" equaling no pain, "5" moderate pain and "10" the worst pain ever. Pain relief was obtained in up to 88% of patients with a median duration of 10 weeks pain scores were significant lower compared with baseline at 2, 4, 8 and 12 weeks after EUS-CPN.[2] Subsequently, a prospective study by the same group including 58 patients with inoperable PDAC found decline in pain scores in 78% patients after EUS-CPN, pain scores were lower 2 weeks after the neurolysis, an effect that was sustained for 24 weeks when adjusted for morphine use and adjuvant therapy.[13]

In a meta-analysis of eight studies of EUS-CPN for PDAC in 283 patients, Puli *et al*. reported 80% of patients experienced pain relief. The majority (6/8) of the studies included in this meta-analysis used VAS pain scores to evaluate pain relief.[14] Although the authors could not determine whether EUS-CPN reduced narcotic requirements due to heterogeneous reporting in the included studies, an earlier meta-analysis by Yan and Myers reported a significant reduction in narcotic use with non-EUS guided CPN in 302 patients, in addition to decreased VA scores and constipation in the CPN group.[15] A recent Cochrane meta-analysis including six randomized controlled trials (358 patients) similarly showed a significant decrease in VAS score at 4 weeks and decreased in opioid consumption with percutaneous CPN approach.[16] In another meta-analysis by Kaufman *et al*.[17] which included three studies of EUS-CPN in PDAC pain (119 patients), EUS-guided CPN alleviated pain in 73% of patients.[17] This study did not evaluate opioid use. In a recent systematic review by Nagels *et al*., which included six observational studies of EUS-CPN in PDAC pain concluded that evidence suggest that EUS-CPN improves pain, but no conclusion could be made on opioid consumption.[18]

In a small abstract by Wallace *et al*., 36 patients were randomized to EUS-CPN versus sham. This trial found no difference in pain scores and quality of life (QOL) between the two groups however study is limited by small sample size and very short life expectancy at the time of diagnosis, as only 15 patients reached the 1 month end-point.[19] Finally, a double-blind, controlled trial by Wyse *et al*. which included 96 patients with advanced PDAC, early EUS-CPN provided greater pain relief compared to conventional therapy at 1 month and significantly greater at 3 months. Morphine consumption was similar in both groups at 1 month but tended toward lower consumption at 3 months in the neurolysis group.[20]

COMPLICATIONS OF ENDOSCOPIC ULTRASOUND-CELIAC PLEXUS NEUROLYSIS

Endoscopic ultrasound-CPN is a safe procedure, and serious complications are uncommon.[21] A recent review included 15 studies (661 patients) of EUS-CPN found complications occurred in 21% of patients. The most common adverse events were diarrhea in 10% and hypotension (responding to intravenous fluids) in 5%. These were minor and self-limited, usually lasted <48 h and were attributed to disruption of the sympathetic activity. Transient pain exacerbation occurred in 4%. This increased pain usually started shortly after the procedure and could last up to 48 h, requiring transient higher analgesic doses and rarely hospitalization.[22] Inebriation occurred in seven patients.[9,22,23] It is controversial whether direct ganglia injection and immediate pain after the procedure is associated with long lasting pain relief.[22]

Serious complications were rare and reported in 0.2% of EUS-CPN cases.[22] Self-limited retroperitoneal bleeding by laceration of left adrenal artery was reported in one anticoagulated patient with EUS-CPN using the bilateral approach.

Anticoagulation was stopped before the EUS-CPN, but patient bled when it was re-started several days later.[24]

Ischemia-related complications resulting in severe visceral injury and death have also been reported. Loeve and Mortensen[25] reported death from necrotic gastric perforation in a patient with chronic pancreatitis who underwent 13 injections of absolute alcohol over a period of 4 years. In this patient, laparotomy revealed a 5 cm profusely bleeding necrotic area of the aorta just above the celiac trunk and a large perforation of the posterior wall of the stomach. Vascular intervention was impossible, and the patient died of exsanguination. In another case, Gimeno-García *et al*.[26] reported that a CT 1 day after bilateral EUS-CPN showed complete thrombosis of the celiac artery take-off resulting in fatal hepatic, splenic and right kidney infarction and pneumatosis of the gut. In another case, Jang *et al*. reported a fatal case with hepatic and splenic infarction, as well as ischemia of the stomach and proximal small bowel after EUS-CPN (central injection).[27] Diffusion of ethanol into the celiac artery resulting in arterial vasospasm, the sclerosing effect of absolute alcohol and arterial embolisms after injection are a plausible mechanism for injury.[22,27]

Paralysis due to anterior spinal cord infarction has been recently reported in a patient with unresectable PDAC, who underwent EUS-CGN.[28,29] Anterior spinal cord syndrome secondary to CPN may be related to injury of the lumbar artery leading into the artery of Adamkiewicz, which originates from the aorta, supplies the lower two-thirds of the anterior spinal artery, and anatomically is closely related to the celiac ganglion. The mechanism of acute spinal cord ischemia after vascular puncture may involve vasospasm due to high alcohol concentration and high-volume, needle injury causing acute thrombosis, or propagation of alcohol along segmental arteries causing multiple artery spasm. Periprocedural prolonged hypotension may also contribute in some patients.[29]

Infectious complications have been reported with celiac plexus block including retroperitoneal abscess[21,30,31] and empyema.[32] The only infectious event after CPN was a brain abscess in a patient with lymphopenia, which was successfully treated with antibiotics.[33]

LIMITATIONS OF ENDOSCOPIC ULTRASOUND-CELIAC PLEXUS NEUROLYSIS

There are few limitations to the EUS approach for celiac neurolysis. The inability to visualize anatomical landmarks to ensure correct needle-tip placement may rarely occur after previous surgery or with a large tumor mass. Furthermore, cachexia can cause loss of the soft-tissue space between the gastric wall and the aorta leaving little room to place the tip of the needle. Finally, an ectatic aorta or an eccentric origin of the celiac artery may create technical difficulties as well. Celiac ganglia can be difficult to visualize in about 20% of patients, which makes direct ganglia injection impossible.[10,34]

GANGLIA INJECTION

Endoscopic ultrasound can identify celiac ganglia in 62-89% of patients; in 62-88% of patients with pancreatic cancer and 81-88% of unselected patients.[8,9,10,11] In our experience, celiac ganglia can be visualized in approximately 70% of subjects. Rate of ganglia detection appears to vary among endosonographers, and an earlier study suggest ganglia are best visualized with the curvilinear scope.[9,10,11,35] Interest has developed in direct celiac ganglia injection (CGN) to improve the efficacy of CPN [Figure 2]. Levy *et al*. retrospectively reported results of CGN in 33 patients, including 18 patients with PDAC[12] and found that 94% of patients reported pain relief at weeks 2-4. In addition, initial pain exacerbation occurred in 34% of patients and correlated with better pain relief. In a recent randomized, multicenter controlled trial including 68 patients with upper abdominal cancer pain (90% PDAC), celiac ganglion neurolysis was more effective than CPN in relieving pain (73.5% *vs*. 45.5%, respectively; $P = 0.02$).[9] Despite the superiority of EUS-CPG over CPN in achieving pain control, in patients with advanced malignancy in which ganglia cannot be visualized we still believe celiac neurolysis should be performed, given overall safety of procedure and effectiveness in pain relief provided by neurolysis.

BILATERAL VERSUS CENTRAL INJECTION IN ENDOSCOPIC

ULTRASOUND-CELIAC PLEXUS NEUROLYSIS

In a nonrandomized study, Sahai *et al*. evaluated the efficacy of bilateral injection compared with central injection in 160 consecutive patients (72 patients with PDAC).[24] The authors found that the bilateral injection was the only predictor of >50% pain reduction by day 7. Celiac ganglia were neither targeted nor avoided. Bilateral injection included areas lateral to the superior mesenteric artery (SMA) and celiac take-off. There was one serious complication in this study, which was self-limited retroperitoneal bleeding due to laceration of the adrenal artery following bilateral block in an anticoagulated patient. In a subsequent a single-blinded trial, LeBlanc *et al*. randomized 50 patients with PDAC to central or bilateral CPN and found no difference in efficacy between both groups.[36] Celiac ganglia were not targeted in this study. In a meta-analysis by Puli *et al*., including 283 patients, a subgroup analysis showed that with bilateral injection, the proportion of patients with pain relied was 84% and with central injection the proportion was much lower at 46%.[14]

DOSE OF ALCOHOL AND ANESTHETIC

The dose of alcohol used for EUS-CPN is not standardized and ranges from 2 to 20 ml[2,12,13,24,37,38] LeBlanc *et al*. found that CPN (ganglia or central injection) with 10 or 20 ml of 98% alcohol resulted in similar complications and pain relief between the two groups.[37]

As observed by Wiersema and Wiersema during the initial description of EUS-CPN, injection of alcohol produces objective evidence of discomfort despite moderate sedation. Since then, anesthetic is employed prior to alcohol injection to minimize this effect.[2] The type, dose and concentration of anesthetic used during EUS-CPN is not standardized. In most studies, bupivacaine was used in a concentration ranging between 25% and 75% and in a dose ranging between 3 and 20 ml.[2,6,12,13,24,36,39] Other studies have used lidocaine 1%, dose ranging from 3 to 10 ml.[8,38] Currently, there are no studies accessing effectiveness of different anesthetics or dosage. In addition, it is unclear if when neurolysis is being performed with anesthesiologist support the use of anesthetic is needed. It is, however, our current practice to use as we perform CGN whenever feasible, which can be associated with exacerbation of pain shortly after the procedure.

TYPE OF NEEDLE

A variety of commercially available FNA needles is currently available which range in size from 19 to 25-gauge. Most endosonographers perform CPN with standard 22-gauge FNA needles which are widely availability and easy to use. This needle, however, may require slow, forceful injection to disseminate the alcohol during CPN. A 20-gauge needle specifically designed for EUS-guided celiac plexus interventions (EchoTip celiac plexus needle; Cook Medical, Winston-Salem NC; USA) differs from other EUS needles in that it does not have a removable stylet. Rather, this device has a solid, sharp, conical tip, and an array of side holes for radial delivery of the desired agent into the celiac plexus and/or the perineural space.[40] This “spray” needle provides easy and quick injection, with multidirectional delivery of the agent in the celiac area, however echogenic “blush” is not seen at the time of injection. Furthermore, this needle is not available in some countries.[6] A 19-gauge needle offers little if any resistance to injection however transgastric puncture can be difficult in some patients. At present, there are no studies specifically comparing various needle types or sizes in CPN.

PREDICTORS OF RESPONSE

Injection of visualized ganglia appears to be the best predictor of pain response in EUS-CPN. A retrospective study by Ascunce *et al*.[8] compared patients with PDAC who underwent EUS-CPN with direct ganglia injection (when visible) versus bilateral injection. Of the 64 patients enrolled, 40 (62.5%) had visible celiac ganglia, with a media of 2 ganglia identified (range: 1-4). At week 1, 50% of patients had symptomatic pain improvement and in a multivariate analysis, visualization of the ganglia was the best predictor of response. Specifically, patients with visible ganglia were over 15 times more likely to respond (odds ratio [OR]: 15.7; $P < 0.001$). Tumors located outside the head of the pancreas and

patients with higher baseline pain level were weakly associated with a good response. In the randomized pilot study by LeBlanc *et al*. comparing 10 and 20 ml of alcohol injection during neurolysis, there was no difference in complete pain response between the two groups, and two-thirds of complete responders in each group had direct injection of celiac ganglia.[37] Finally, in a recent randomized multicenter trial by Doi *et al*., including 68 patients with upper abdominal cancer pain (90% PDAC), CGN was more effective than CPN (central injection) in providing pain relief (73.5% *vs*. 45.5%, respectively; $P = 0.02$).[9] In another study by Iwata *et al*., which included 47 consecutive patients who underwent EUS-CPN (central injection) with absolute ethanol containing a contrast medium, pain relief occurred in 68% of patients and on multivariate analysis direct invasion of the celiac trunk and distribution of ethanol only on the left side of the celiac artery were significant factors for a negative response to EUS-CPN (OR = 4.82 and 8.67, $P = 0.03$ and 0.02, respectively).[23]

NEW TECHNIQUES

Repeat celiac plexus neurolysis

Patient survival can in times exceed the benefit of CPN, and therefore occasionally repeat CPN may be considered. In a retrospective study including 24 patients with PDAC in which repeat percutaneously guided neurolysis was performed, the success rate decreased from 67% after initial CPN to 29% following repeat CPN ($P = 0.13$) with an associated decrease in mean duration of pain relief from 3.4 months for initial CPN to 1.6 months of repeat CPN ($P = 0.03$).[41] In a recent retrospective study by our group,[42] including 50 patients with PDAC in which repeat EUS- CPN was performed, the mean number of EUS-CPN was 2.2. The mean duration of pain relief after the first CPN was 13 weeks and after the second CPN 8 weeks. Response to the first CPN was associated with response to the second CPN ($P < 0.0001$). Surprisingly direct ganglia injection was not associated with the pain response. Repeat EUS-CPN was safe, only one minor complication occurred after the first CPN (postprocedural abdominal pain) and there was no major complications reported-up to the forth CPN. Prospective studies are needed to further confirm the safety and determine efficacy of repeat EUS-CPN.

ENDOSCOPIC ULTRASOUND-GUIDED BROAD PLEXUS NEUROLYSIS OVER THE SUPERIOR MESENTERIC ARTERY

Sakamoto *et al*.[38] presented a single-center study comparing the pain-relieving effectiveness of standard EUS-CPN with EUS-guided broad plexus neurolysis (EUS-BPN) in 67 patients with advanced abdominal cancer (89% of those PDAC). EUS-BPN uses 25-gauge needle to inject both sides of the SMA. Postprocedure CT was used to assess the spread of the neurolytic agent (mixed with contrast) around the celiac, superior and inferior mesenteric areas and evaluate the relationship between pain relief and the number of contrast-bearing areas. The EUS-BPN group had more patients with six contrast-bearing areas (42%) than the EUS-CPN group (0%). These patients had significantly better short-term and long-lasting pain relief than patients with <5 contrast-bearing areas. EUS-BPN patients exhibited significantly greater reductions in days 7 and 30 visual analog pain scale scores than EUS-CPN patients. Although those results are promising, those results should be interpreted with caution as this study was retrospective and nonrandomized.[43] Further studies are needed to better determine the efficacy of this new approach.

ENDOSCOPIC ULTRASOUND-GUIDED CELIAC GANGLION IRRADIATION WITH IODINE-125 SEEDS

Brachytherapy involves the insertion of a radioactive seed directly into a pancreatic tumor for localized therapy. The most common radioactive seed used clinically is iodine-125, which has a half-time of 59.7 days and tissue penetration of 1.7 cm.[44] Currently, in the three series reporting brachytherapy with EUS implanted seeds in advanced PDAC, no significant survival benefit occurred, however pain scores were significantly reduced.[45,46,47] In the most recent and largest series[46] of 100 patients with advanced PDAC undergoing brachytherapy with EUS implanted seeds, pain scores dropped dramatically after 1-week postimplantation, with sustained results until the 3rd month. The same group

then reported the use of iodine-125 as a neurolytic agent in 23 patients undergoing EUS-guided CGN for unresectable PDAC.[48] The mean number of seeds implanted in the celiac ganglion was 4 (range: 2-6). Immediately after the procedure, pain relief and analgesic consumption showed no significant changes compared to pre-CPG values and 26% of patients reported pain exacerbation. However, at week 2, 82% of patients had a reduction in pain score on a VAS, and the mean narcotic consumption had decreased. This effect lasted until the study conclusion at 5 months follow-up when only two patients were still alive. No major complications occurred. The authors postulate that iodine-125 may be a superior neurolytic agent compared with ethanol due to its longer half-life and deeper tissue penetration, although this has yet to be confirmed in controlled clinical trial. Larger studies are needed to further evaluate this technique, including assessment of patient safety studies as well as safety of handling and storing radioactive material at endoscopy suites.

SELECTION OF PATIENTS FOR ENDOSCOPIC ULTRASOUND-CELIAC PLEXUS NEUROLYSIS

Patients with PDAC are most commonly seen by gastroenterologists only at the time of initial diagnosis for biopsy or stenting. If a PDAC is an unresectable tumor and pain affecting QOL or requiring narcotics (usually body and tail cancers) at the time of presentation then, EUS-CPN should be offered simultaneously with the planned EUS-FNA, and this is our current practice. In a study by Ascunce *et al*., tumors located outside the head of the pancreas and patients with higher baseline pain level were associated with a good response.[8] Patients who fail medical management should not be the only ones considered. Earlier therapy may be better than waiting for medical failure. In a study by Wyse *et al*., early EUS-CPN at the time of EUS-FNA reduced pain in patients with inoperable PDAC.[20] Patients with resectable tumors usually do not have pain, so these are less likely to be candidates for EUS-CPN at the time of diagnostic EUS. Patients should be offered repeat CPN if it initially aids but the pain the effect wears off, although evidence is limited.[41,42] These repeat referrals are usually directed by the oncologist or surgeon.

CONCLUSION

Endoscopic ultrasound permits real-time visualization and utilizes an anterior approach for CPN, which allows more precise needle placement and avoidance of intervening structures. Since first description of EUS-CPN, investigators have employed several technical variations in terms of target of injection, composition and volume of the injectate. Until date, targeted injection at the visualized celiac ganglia has been shown to be the best predictor of pain response in EUS-CPN. Further prospective studies are needed to evaluate the clinical utility of different approaches for EUS-CPN.

Footnotes

Source of Support: Nil.

Conflict of Interest: None declared.

REFERENCES

1. Kappis M. Erfahrungen mit local anasthesie bie bauchoperationen. Vehr Dtsch Gesellsch Chir. 1914;43:87–9.
2. Wiersema MJ, Wiersema LM. Endosonography-guided celiac plexus neurolysis. Gastrointest Endosc. 1996;44:656–62. [PubMed: 8979053]
3. NCCN guidelines. 2014 for Pancreatic Adenocarcinoma. [Last accessed on 2014 February]. Available from: http://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf .
4. Soweid AM, Azar C. Endoscopic ultrasound-guided celiac plexus neurolysis. World J Gastrointest Endosc. 2010;2:228–31. [PMCID: PMC2999129] [PubMed: 21160938]
5. Ward EM, Rorie DK, Nauss LA, et al. The celiac ganglia in man: Normal anatomic variations. Anesth Analg. 1979;58:461–5. [PubMed: 574729]
6. Penman ID, Gilbert D. Basic technique for celiac plexus block/neurolysis. Gastrointest Endosc. 2009;69:S163–5.

[PubMed: 19179148]
7. Brown DL, Moore DC. The use of neurolytic celiac plexus block for pancreatic cancer: Anatomy and technique. J Pain Symptom Manage. 1988;3:206–9. [PubMed: 3192964]
8. Ascunce G, Ribeiro A, Reis I, et al. EUS visualization and direct celiac ganglia neurolysis predicts better pain relief in patients with pancreatic malignancy (with video) Gastrointest Endosc. 2011;73:267–74. [PubMed: 21295640]
9. Doi S, Yasuda I, Kawakami H, et al. Endoscopic ultrasound-guided celiac ganglia neurolysis vs. celiac plexus neurolysis: A randomized multicenter trial. Endoscopy. 2013;45:362–9. [PubMed: 23616126]
10. Gleeson FC, Levy MJ, Papachristou GI, et al. Frequency of visualization of presumed celiac ganglia by endoscopic ultrasound. Endoscopy. 2007;39:620–4. [PubMed: 17549662]
11. Ha TI, Kim GH, Kang DH, et al. Detection of celiac ganglia with radial scanning endoscopic ultrasonography. Korean J Intern Med. 2008;23:5–8. [PMCID: PMC2686954] [PubMed: 18363273]
12. Levy MJ, Topazian MD, Wiersema MJ, et al. Initial evaluation of the efficacy and safety of endoscopic ultrasound-guided direct Ganglia neurolysis and block. Am J Gastroenterol. 2008;103:98–103. [PubMed: 17970834]
13. Gunaratnam NT, Sarma AV, Norton ID, et al. A prospective study of EUS-guided celiac plexus neurolysis for pancreatic cancer pain. Gastrointest Endosc. 2001;54:316–24. [PubMed: 11522971]
14. Puli SR, Reddy JB, Bechtold ML, et al. EUS-guided celiac plexus neurolysis for pain due to chronic pancreatitis or pancreatic cancer pain: A meta-analysis and systematic review. Dig Dis Sci. 2009;54:2330–7. [PubMed: 19137428]
15. Yan BM, Myers RP. Neurolytic celiac plexus block for pain control in unresectable pancreatic cancer. Am J Gastroenterol. 2007;102:430–8. [PubMed: 17100960]
16. Arcidiacono PG, Calori G, Carrara S, McNicol ED, Testoni PA. Celiac plexus block for pancreatic cancer pain in adults. Cochrane Database Syst Rev. 2011;16:CD007519. [PubMed: 21412903]
17. Kaufman M, Singh G, Das S, et al. Efficacy of endoscopic ultrasound-guided celiac plexus block and celiac plexus neurolysis for managing abdominal pain associated with chronic pancreatitis and pancreatic cancer. J Clin Gastroenterol. 2010;44:127–34. [PubMed: 19826273]
18. Nagels W, Pease N, Bekkering G, et al. Celiac plexus neurolysis for abdominal cancer pain: A systematic review. Pain Med. 2013;14:1140–63. [PubMed: 23802777]
19. Wallace MB, Woodward TA, Hoffman BJ, et al. A prospective double blind randomized controlled trial of EUS guided celiac neurolysis vs. sham for pancreatic cancer pain. Gastrointest Endosc. 2010;71:AB224.
20. Wyse JM, Carone M, Paquin SC, et al. Randomized, double-blind, controlled trial of early endoscopic ultrasound-guided celiac plexus neurolysis to prevent pain progression in patients with newly diagnosed, painful, inoperable pancreatic cancer. J Clin Oncol. 2011;29:3541–6. [PubMed: 21844506]
21. O'Toole TM, Schmulewitz N. Complication rates of EUS-guided celiac plexus blockade and neurolysis: Results of a large case series. Endoscopy. 2009;41:593–7. [PubMed: 19588286]
22. Alvarez-Sánchez MV, Jenssen C, Faiss S, et al. Interventional endoscopic ultrasonography: An overview of safety and complications. Surg Endosc. 2014;28:712–34. [PubMed: 24196551]
23. Iwata K, Yasuda I, Enya M, et al. Predictive factors for pain relief after endoscopic ultrasound-guided celiac plexus neurolysis. Dig Endosc. 2011;23:140–5. [PubMed: 21429019]
24. Sahai AV, Lemelin V, Lam E, et al. Central vs. bilateral endoscopic ultrasound-guided celiac plexus block or neurolysis: A comparative study of short-term effectiveness. Am J Gastroenterol. 2009;104:326–9. [PubMed: 19174816]
25. Loeve US, Mortensen MB. Lethal necrosis and perforation of the stomach and the aorta after multiple EUS-guided celiac plexus neurolysis procedures in a patient with chronic pancreatitis. Gastrointest Endosc. 2013;77:151–2. [PubMed: 22624792]
26. Gimeno-García AZ, Elwassief A, Paquin SC, et al. Fatal complication after endoscopic ultrasound-guided celiac plexus neurolysis. Endoscopy. 2012;44(Suppl 2 UCTN):E267. [PubMed: 22814913]
27. Jang HY, Cha SW, Lee BH, et al. Hepatic and splenic infarction and bowel ischemia following endoscopic ultrasound-guided celiac plexus neurolysis. Clin Endosc. 2013;46:306–9. [PMCID: PMC3678073] [PubMed: 23767046]
28. Fujii L, Clain JE, Morris JM, et al. Anterior spinal cord infarction with permanent paralysis following endoscopic ultrasound celiac plexus neurolysis. Endoscopy. 2012;44(Suppl 2 UCTN):E265–6. [PubMed: 22814912]
29. Mittal MK, Rabinstein AA, Wijdicks EF. Pearls & oy-sters: Acute spinal cord infarction following endoscopic ultrasound-guided celiac plexus neurolysis. Neurology. 2012;78:e57–9. [PubMed: 22371417]
30. Gress F, Schmitt C, Sherman S, et al. A prospective randomized comparison of endoscopic ultrasound- and computed tomography-guided celiac plexus block for managing chronic pancreatitis pain. Am J Gastroenterol.

1999;94:900–5. [PubMed: 10201454]
31. Muscatiello N, Panella C, Pietrini L, et al. Complication of endoscopic ultrasound-guided celiac plexus neurolysis. Endoscopy. 2006;38:858. [PubMed: 17001583]
32. Mahajan R, Nowell W, Theerathorn P. Empyema after endoscopic ultrasound-guided celiac plexus (EUS-CPB) in chronic pancreatitis (CP): Experience at an academic center. Gastrointest Endosc. 2002;55:AB101.
33. Lalueza A, Lopez-Medrano F, del Palacio A, et al. Cladosporium macrocarpum brain abscess after endoscopic ultrasound-guided celiac plexus block. Endoscopy. 2011;43(Suppl 2 UCTN):E9–10. [PubMed: 21271535]
34. Penman ID, Rösch T. EUS 2008 Working Group. EUS 2008 Working Group document: Evaluation of EUS-guided celiac plexus neurolysis/block (with video) Gastrointest Endosc. 2009;69:S28–31. [PubMed: 19179165]
35. Seicean A. Celiac plexus neurolysis in pancreatic cancer: The endoscopic ultrasound approach. World J Gastroenterol. 2014;20:110–7. [PMCID: PMC3885999] [PubMed: 24415863]
36. LeBlanc JK, Al-Haddad M, McHenry L, et al. A prospective, randomized study of EUS-guided celiac plexus neurolysis for pancreatic cancer: One injection or two? Gastrointest Endosc. 2011;74:1300–7. [PubMed: 22000795]
37. Leblanc JK, Rawl S, Juan M, et al. endoscopic ultrasound-guided celiac plexus neurolysis in pancreatic cancer: A prospective pilot study of safety using 10 mL versus 20 mL Alcohol. Diagn Ther Endosc 2013. 2013:327036. [PMCID: PMC3556397]
38. Sakamoto H, Kitano M, Kamata K, et al. EUS-guided broad plexus neurolysis over the superior mesenteric artery using a 25-gauge needle. Am J Gastroenterol. 2010;105:2599–606. [PubMed: 20823834]
39. Harada N, Wiersema MJ, Wiersema LM. Endosonography-guided celiac plexus neurolysis. Gastrointest Endosc Clin N Am. 1997;7:237–45. [PubMed: 9101264]
40. Adler DG, Conway JD, Coffie JM, et al. EUS accessories. Gastrointest Endosc. 2007;66:1076–81. [PubMed: 17892880]
41. McGreevy K, Hurley RW, Erdek MA, et al. The effectiveness of repeat celiac plexus neurolysis for pancreatic cancer: A pilot study. Pain Pract. 2013;13:89–95. [PubMed: 22568823]
42. Sey MA, Dewitt JM, Leblanc JK. Repeat endoscopic ultrasound-guided celiac plexus block and neurolysis: What is the efficacy and safety? Am J Gastroenterol. 2013;108:s572–620.
43. Virtue MA, Levy MJ. Editorial: Neurolysis for pancreatic cancer pain: Same song, diff erent verse? Am J Gastroenterol. 2010;105:2607–9. [PubMed: 21131929]
44. Jin Z, Chang KJ. Endoscopic ultrasound-guided fiducial markers and brachytherapy. Gastrointest Endosc Clin N Am. 2012;22:325–31. x. [PubMed: 22632954]
45. Jin Z, Du Y, Li Z, et al. Endoscopic ultrasonography-guided interstitial implantation of iodine 125-seeds combined with chemotherapy in the treatment of unresectable pancreatic carcinoma: A prospective pilot study. Endoscopy. 2008;40:314–20. [PubMed: 18283622]
46. Du Y, Jin Z, Meng H, et al. Long-term effect of gemcitabine-combined endoscopic ultrasonography-guided brachytherapy in pancreatic cancer. J Interv Gastroenterol. 2013;3:18–24.
47. Sun S, Xu H, Xin J, et al. Endoscopic ultrasound-guided interstitial brachytherapy of unresectable pancreatic cancer: Results of a pilot trial. Endoscopy. 2006;38:399–403. [PubMed: 16680642]
48. Wang KX, Jin ZD, Du YQ, et al. EUS-guided celiac ganglion irradiation with iodine-125 seeds for pain control in pancreatic carcinoma: A prospective pilot study. Gastrointest Endosc. 2012;76:945–52. [PubMed: 22841501]

Figures and Tables

Figure 1

Linear-array eus imaging of the aorta (AO) at the level of the celiac artery (CX) and superior mesenteric artery (SMA) take-off

Figure 2

Linear-array EUS images of direct celiac ganglia injection. CEL AX: Celiac Axis; GANG: Ganglia

---