International Journal of Gastrointestinal Intervention

journal homepage: www.ijgii.org

Review Article

Recent topics on endoscopic ultrasonography-guided celiac plexus neurolysis

Ichiro Yasuda^{1,*}, Tatsuyuki Hanaoka¹, Kosuke Takahashi¹, Yasuhiro Araki¹, Shinpei Doi², Takuji Iwashita³, Keisuke Iwata⁴, and Tsuyoshi Mukai⁵

A B S T R A C T

Endoscopic ultrasonography-guided celiac plexus neurolysis (EUS-CPN) is a widely practiced technique. Three sets of guidelines have recently been published and this procedure has become a major EUS technique. However, there are still several unanswered questions. The purpose of this manuscript is to review the recent literature pertaining to EUS-CPN. Currently, the main indication of EUS-CPN is pancreatic cancer pain. It is also performed for patients with chronic pancreatitis, but the indication is controversial due to its limited efficacy and a high incidence of infectious complications. Various techniques, such as central and bilateral EUS-CPN, and EUS-guided direct celiac ganglia neurolysis (EUS-CGN) have been performed. However, the efficacies of these techniques remain controversial. Complications related to the procedures are generally not serious, but major adverse events, such as paraplegia and ischemic complications, have been reported. The impacts of EUS-CPN on survival have also been evaluated. Although increased survival was expected via improvements in the quality of life, data suggests that EUS-CPN related procedures, especially EUS-CGN, might reduce the survival time. However, precise mechanisms have not been elucidated. In addition to conventional techniques, new techniques, such as EUS-guided celiac ganglion radiofrequency ablation (EUS-RFA) and the use of highly viscous phenol-glycerol, dexmedetomidine, and contrast-enhanced agents, have been introduced. However, these techniques are still in experimental stages. Additional studies need to be conducted to address these gaps in the literature.

Copyright © 2020, Society of Gastrointestinal Intervention.

Keywords: Celiac plexus; Endoscopic ultrasonography; Neurolysis; Pancreatic cancer

Introduction

The celiac plexus is a nerve bundle that transmits pain sensations from the upper abdominal organs. Celiac plexus neurolysis (CPN) involves the injection of a neurolytic or analgesic agent into the celiac plexus to disrupt the transmission of pain signals from afferent nerves to the spinal cord. This technique has been performed intraoperatively or under the guidance of fluoroscopy, computed tomography, or ultrasonography. Furthermore, endoscopic ultrasonography-guided CPN (EUS-CPN) was introduced by Faigel et al¹ and Wiersema and Wiersema² in 1996. The EUS-guided approach seems to be safer, more effective, and more convenient compared to previous approaches because it can be

performed using real-time precise imaging with color Doppler assessment as a guide. EUS-CPN is widely practiced and has become a major interventional EUS technique. The purpose of this manuscript is to review the recent literature regarding the safety and efficacy of EUS-CPN.

Methods

We used MEDLINE and PubMed to search for manuscripts that were written in English and published between January 2015 and July 2020. The keywords “EUS” OR “endoscopic ultrasound” AND “celiac plexus” were used. The initial search identified 67 articles. Forty-three articles were deemed relevant to this review

¹Third Department of Internal Medicine, University of Toyama, Toyama, Japan

²Department of Gastroenterology, Teikyo University Mizonokuchi Hospital, Kawasaki, Japan

³First Department of Internal Medicine, Gifu University, Gifu, Japan

⁴Department of Gastroenterology, Gifu Prefectural Medical Center, Gifu, Japan

⁵Department of Gastroenterology, Gifu Municipal Hospital, Gifu, Japan

Received August 10, 2020; Accepted September 3, 2020

* Corresponding author. Third Department of Internal Medicine, University of Toyama, 2630 Sugitani, Toyama 930-0194, Japan.

E-mail address: yasudaic@med.u-toyama.ac.jp (I. Yasuda).

after screening their titles. After reviewing the abstracts, complete texts were obtained for potentially relevant articles. Manual recursive searches of the reference sections of these articles were conducted to identify other potentially relevant articles, which were then reviewed in detail.

Indications

Currently, pain associated with pancreatic cancer is the main indication for EUS-CPN. Approximately 90% of patients with advanced pancreatic cancer report pain as a common symptom and it is a major issue associated with treatment in these patients.³

EUS-CPN is also used to alleviate pain originating from chronic pancreatitis. Local analgesic agents, such as bupivacaine, and steroids are usually used to alleviate pain associated with benign diseases; this procedure is called EUS-guided celiac plexus block (EUS-CPB). However, the use of EUS-CPB in patients with chronic pancreatitis remains controversial due to its limited efficacy and a higher incidence of serious complications compared to EUS-CPN, which is used for pancreatic cancer pain. In addition, repeated procedures are required for a long prognosis of benign diseases; however, an excessive number of sessions may cause vascular injuries and ischemic complications.^{3,4} To address these concerns, Sey et al⁵ evaluated the effectiveness and safety of repeated EUS-CPB for pain in patients with chronic pancreatitis. A total of 248 patients underwent a mean of 3.1 procedures. After the first EUS-CPB, 76% of the patients obtained pain relief and the median duration of pain relief was 10 weeks. Older age at the time of the first EUS-CPB and pain relief after the first EUS-CPB were significantly associated with pain relief after subsequent EUS-CPB procedures. Adverse events included peri-procedural hypoxia ($n = 2$), hypotension ($n = 1$), postprocedural orthostasis hypotension ($n = 1$), and diarrhea ($n = 4$). No major adverse events occurred. That study concluded that performing repeated EUS-CPB procedures is safe.

A case study reported that EUS-CPB using triamcinolone and bupivacaine was effective for chronic abdominal pain secondary to mesenteric panniculitis.⁶ As mentioned above, any pain originating from the upper abdominal organs can be an indication for EUS-CPN/EUS-CPB.

Conventional Techniques

Various techniques related to EUS-guided celiac plexus ablation have been introduced (Fig. 1).³ Classic EUS-CPN approaches are represented by the central technique and bilateral technique. The neurolytic agent is injected at the base of the celiac axis (CA) in the central technique, and on both sides of the CA (in a position lateral to the point where the superior mesenteric artery [SMA] originates from the aorta) in the bilateral technique. In addition, EUS-guided broad plexus neurolysis (EUS-BPN) is modified from the bilateral EUS-CPN technique.⁷ In EUS-BPN, the needle is advanced deeper than in the conventional bilateral technique, over the level of the SMA to distribute the agent more widely. Another major technique is EUS-guided direct celiac ganglia neurolysis (EUS-CGN).⁸ In this technique, the celiac ganglion is identified and punctured with a needle before ethanol is injected.

Efficacy and Prognostic Factors following Treatment

Two recent meta-analyses demonstrated that pain relief was experienced by 73%–80% of patients with pancreatic cancer and in 51%–59% of patients with chronic pancreatitis after EUS-

CPN.^{9,10}

Some data also suggested that broad distribution of the injected ethanol was an important factor associated with a good response.^{7,11} A previous meta-analysis revealed that the rate of pain relief was much higher in pancreatic cancer patients treated with bilateral EUS-CPN compared to those treated using central EUS-CPN (84.5% vs 46.0%, respectively).⁹ Furthermore, a randomized controlled trial (RCT) revealed that the mean pain reduction score was significantly higher in the bilateral EUS-CPN group than in the central EUS-CPN group (70.4% vs 45.9%, respectively). A positive response (> 50% reduction in pain score) was also significantly more frequent in the bilateral EUS-CPN group than in the central EUS-CPN group (77.5% vs 50.7%, respectively). On the other hand, another RCT found no significant difference in pain relief between the central and bilateral EUS-CPN groups (69% vs 81%, respectively).¹² Another retrospective study also showed similar amounts of pain reduction in the central and bilateral EUS-CPN groups (50% vs 60%, respectively).¹³ The most recent meta-analysis by Lu et al¹⁴ included 437 patients from six eligible studies and analyzed the analgesic efficacy and safety of bilateral EUS-CPN compared to central EUS-CPN. The short-term analgesic effects and general risks of bilateral EUS-CPN were comparable with those of central EUS-CPN, but the study revealed that the bilateral approach significantly reduced postoperative analgesic use.

Our previous multicenter RCT revealed that the EUS-CGN showed a higher positive response and complete response rates than the central EUS-CPN, with rates of 73.5% vs 45.5% and 50.0% vs 18.2%, respectively.¹⁵ Additionally, two other retrospective cohort studies demonstrated that the performance of EUS-CGN was a predictor of a good response.^{16,17} However, one recent RCT did not demonstrate a significant difference between the EUS-CPN and EUS-CGN groups. The response rates at 12 weeks were 40.4% vs 46.2% for EUS-CPN and EUS-CGN, respectively ($P = 0.84$).¹⁸

Recently, Kappelle et al¹⁹ compared the spread of ethanol after various EUS-CGN and EUS-CPN procedures in human cadavers. EUS-CGN was performed with 1 mL of ethanol per ganglion using a 25-gauge needle (Technique 1) or a 22-gauge needle (Tech-

Fig. 1. Various techniques related to endoscopic ultrasonography (EUS)-guided celiac plexus ablation. ① Central technique, ② bilateral technique, ③ EUS-guided direct celiac ganglia neurolysis, ④ EUS-guided broad plexus neurolysis.

nique 2) for all two visualized ganglia; 1 mL of ethanol was used for the largest ganglion using a 25-gauge needle (Technique 3) or with 4 mL ethanol per ganglion using 22-gauge needle (Technique 4). EUS-CPN was performed using the central (20 mL, Technique 5) or bilateral (2 × 10 mL, Technique 6) approach. Ethanol spread was seen well beyond the target ganglion even after low-volume EUS-CGN procedures (Techniques 1–3), while a larger ethanol spread was seen after the high-volume EUS-CGN (Technique 4). Unidentified celiac ganglia were better reached with high-volume EUS-CGN, which was likely to result in a more thorough neurolysis. On the other hand, the spread was comparable to the spread after the central and bilateral EUS-CPN procedures.

To determine other prognostic factors, Facciorusso et al²⁰ analyzed the influences of sarcopenia on treatment outcomes after EUS-CPN. Their study revealed that non-sarcopenic patients showed better treatment responses and a longer duration of pain relief compared to sarcopenic patients.

In order to compare medications using oxycodone and/or fentanyl with and without EUS-CPN, Kanno et al²¹ recently evaluated the efficacy of EUS-CPN for pancreatic cancer pain. As a result, EUS-CPN did not improve pain, quality of life (QOL), or opioid consumption compared to patients who did not undergo EUS-CPN or receive oxycodone and/or fentanyl. In addition, opioid-related adverse events, such as constipation, nausea, and drowsiness, were considerably mild or well-controlled. Therefore, they concluded that EUS-CPN did not have a large enough impact to be routinely performed for all patients with pain, although it can be an option for those receiving oxycodone/fentanyl.

Evaluation of Repeated EUS-CPN

Repeated EUS-CPN may cause vascular injuries and ischemic complications. Furthermore, it may lead to the tolerance of the procedure. Facciorusso et al²² recently analyzed 156 patients to assess the efficacy of repeated EUS-CPN for pancreatic cancer pain. The results revealed that 32.6% of the patients experienced treatment response, while 3.8% of the patients experienced complete pain suppression. The median duration of pain relief was 6 weeks (range, 2–8 weeks). The logistic regression model and artificial neural network model using a machine learning approach were also built to predict the pain response after the treatment. The univariate and multivariate logistic regression analyses showed that the tumor stage, length of time between the initial and repeat treatments, responses to initial neurolysis, and tumor progression between the two treatments were significant predictors of pain response. The performance of the artificial neural network was higher than the regression model for predicting treatment response.

Complications

Common complications related to EUS-CPN include transient diarrhea, transient pain exacerbation, transient hypotension, and inebriation, which occurs in up to 36% of patients. However, these complications are not serious in most cases. Furthermore, several major adverse events have been reported. Among them, paraplegia after EUS-CPN has been reported in four cases.^{3,23} The postulated mechanism of spinal cord injury in these cases involved spasms of radicular arteries because of the propagation of ethanol. The artery of Adamkiewicz originates from the posterolateral end of the aorta and is the main artery supplying the anterior spinal artery in the thoracolumbar region. Therefore, major neurological complications related to spinal cord infarction

occur more commonly with percutaneous posterior approaches in 1%–2% of patients. However, it can also occur during the anterior approach when the needle is punctured deeply and/or a high volume of ethanol is injected.

Impact on Survival

In their recent retrospective case-control study, Fujii-Lau et al²⁴ evaluated the ability of CPN to provide survival advantages for pancreatic cancer patients. A total of 417 patients underwent CPN and were compared with 840 controls with pancreatic cancer. Although better survival outcomes were expected via improvements in their QOL, the median survival of patients who underwent CPN was shorter compared with the controls (193 days vs 246 days). Although patients were stage-matched in this study, the shorter survival among the CPN group might be related to a lower performance status, as indicated by the greater initial weight loss, presence of pain, opioid use, and less-common use of chemotherapy and/or radiation therapy. Additional sub-analysis also showed that EUS-CPN was associated with longer survival compared to other non-EUS approaches. Patients who received CPN had a longer survival compared to those who underwent CGN; however, there was no difference in survival for patients receiving central or bilateral injection. Later, the same researchers conducted an RCT to compare the effects of combined EUS-CGN and EUS-CPN to those of CPN alone regarding pain, QOL, and survival.¹⁸ They found that CGN reduced the median survival time (5.59 months vs 10.46 months) without improving pain, QOL, or adverse events, compared to CPN. They suggested that injecting a caustic agent within the celiac ganglia might induce local or systemic immune, inflammatory, or metabolic pathways that enhanced tumor growth and spread, thereby promoting tumor-associated death. Otherwise, CGN might negatively impact other organs and, therefore, secondarily impact survival. However, there are no data supporting possible mechanisms associated with CGN that may reduce the survival in cancer patients.

New Techniques

Recently, several new techniques related to EUS-CPN have been introduced. Manta et al²⁵ introduced a multimodal “one-session three endoscopic procedures (one-STEP)” technique in selected patients diagnosed with an advanced pancreatic cancer presenting with biliary obstruction, duodenal stenosis, and severe pain. The one-STEP endoscopic approach included biliary and duodenal stenting and EUS-CPN. The procedure was successful in 13 of 15 cases (87%). The procedure seems cumbersome, but it may reduce costs and the duration of hospital stays.

Ishiwatari et al²⁶ introduced EUS-CPN using highly viscous phenol-glycerol as a neurolytic agent; they hypothesized that a highly viscous neurolytic agent would remain around the celiac plexus and provide better pain relief. As a result, positive responses were obtained in eight out of nine patients (89%), while four patients (44%) achieved complete resolution of pain. The median duration of pain relief was estimated to be 19.1 weeks. Saleh et al²⁷ reported that the addition of dexmedetomidine to bupivacaine in EUS-CPN was beneficial, in regards to the degree and duration of pain relief. In addition, a case report suggested that endoscopic ethanol ablation of tumors combined with CPN might improve pain control in a patient with pancreatic cancer.²⁸ However, the efficacy and safety should be evaluated in future cases. Recently, Bang et al²⁹ conducted an RCT to compare the effectiveness of EUS-guided celiac ganglion radiofrequency ablation (EUS-RFA)

Table 1 Guidelines on EUS-CPN

Statement	EFSUMB (2016)	Endoscopic Ultrasound (2017)	AEG (2018)
Indication	EUS-guided CPN combined with standard analgesic treatment is superior to analgesic treatment alone in reducing pain in patients with pancreatic and upper gastrointestinal cancer.		EUS-guided CPN is recommended in patients suffering from pain due to unresectable upper abdominal cancer, particularly for pancreatic cancer.
	For chronic pancreatitis, percutaneous CPB has inferior efficacy compared with EUS-guided CPB, and therefore it is not recommended for use in clinical practice.	We recommend against EUS-CPN for the treatment of chronic pancreatitis pain.	EUS-guided CPN for treatment of pain arising from chronic pancreatitis is not recommended.
Efficacy	EUS-guided CPB induces moderate pain improvement compared to analgesic drugs only.	Without availability of direct comparison between techniques, EUS-CPN appears equal or more effective in controlling pain.	The EUS-guided approach is recommended over percutaneous image-guided techniques for celiac plexus ablation.
Technique	Antibiotic prophylaxis should be considered before EUS-guided CPB when steroids are used.		Prophylactic antibiotics are suggested to be given when bupivacaine with steroids is used for EUS-CPB.
	The injection technique (central vs. bilateral) has no significant influence on the efficacy and safety of EUS-guided CPN and CPB.	Bilateral EUS-CPN (with needle advancement caudally, beyond the level of the celiac axis) is superior, but technical feasibility and operator comfort justify central injection as an acceptable option.	Celiac broad plexus neurolysis may be associated with improved efficacy but routine use is not recommended.
			10–20 mL of absolute ethanol is recommended for EUS-CPN and the volume may be reduced in EUS-CGN.
			Phenol may be used instead of alcohol for EUS-guided CPN in patients with alcohol intolerance due to aldehyde dehydrogenase deficiency, but the comparative efficacy and safety of the two agents is uncertain.
			In order to perform EUS-CGN, the celiac ganglia can be identified between the aorta and the left adrenal gland in most patients. Otherwise, they may be located cephalad to the origin of the celiac axis in others.
	In patients with painful non-resectable pancreatic and upper gastrointestinal cancer, EUS-guided CPN should be considered early in the course of the disease.	When on-site cytopathology is available, patients with painful inoperable pancreas cancer should undergo EUS-CPN at time of diagnosis (early).	Early EUS-CPN at the time of EUS-guided fine needle aspiration (FNA) is recommended as it reduces pain and may moderate opioid consumption compared with best medical therapy.
	In patients with visible ganglia, EUS-guided CGN should be preferred to conventional EUS-guided CPN as it provides greater pain relief.	There is no clear evidence that CGN is more superior to bilateral or broad plexus EUS-CPN (with needle advancement caudal to the base of the celiac axis). Therefore, EUS-guided CGN is not necessary.	EUS-guided CGN is recommended over single or bilateral injections around the celiac artery for improved pain relief.
			When the ganglion cannot be identified, EUS-CPN is performed by single or bilateral injections but evidence is contradictory on which approach is superior.
Complications	The safety profile of EUS-guided CPN and CPB is favorable. However, due to some serious adverse events that have been reported with EUS-guided CPN, its use in patients with benign conditions should be considered with caution	Although the evidence for efficacy outweighs the risks, the small incidence of serious adverse events should be disclosed to the patient.	The complications of EUS-CPN and CGN are generally minor and do not need specific treatment.
			Repeated injections for chronic pancreatitis should be avoided to prevent development of major complications.
Training			Training in EUS-guided celiac plexus ablation is recommended in endoscopists experienced in EUS and EUS-FNA.

EUS, endoscopic ultrasonography; CPN, celiac plexus neurolysis; EFSUMB, European Federation of Societies for Ultrasound in Medicine and Biology; AEG, Asian EUS Group; CPN, celiac plexus neurolysis; CPB, celiac plexus block; CGN, celiac ganglia neurolysis.

with that of EUS-CPN as a palliative technique for patients with pancreatic cancer. As a result, EUS-RFA provided more pain relief and improved the QOL in patients, when compared to EUS-CPN. The EUS-RFA cohort experienced significantly less severe gastrointestinal symptoms, were able to plan more for the future, and had better emotional functioning compared with the EUS-CPN group.

Besides these EUS-guided techniques, Wang et al³⁰ introduced contrast-enhanced external ultrasound (CEUS)-guided CPN. They suggested that the CEUS image allows visualization of the puncture path and observation of drug dispersion. It may also be helpful to evaluate the dispersion of ethanol during the EUS approach.

Guidelines

The European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB),³¹ *Endoscopic Ultrasound* journal,³² and the Asian EUS Group (AEG)⁴ established guidelines regarding the use of EUS-CPN. Each set of guidelines includes 8, 6, and 14 statements, respectively, and some statements are similar (Table 1). For example, not all of the guidelines recommend EUS-CPB/EUS-CPN for the treatment of chronic pancreatitis pain due to limited efficacy and a high incidence of complications. All guidelines do recommend that EUS-CPN is performed early for cancer pain. Two guidelines recommended the use of prophylactic antibiotics before EUS-CPB. On the other hand, there are some discrepancies regarding the technical aspects of these procedures. The EFSUMB and AEG guidelines recommended EUS-CGN over conventional EUS-CPN (specifically central or bilateral injections around the celiac artery) for improved pain relief. However, the third guideline did not recommend EUS-CGN over the other procedures.

Conclusions

EUS-CPN related techniques have been widely practiced to date and this manuscript reviewed the recent five-year topics on EUS-CPN. Although the techniques are widely used, there are still questions regarding their real efficacy, which technique is the most effective, and the survival outcomes associated with the techniques. Future studies should be designed to address these questions and determine the efficacy of these techniques for cancer patients.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

ORCID

Ichiro Yasuda, <https://orcid.org/0000-0002-6888-0310>
 Kosuke Takahashi, <https://orcid.org/0000-0003-2361-5043>
 Shinpei Doi, <https://orcid.org/0000-0003-3030-223X>
 Takuji Iwashita, <https://orcid.org/0000-0003-4978-1787>
 Keisuke Iwata, <https://orcid.org/0000-0003-0564-8669>
 Tsuyoshi Mukai, <https://orcid.org/0000-0002-5198-9475>

References

1. Faigel DO, Veloso KM, Long WB, Kochman ML. Endosonography-guided celiac plexus injection for abdominal pain due to chronic pancreatitis. *Am J Gastroenterol*. 1996;91:1675.
2. Wiersma MJ, Wiersma LM. Endosonography-guided celiac plexus neurolysis. *Gastrointest Endosc*. 1996;44:656–62.
3. Yasuda I, Wang HP. Endoscopic ultrasound-guided celiac plexus block and neu-

- rolysis. *Dig Endosc*. 2017;29:455–62.
4. Teoh AYB, Dhir V, Kida M, Yasuda I, Jin ZD, Seo DW, et al. Consensus guidelines on the optimal management in interventional EUS procedures: results from the Asian EUS group RAND/UCLA expert panel. *Gut*. 2018;67:1209–28.
5. Sey MS, Schmaltz L, Al-Haddad MA, DeWitt JM, Calley CS, Juan M, et al. Effectiveness and safety of serial endoscopic ultrasound-guided celiac plexus block for chronic pancreatitis. *Endosc Int Open*. 2015;3:E56–9.
6. Alhazzani W, Al-Shamsi HO, Greenwald E, Radhi J, Tse F. Chronic abdominal pain secondary to mesenteric panniculitis treated successfully with endoscopic ultrasonography-guided celiac plexus block: a case report. *World J Gastrointest Endosc*. 2015;7:563–6.
7. Sakamoto H, Kitano M, Kamata K, Komaki T, Imai H, Chikugo T, et al. EUS-guided broad plexus neurolysis over the superior mesenteric artery using a 25-gauge needle. *Am J Gastroenterol*. 2010;105:2599–606.
8. Levy MJ, Topazian MD, Wiersma MJ, Clain JE, Rajan E, Wang KK, 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.
9. Puli SR, Reddy JB, Bechtold ML, Antillon MR, Brugge WR. 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.
10. Kaufman M, Singh G, Das S, Concha-Parra R, Erber J, Micames C, 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.
11. Iwata K, Yasuda I, Enya M, Mukai T, Nakashima M, Doi S, et al. Predictive factors for pain relief after endoscopic ultrasound-guided celiac plexus neurolysis. *Dig Endosc*. 2011;23:140–5.
12. LeBlanc JK, Al-Haddad M, McHenry L, Sherman S, Juan M, McGreevy K, 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.
13. Téllez-Ávila FI, Romano-Munive AF, Herrera-Esquivel Jde J, Ramirez-Luna MA. Central is as effective as bilateral endoscopic ultrasound-guided celiac plexus neurolysis in patients with unresectable pancreatic cancer. *Endosc Ultrasound*. 2013;2:153–6.
14. Lu F, Dong J, Tang Y, Huang H, Liu H, Song L, et al. Bilateral vs. unilateral endoscopic ultrasound-guided celiac plexus neurolysis for abdominal pain management in patients with pancreatic malignancy: a systematic review and meta-analysis. *Support Care Cancer*. 2018;26:353–9.
15. Doi S, Yasuda I, Kawakami H, Hayashi T, Hisai H, Irisawa A, et al. Endoscopic ultrasound-guided celiac ganglia neurolysis vs. celiac plexus neurolysis: a randomized multicenter trial. *Endoscopy*. 2013;45:362–9.
16. Asuncion G, Ribeiro A, Reis I, Rocha-Lima C, Sleeman D, Merchan J, 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.
17. Minaga K, Kitano M, Sakamoto H, Miyata T, Imai H, Yamao K, et al. Predictors of pain response in patients undergoing endoscopic ultrasound-guided neurolysis for abdominal pain caused by pancreatic cancer. *Therap Adv Gastroenterol*. 2016;9:483–94.
18. Levy MJ, Gleeson FC, Topazian MD, Fujii-Lau LL, Enders FT, Larson JJ, et al. Combined celiac ganglia and plexus neurolysis shortens survival, without benefit, vs plexus neurolysis alone. *Clin Gastroenterol Hepatol*. 2019;17:728–38.e9.
19. Kappelle WFW, Bleys RLAW, van Wijck AJM, Siersema PD, Vleggaar FP. EUS-guided celiac ganglia neurolysis: a clinical and human cadaver study (with video). *Gastrointest Endosc*. 2017;86:655–63.
20. Facciorusso A, Antonino M, Muscatiello N. Sarcopenia represents a negative prognostic factor in pancreatic cancer patients undergoing EUS celiac plexus neurolysis. *Endosc Ultrasound*. 2020;9:238–44.
21. Kanno Y, Koshita S, Masu K, Ogawa T, Kusunose H, Murabayashi T, et al. Efficacy of EUS-guided celiac plexus neurolysis compared with medication alone for unresectable pancreatic cancer in the oxycodone/fentanyl era: a prospective randomized control study. *Gastrointest Endosc*. 2020;92:120–30.
22. Facciorusso A, Del Prete V, Antonino M, Buccino VR, Muscatiello N. Response to repeat echoendoscopic celiac plexus neurolysis in pancreatic cancer patients: a machine learning approach. *Pancreatol*. 2019;19:866–72.
23. Minaga K, Kitano M, Imai H, Miyata T, Kudo M. Acute spinal cord infarction after EUS-guided celiac plexus neurolysis. *Gastrointest Endosc*. 2016;83:1039–40; discussion 1040.
24. Fujii-Lau LL, Bamlet WR, Eldrige JS, Chari ST, Gleeson FC, Abu Dayyeh BK, et al. Impact of celiac neurolysis on survival in patients with pancreatic cancer. *Gastrointest Endosc*. 2015;82:46–56.e2.
25. Manta R, Conigliaro R, Mangiafico S, Forti E, Bertani H, Frazzoni M, et al. A multimodal, one-session endoscopic approach for management of patients with advanced pancreatic cancer. *Surg Endosc*. 2016;30:1863–8.
26. Ishiwatari H, Hayashi T, Yoshida M, Ono M, Sato T, Miyanishi K, et al. EUS-guided celiac plexus neurolysis by using highly viscous phenol-glycerol as a neurolytic agent (with video). *Gastrointest Endosc*. 2015;81:479–83.
27. Saleh AAG, Sultan A, Hammouda MA, Shawki A, El Ghaffar MA. Value of adding dexmedetomidine in endoscopic ultrasound-guided celiac plexus neurolysis for treatment of pancreatic cancer-associated pain. *J Gastrointest Cancer*. 2020. doi: 10.1007/s12029-020-00449-1. [Epub ahead of print]
28. Facciorusso A, Maso MD, Barone M, Muscatiello N. Echoendoscopic ethanol ablation of tumor combined to celiac plexus neurolysis improved pain control in a patient with pancreatic adenocarcinoma. *Endosc Ultrasound*. 2015;4:342–4.

29. Bang JY, Sutton B, Hawes RH, Varadarajulu S. EUS-guided celiac ganglion radio-frequency ablation versus celiac plexus neurolysis for palliation of pain in pancreatic cancer: a randomized controlled trial (with videos). *Gastrointest Endosc.* 2019; 89:58-66.e3.
30. Wang L, Lu M, Wu X, Cheng X, Li T, Jiang Z, et al. Contrast-enhanced ultrasound-guided celiac plexus neurolysis in patients with upper abdominal cancer pain: initial experience. *Eur Radiol.* 2020;30:4514-23.
31. Fusaroli P, Jenssen C, Hocke M, Burmester E, Buscarini E, Havre RF, et al. EF-SUMB guidelines on Interventional Ultrasound (INVUS), Part V. *Ultraschall Med.* 2016;37:77-99.
32. Wyse JM, Battat R, Sun S, Saftoiu A, Siddiqui AA, Leong AT, et al. Practice guidelines for endoscopic ultrasound-guided celiac plexus neurolysis. *Endosc Ultrasound.* 2017;6:369-75.