# **Systematic Review**

# Efficacy and Safety of Celiac Plexus Neurolysis Versus Splanchnic Nerve Neurolysis in the Management of Abdominal Cancer Pain: A Meta-analysis of 359 Patients

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Free full manuscript: www.painphysicianjournal.com **Background:** Splanchnic nerve neurolysis (SNN) is commonly used as an alternative pain control technique to celiac plexus neurolysis (CPN) in patients with distortion of anatomy, but the analgesic effect and relative risks of the 2 procedures remain controversial in general condition.

**Objectives:** The aim of this study was to evaluate the pain condition, safety, and symptom burden of SNN compared with CPN.

**Study Design:** A systematic review and meta-analysis of neurolysis therapy for intractable cancer-related abdominal pain.

**Methods:** A systematic search was performed for randomized controlled trials comparing SNN and CPN using the PubMed, Medline, Cochrane Library, Web of Science, Google Scholar, and China National Knowledge Infrastructure databases. Meta-analysis was performed using Stata Version 15.0. Outcomes included pain condition, opioid consumption, adverse effects, quality of life (QOL), and survival rate. Standardized mean difference (SMD) was calculated for continuous outcomes with its corresponding 95% CI.

**Limitations:** Study limitations include challenges to make subgroup analysis by intervention measures and addressing inevitable heterogeneity. Larger studies are needed for survival rates and further insights.

**Results:** Seven studies involving 359 patients were included. No significant difference was found in pain condition at 2 weeks [SMD = 0.75, 95% CI (-0.25, 1.74), P > 0.05], 2 months [SMD = 1.10, 95% CI (-0.21, 2.40), P > 0.05] and 6 months [SMD = 0.53, 95% CI (-0.02, 1.08), P > 0.05] between SNN and CPN. Opioid consumption was comparable at 2 weeks [SMD = 0.57, 95% CI (-1.21, 2.34), P > 0.05] and one month [SMD = 0.37, 95% CI (-1.33, 2.07), P > 0.05]. However, SNN was associated with a statistically significant reduction in the opioid consumption at 2 months postoperatively [SMD = 0.99, 95% CI (0.68, 1.30), P < 0.05]. A systematic review was performed for adverse effects and QOL.

**Conclusions:** Our evidence supports that the analgesic effect of SNN is equivalent to that of CPN, independent of changes in the anatomical structure of the abdominal nerve plexus. SNN requires less use of opioids at 2 months and does not show greater improvement in pain burden compared to CPN.

Key words: Cancer pain, celiac plexus, meta-analysis, neurolysis, splanchnic nerve

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eliac plexus neurolysis (CPN) was first performed as an invasive procedure for analgesia by Kappis in 1914 (1) and is currently becoming a widely used and effective analgesic technique for the management of abdominal and back pain in patients with upper gastrointestinal malignancies. This procedure provides benefits not only for analgesia, but also to reduce opioid use and pain interference (2,3). Hegedüs (4) first reported the use of radiography-guided CPN in 1979, and since then approaches, including computerized tomography and endoscopic ultrasound, have been described to achieve neurolysis (5,6). The antecrural technique is a classical insertion pathway that targets the abdominal trunk and the root of the superior mesenteric artery anterior to the crura of the diaphragm (7,8). However, the celiac plexus is located adjacent to the abdominal aorta and gastrointestinal tract and can be proximal to malignant lesions, which increases the risk of severe adverse events (9). In addition, altered neurotic anatomy or regional metastasis may hinder agent diffusion and cause subsequent incomplete blockade.

Splanchnic nerve neurolysis (SNN) may represent another promising analgesic option for abdominal cancer pain. This technique does not require needle penetration of the crura, and usually, the neurolytic solution is applied into the narrow space between the lateral border of the T12-L1 vertebra and diaphragm (10,11). The innervation of the upper abdominal organs consists of afferent fibers derived from the thoracic splanchnic nerve, which is composed of the greater, lesser, and least ganglion and descends through the diaphragm to form the partial celiac nerve plexus (12). Besides chemical degeneration, splanchnicectomy is a frequently applied method for SNN (13,14). A recent multicenter randomized controlled trial (RCT) (15) showed that SNN significantly reduced pain levels and opioid consumption in patients with unresectable pancreatic cancer in the first 3 months compared with that of normal saline injection. Notably, the mechanism of abdominal cancer pain is intimately related to tumor regional progression and perineural invasion (16,17); therefore, SNN was recognized as an alternative to CPN for patients with celiac plexus invasion (18).

However, controversy remains whether SNN can be applied as a substitute for CPN in general conditions. A few RCTs and retrospective studies have been conducted to compare the efficacy and safety of the 2 methods. Therefore, this meta-analysis aimed to evaluate the pain condition, opioid consumption, complications, quality of life (QOL), and survival rate in patients with upper abdominal cancer pain treated with either CPN or SNN.

## **M**ETHODS

#### **Search Strategy and Selection Criteria**

The study protocol was registered with the International Prospective Register of Systematic Reviews and assigned the identification number CRD42023425502. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement was used for systematic review and guidance in this metaanalysis (19). We conducted a detailed search of the PubMed, Medline, Cochrane Library, Web of Science, Google Scholar, and China National Knowledge Infrastructure databases from January 1990 to December 2022. The search formula, composed of Medical Subject Headings, was ("celiac plexus") and ("splanchnic nerve" or "splanchnicectomy") and ("retrocrural" or "antecrural" or "neurolysis" or "block"). The systematic search strategy for the PubMed database is shown in the Appendix. Studies were selected if the following inclusion criteria were achieved: chronic upper abdominal pain or back pain caused by gastrointestinal malignancies with baseline pain score > 3, studies involving interventions of abdominal plexus or splanchnic nerve neurolysis, and studies comparing the antecrural and retrocrural technique for celiac plexus block. Studies were excluded if SNN was used only as an alternative or complementary treatment or when patients had non-cancer pain or received other invasive analgesic techniques during observation.

#### **Assessment of Risk of Bias**

Methodological quality assessment was conducted independently by 2 review investigators (FL and XHL) using a standardized approach. The Cochrane Collaboration tool (20) was utilized to assess the risk of bias in RCTs on the items of random sequence generation, blinding, allocation concealment, selective reporting, incomplete outcome data, and other sources of bias. Judgment was made for "low risk," "high risk," or "unclear" (lack of information or uncertainty over the bias) for each study. Additionally, the Newcastle-Ottawa Scale (NOS) was employed to assess the methodological quality of cohort and case-control studies, considering factors, such as selection of study groups, comparability of groups, and ascertainment of outcomes. The total score on the NOS can range from 0 to 9, with a higher score indicating a lower risk of bias and higher quality of the study.

#### **Data Extraction and Management**

All studies were screened by 2 independent researchers (FL and XHL) using the inclusion and exclusion criteria. Data were extracted for study design, authors, publication time, course of disease, intervention measures, and outcome indicators. The primary outcome was pain intensity (recorded for Visual Analog Scale, VAS) at different time points (i.e., 2 weeks, one month, 2 months, 6 months) after treatment, and the secondary outcomes included opioid consumption, QOL, survival rates, and adverse reactions (e.g., dizziness, diarrhea, nausea and vomiting, surgical pain, hypotension, etc). We contacted the original authors if the data were incomplete. If the units or statistical expression of the data were inconsistent, a conversion was made according to the Cochrane Handbook for Systematic Review of Interventions (20).

or because of duplicate publications (Fig. 1). A total of 27 articles were considered eligible for full-text assessment, of which 20 were excluded because they were a review article (n = 9), case report (n = 2), nonmalignant pain treatment (n = 3), considered SNN as a complementary strategy (n = 4), or had incomplete data or were not available after contacting the authors (n = 2). Therefore, 7 studies were examined for inclusion in our meta-analyses (Fig. 1).

### **Methodological Evaluation of Studies**

We used the Cochrane Collaboration Risk of Bias Tool and NOS scale to perform methodological quality assessment for all included studies. All studies reported the baseline conditions of patients with complete outcome data. Two studies (21,22) used random numbers in sequence generation, and 2 studies (21,23) mentioned the use of envelope methods and a central telephone randomization system for allocation concealment, respectively. In Süleyman et al (21), the follow-up evaluations were conducted by an anesthesiologist who was unaware of the procedure, ensuring blinding of the

## **Statistical Analysis**

Statistical analysis was performed using Stata Version 15.0 (StataCorp LP, College Station, TX) and SPSS Version 26.0 (IBM Corporation, Armonk, NY). Data were divided into the CPN or SNN group. The VAS scores and opioid consumption were calculated as standardized mean difference (SMD), both with a 95% CI. The I<sup>2</sup> statistic and chi-square test were calculated to measure the heterogeneity of the selected studies. Meta-analysis was performed with a random effects model if the heterogeneity was considered significant (P < 0.10 or  $I^2 > 50\%$ ), otherwise, a random-effects model was used. Descriptive qualitative analysis was applied when the original data were insufficient for metaanalysis. A funnel plot and Egger's test (P < 0.05 indicates a significant publication bias) were used to assess potential publication bias.

## RESULTS

## **Search and Selection of Studies**

We retrieved 353 citations from the electronic databases and references, 326 of which were excluded through screening of titles and abstracts according to the criteria



VAS (Fig. 2).

evaluator. Additionally, Peng et al (22) reported doubleblinding, where both the patients and the follow-up observers were unaware of the treatment assignment. Two additional nonrandomized studies (14,26) were included in the analysis, and their methodological quality was assessed using the NOS, with the scores of 7 and 8, respectively, suggesting a lower risk of bias and higher methodological quality. The methodological quality assessment results are presented in Table 1.

#### **Study Characteristics and Clinical Outcome**

A total of 7 studies with 359 patients were enrolled in the meta-analysis, including 5 randomized clinical trial studies (21-25), one prospective clinical trial (14), and one retrospective observational study (26). All studies compared the effects of CPN and SNN on upper abdominal pain caused by pancreatic cancer or other upper gastric tract tumors. Stefaniak et al (14) and Johnson et al (23) used thoracoscopic splanchnicectomy to achieve visceral nerve denervation; whereas, the other studies used neurolytic agents in CPN and SNN. Of these, the use of alcohol from 70% to 100% was reported in 5 studies (22-26), while 50% to 75% ethanol was reported in the other 2 studies (14,21). The total agent dosage was between 20 mL to 40 mL. The primary outcome was pain scores assessed by the VAS, Numeric Rating Scale (NRS-11), or Brief Pain Inventory (BPI) from the first day to the 6 months after the procedure. The QOL was assessed by different scales, such as functional assessment of cancer therapy scale (14), the European Organization for Research and Treatment of Cancer quality of life questionnaire (EORTC QLQ-C30) (14,23,24), performance status scale (PS), and patient satisfaction scale (PSS) (21). All trials reported the changes in analgesic consumption and adverse effects. In addition, 3 studies (21,23,24) evaluated the survival rates with Kaplan-Meier curves. Study characteristics are shown in Table 2.

## **Pain Condition**

The intensity of pain between CPN and SNN was assessed via VAS, except for 2 studies that used BPI pain scores (23) and NRS-11 (26), which were both converted to mean  $\pm$  SD with parameters ranged in scores from 0 to 10. In addition, the pain scores were presented graphically by Stefaniak et al (14) and Tewari et al (26), and therefore numerical data were obtained by contacting the authors. We compared the pain scores for the 2 groups at 2 weeks and 2 and 6 months (Fig. 2A, B, and C, respectively) after treatment, which were cant at 2 weeks (P = 0.000,  $I^2 = 94.2\%$ ), 2 months (P = 0.000,  $I^2 = 95.2\%$ ), and 6 months (P = 0.018,  $I^2 = 70.3\%$ ).

The occurrence of heterogeneity was not unexpected in the analysis of VAS, which may be caused by the variable understanding of pain from different regions and beliefs as VAS is a subjective assessment. The funnel plot and Egger's test showed no publication bias in pain scores at each follow-up time point (2 weeks: P =0.108; 2 months: P = 0.217; 6 months: P = 0.734). Overall, 346, 266, and 185 patients were included at 2 weeks, 2 months, and 6 months, respectively. All results were obtained using a random effects model [2 weeks: SMD = 0.75, 95% CI (-0.25-1.74); 2 months: SMD = 1.10, 95% CI (-0.21-2.40); 6 months: SMD = 0.53, 95% CI (-0.02-1.08)]. This indicated that there was no significant difference in postoperative pain scores (Fig. 2).

represented by a forest plot of the mean difference of

Heterogeneity was found to be statistically signifi-

#### **Analgesic Consumption and Adverse Effects**

The studies calculated opioid consumption at different times after the procedure, with eligible data available at 2 weeks and 1 and 2 months, postoperatively (Fig. 3). For Peng et al (22) and Pisheng et al (25), the analgesic consumption was not available for calculation. Johnson et al (23) demonstrated the number and proportion of patients who used opioids and adjuvants regularly, rather than the analgesic dosage. Different types of opioids were converted into the equivalent dosage of morphine and presented as mean ± SD. The forest plots for the mean difference in morphine use (mg) at 2 weeks and 1 and 2 months are shown in Fig. 3A, B, and C, respectively.

Heterogeneity was found to be statistically significant at 2 weeks (P = 0.000,  $I^2 = 97\%$ ) and 1 month (P= 0.000,  $I^2$  = 95.7%); whereas, no heterogeneity was shown among studies at 2 months (P = 0.336,  $I^2 = 11.3\%$ ), which was confirmed by the funnel plot symmetry (Fig. 4). The observed heterogeneity may be attributed to the limited number of studies included in the analysis of opioids consumption at specific time points. Egger's test showed no publication bias at 2 weeks or 1 or 2 months (P = 0.745, 0.326, and 0.415, respectively). Opioid consumption did not significantly differ at 2 weeks [SMD = 0.57, 95% CI (-1.21-2.34)] or 1 month [SMD = 0.37, 95% CI (-1.33-2.07)] between CPN and SNN. However, morphine consumption was significantly lower in the SNN group at 2 months [SMD = 0.99, 95% CI (0.68-1.30)]. Adverse events were reported in all studies. Five studies

Table 1. Assessment	in methodologic	al quality of	included studies.							
					Coc	hrane Collabor	ation Tool			
Study Name	Study Type	Sequen	ce Generation	Alloc Concea	ation dment	Blinding	Data In	tegrity	Selective Reporting	Other Bias
Johnson CD (2009)	RCT		Unclear	Telep	hone	Unclear	Low	risk	Low risk	Low risk
Shwita AH (2015)	RCT		Unclear	Unc	lear	Unclear	Low	risk	Low risk	Unclear
Süleyman N (2004)	RCT	Ranc	lom numbers	Enve	lope	Low risk	Low	risk	Low risk	Low risk
Pisheng Q (2009)	RCT		Unclear	Unc	lear	Unclear	Low	risk	Low risk	Unclear
Peng Y (2007)	RCT	Rano	lom numbers	Unc	lear	Low risk	Low	risk	Low risk	Low risk
						SON				
		Definition Adequate	Representativeness	Selection of Controls	Definition of Controls	Comparability on the Basis	Ascertainment of Exposure	Nonresponse Rate	Same Method of Ascertainment	Score
Stefaniak T (2005)	Prospective	*	*	Ι	*	*	*	*	*	2
Tewari S (2016)	Retrospective	*	*		*	* *	*	*	*	8
									A	
* represents 1 point; **	represents 2 poir	nts								

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Table 2. Gener	ral character	ristics of studies	used for meta-	analysis.							
Study	Country	Design	Treatment	Number of Patients	M/W	Age (y)	Unbearable Time of Pain	Procedures	Dosage (mL)	Follow- up	Outcome
Stefaniak T			CPN	35	21/14	61.20	1.7 mo	50% ethanol			VAS, QOL (FACIT and
(2005)	Poland	Prospective	NNS	24	14/10	63.50	2.1 mo	or incision, 1 center	20-30	8 wk	QLQ-C30), opioid use, adverse effects
Iohnson CD			CPN	20	10/10	60.5 (9.22)	NA	100% alcohol			BPI pain score, QOL
(2009)	UK	RCT	NNS	21	6/15	60.2 (9.31)	NA	or incision, 4 centers	NA	2 mo	(QLQ-C30), opioid use, survival, adverse events
Tewari S	Ladia	Datus and its	CPN	28	12/16	51.2 (12.9)	NA	100% alcohol, 1	06	,	NRS-11, QOL, morphine
(2016)	India	ketrospective	SNN	36	16/20	52.7 (15.8)	NA	center	00	0 III 0	consumption, side effects
Shwita AH		НСа	CPN	30	16/14	46 (19)	1.5 mo	70% alcohol, 1	υι	-1 10	VAS, QOL (QLQ-C30),
(2015)	Egypt	IVUI	SNN	30	18/12	49 (21)	1.3 mo	center	70	24 WK	survival, side effects
Sülevman N			CPN	19	14/5	57 (7)	NA	75% ethanol. 1			VAS, QOL (PSS and PS),
(2004)	Turkey	RCT	NNS	20	12/8	61(8)	NA	center	40	18 wk	opioid consumption, survival, side effects
Pisheng Q		ЦU	CPN	24	14/10	66 (9)	NA	95% alcohol, 1	υı	, ,	VAS, response,
(2009)	Cuina	INU	SNN	24	15/9	64(10)	NA	center	07	ош с	medication, complication
Peng Y		туп	CPN	24	10/20	C 12	121-	100% alcohol, 1	36 06	,	VAS, response,
(2007)	Cnina	RUI	SNN	24	17//7	7.10	12 WK	center	67-07	om c	medication, complication
M = men; W = .	women; Age	: mean (SD).									

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(14,21,22,24,25) demonstrated that CPN was associated with higher incidences of hypotension, transient backache, fatigue, diarrhea, and hemodynamic disturbances (Table 3). However, Tewari et al (26) reported contradictory results in transient backache (50% vs 61%), diarrhea (14.3% vs 16.7%), and hypotension (21.4% vs 22.2%) between the CPN and SNN groups. In addition, increased complications (e.g., wound infection and intraoperative bleeding) were shown in the SNN group when splanchnicectomy was applied to achieve denervation of the splanchnic nerve (23).

## Pain-Related Quality of Life and Survival Time

Five studies (14,21-25) compared postoperative QOL between the CPN and SNN groups and showed discrepant results. Evaluation of the QOL by Süleyman



et al (21) showed a greater improvement of PS and PSS during the 2 to 18 weeks follow-up in the CPN group, with a significant difference present at 4 and 6 weeks. Stefaniak et al (14) reported that CPN treatment produced a significant improvement for social support and emotional and physical well-being, as assessed by QLQ-C30. Conversely, Shwita et al (24) described a contrary result, where SNN produced better outcomes for assessment of physical and emotional symptoms, social roles, and cognitive scales. However, due to limited sample sizes, a meta-analysis of the QLQ-C30 results was not feasible. Two other studies (23,26) found that pain relief did not correlate well with overall QOL in the 2 groups. The survival rate of the CPN group (45.37 ± 5.82 days; 95% CI: 33.96-56.78) was lower than that of the SNN group (68.85 ± 7.30 days; 95% CI: 54.54-83.16) (P = 0.072), but with no statistically significant difference (21). Two studies (23,24) both revealed that the patient survival period was comparable between the 2 groups.

## DISCUSSION

Cancer-related chronic pain is one of the most common manifestations in patients with malignancy, occurring in 48% of cases with early tumors, and 75% of those with terminal diseases and has a significant impact on QOL and survival time (27,28). Pain is the most significant and frequent symptom of pancreatic cancer, which is the seventh leading cause of cancer mortality globally (29). The severity of pain correlates with tumor location (i.e., body or tail of pancreas) and autonomic plexus invasion through regional progression and retroperitoneal invasion (17). In addition, gastric, esophageal, hepatobiliary malignancies, colorectal cancer, and retroperitoneal lymph node metastasis can cause persistent intractable abdominal pain (30). CPN and SNN therapies that directly target the celiac plexus or splanchnic nerves, respectively, for neuromodulation are widely recognized to achieve effective and rapid analgesic effects in clinical practice. A recent study (31) supports the early use of CPN for pain control in patients with an unsatisfactory response to opioids. Notably, a prospective study (32) demonstrated that splanchnicectomy produced significant pain relief and QOL improvement as well as longer survival as a firstline treatment for patients with pancreatic cancer.

Our systematic review found no significant difference in pain scores from 2 weeks to 6 months between the 2 groups, indicating that SNN achieved comparable analgesic effects with those of CPN. Moreover, SNN was comparable to CPN in opioid consumption between 2 weeks to one month. Thus, the comparable pain reduction of the 2 groups was not caused by the difference in the amount of opioid usage after the procedure, but was directly caused by the operation methods. Conversely, the demand for opioids 2 months postoperation was significantly lower with the SNN group than with the CPN group. Although we noted that Stefaniak et al (14) achieved SNN through splanchnicectomy, we suspected that neurectomy may cause a more complete nerve blockade, thereby decreasing postoperative analgesic usage in the SNN group. Therefore, we excluded this study and conducted a subgroup analysis of the opioid consumption at 2 months to obtain the same result that favors the SNN group. Our findings indicate that the analgesic effects of SNN and CPN are comparable and that SNN has fewer analgesic requirements. Therefore, using SNN as an alternative treatment for CPN is a desirable option even if no distortion of anatomy or enlarged celiac lymph nodes is detected.

The risks arising from anatomical variation and



Table 3. Assessment in adverse effects of included studies.

Study	CPN	SNN
Stefaniak T (2005)	Fatigue (stronger)	Fatigue
Johnson CD (2009)	Constipation	Constipation, wound infection, intraoperative bleeding, diarrhea, vomiting
Tewari S (2016)	Backache (14/28), diarrhea (4/28), hypotension (6/28)	Backache (22/36), diarrhea (6/36), hypotension(8/36)
Shwita AH (2015)	Diarrhea (20/30), hypotension (10/30), transient backache (18/30), shoulder pain (4/30)	Diarrhea (20/30), hypotension (8/30), transient backache (16/30), shoulder pain (2/30)
Süleyman N (2004)	Severe pain (2/19),intractable diarrhea (5/19),hemodynamic disturbances (2/19)	Severe pain (1/20)
Pisheng Q (2009)	Diarrhea (18/24), hypotension (-)	Diarrhea (11/24), hypotension (-)
Peng Y (2007)	Hypotension (7/24), alcohol-associated dizziness (2/24), diarrhea (2/24), nausea and vomiting (3/24), procedure pain (2/24)	Hypotension (5/24), alcohol-associated dizziness (3/24), diarrhea (3/24), nausea and vomiting (3/24), procedure pain (1/24)

insertion complexity are generally the first consideration when deciding between CPN and SNN. The celiac plexus, located anterior to the upper retroperitoneal abdominal aorta, comprises the celiac ganglia, superior mesenteric ganglia, aortic renal ganglia, and splanchnic ganglia, which usually vary in size, number, and location (8). Thus, deep insertion is required to perform CPN, which causes difficulty for repeated adjustment of the needle tip position and requires a skilled and experienced operator. Although CPN can be performed with imaging guidance, this procedure involves significant risks, including, but not limited to, retroperitoneal bleeding, abscess, thrombosis, and paraplegia (33). In addition, patients usually require repeated injections for palliative pain management because the duration of a single injection is limited to 3-6 months (34). Thus, retroperitoneal metastases and ascites may occur as the condition changes, all of which reduce the analgesic effectiveness of CPN. By contrast, the injection target of SNN is located on both sides of the vertebral body and in the posterior space of the diaphragm with a fixed and superficial space (35). Furthermore, the splanchnic nerve is the superior innervation of the celiac plexus with a shared etiology, so SNN therapy is believed to proximally block the transmission of pain signals (36).

In our systematic review, the available data indicated that CPN may cause more operation-related risks than caused by SNN and that these were not confined to the common side effects, such as self-limiting diarrhea and hypotension, but also included severe back pain, fatigue, nausea, and vomiting, observed in CPN (14,21,22). Tewari et al (26) revealed that SNN caused higher complication rates, although no significant difference was detected between the 2 groups. The paravertebral injection of SNN could theoretically minimize the risk of postural hypotension and diarrhea and avoid serious complications, such as intestinal and abdominal aorta injury (37). However, implementing SNN with splanchnicectomy may increase surgery-related risks, such as wound infection and intraoperative bleeding (23). We noted that splanchnicectomy was not associated with effective improvement of patient social support or emotional and physical well-being for pain interference (14). These results suggest that invasive surgery may not be the optimal first option for the palliative management of abdominal cancer pain, even under the guidance of thoracoscopy.

Early acceptance of supportive care is recognized as being effective in improving mood and QOL in patients with advanced cancer and reduces the demand for aggressive end-of-life care (38,39). Furthermore, neurolysis for patients with abdominal malignancies can improve QOL and prolong life expectancy, which may be caused by reducing the opioid-related side effects (40,41). CPN and SNN are both well-established verified anesthetic interventions for relieving pain and improving the pain burden for patients with abdominal malignancy (40,41). Nevertheless, we did not identify any consistency between the pluses and minuses considering the effects of CPN and SNN on QOL. Only 3 studies (21,23,24) reported the survival rate, and 2 of them (23,24) showed no significant difference between the 2 groups. Although Süleyman et al (21) suggest that the average survival time of the SNN group is 23.48 days longer than that of the CPN group, this difference may depend on various factors without control and may not be directly explained by improved analgesia or less opioid consumption.

#### Limitations

Our study does have a few limitations. The first limitation is the challenge in distinguishing and clarifying intervention measures guided by thoracoscopy and imaging, due to their different levels of invasiveness. To address this limitation, future studies may need to consider alternative approaches, such as refining the criteria for distinguishing between the 2 methods or conducting separate analyses for each method. Secondly, our subgroup analysis and sensitivity analysis cannot fully address the sources of heterogeneity between studies. Finally, there are too few descriptions of the occurrence of survival rates, and future research needs to increase the sample size for further discussion. Further large-scale randomized, controlled, blind studies are required on this topic.

#### CONCLUSIONS

In summary, SNN treatment is comparable with CPN for pain control in patients with abdominal cancer and is associated with a significant reduction in analgesic consumption 2 months postprocedure. SNN appears to be an effective and safe alternative to CPN, independent of distorted anatomy of the celiac plexus, and has fewer adverse effects and a longer survival rate (though evidence is limited). However, insufficient evidence supports a greater improvement in paininterfered QOL by SNN.

#### Appendix available at www.painphysicianjournal.com

## REFERENCES

- [Kappis M. Erfahrungen mit Lokalansthesie bei Bauchoperationen. Verh Dsch Ges Cire 1914; 43:87-89b.]
- Ambai VT, Singh V, Boorman DW, Neufeld NJ. Celiac plexus neurolysis for abdominal cancers: Going beyond pancreatic cancer pain. *Pain Rep* 2021; 6:e930.
- Agarwal A, Aggarwal A, Shamshery C, Gambhir S, Nazar AH, Rajput AK. Robotic computed tomography-guided celiac plexus neurolysis: Our experience of technique and outcomes. *Pain Manag* 2022; 12:675-680.
- Hegedüs V. Relief of pancreatic pain by radiography-guided block. AJR Am J Roentgenol 1979; 133:1101-1103.
- Gao Y, Zhao X. EUS-Guided celiac plexus neurolysis versus medication alone for unresectable pancreatic cancer. Gastrointest Endosc 2020; 92:1143.
- Abdelbaser I, Shams T, El-Giedy AA, Elsedieq M, Ghanem MA. Direct intraoperative versus percutaneous computed tomography guided celiac plexus neurolysis in non-resectable pancreatic cancer: A randomized, controlled, non-inferiority study. *Rev Esp Anestesiol Reanim (Engl Ed)* 2022; 69:71-78.
- Urits I, Jones MR, Orhurhu V, et al. A comprehensive review of the celiac plexus block for the management of chronic abdominal pain. Curr Pain Headache Rep 2020; 24:42.
- Kambadakone A, Thabet A, Gervais DA, Mueller PR, Arellano RS. CT-Guided celiac plexus neurolysis: A review of anatomy, indications, technique, and tips for successful treatment. *Radiographics* 2011; 31:1599-1621.
- Moore JC, Adler DG. Celiac plexus neurolysis for pain relief in pancreatic cancer. J Support Oncol 2009; 7:83-87,90.
- Silva V, López AG, Martínez L. Splanchnic nerve neurolysis: Double access for abdominal cancer pain. BMJ Support Palliat Care 2021.
- Koyyalagunta D, Engle MP, Yu J, Feng L, Novy DM. The effectiveness of alcohol versus phenol based splanchnic nerve neurolysis for the treatment of intraabdominal cancer pain. *Pain Physician* 2016; 19:281-292.
- Vranken JH, Zuurmond WW, Van Kemenade FJ, Dzoljic M. Neurohistopathologic findings after a neurolytic celiac plexus block with alcohol in patients with pancreatic

cancer pain. Acta Anaesthesiol Scand 2002; 46:827-830.

- Masuda T, Kuramoto M, Shimada S, et al. Splanchnicectomy for pancreatic cancer pain. *Biomed Res Int* 2014; 2014:941726.
- 14. Stefaniak T, Basinski A, Vingerhoets A, et al. A comparison of two invasive techniques in the management of intractable pain due to inoperable pancreatic cancer: Neurolytic celiac plexus block and videothoracoscopic splanchnicectomy. *Eur J Surg Oncol* 2005; 31:768-773.
- Dong D, Zhao M, Zhang J, et al. Neurolytic splanchnic nerve block and pain relief, survival, and quality of life in unresectable pancreatic cancer: A randomized controlled trial. *Anesthesiology* 2021; 135:686-698.
- 16. Lohse I, Brothers SP. Pathogenesis and treatment of pancreatic cancer related pain. *Anticancer Res* 2020; 40:1789-1796.
- Carvajal G. Pancreatic cancer related pain: Review of pathophysiology and intrathecal drug delivery systems for pain management. *Pain Physician* 2021; 24:E583-E594.
- Paul A, Borkar A. Fluoroscopy-Guided splanchnic nerve block for cancerassociated pain. Cureus 2022; 14:e30944.
- Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *BMJ* 2021; 372:n71.
- Higgins JPT, Thomas J, Chandler J, et al. (eds). Cochrane Handbook for Systematic Reviews of Interventions version 6.3 (updated February 2022). Cochrane 2022. Available from www.training. cochrane.org/handbook
- Süleyman Ozyalçin N, Talu GK, Camlica H, Erdine S. Efficacy of coeliac plexus and splanchnic nerve blockades in body and tail located pancreatic cancer pain. Eur J Pain (London, England); 8:539-545.
- Peng YAO, Zhao GX, Jiang CL, Cui JJ, Meng LX. Efficacy of splanchnic nerve and celiac plexus block in treating superior abdominal cancer pain. Chin Clin Med Imaging 2007; 18:265-268.
- Johnson CD, Berry DP, Harris S, et al. An open randomized comparison of clinical effectiveness of protocol-driven opioid analgesia, celiac plexus block or thoracoscopic splanchnicectomy for pain management in patients with pancreatic and other abdominal malignancies. *Pancreatology* 2009; 9:755-763.

- 24. Shwita AH, Amr YM, Okab MI. Comparative study of the effects of the retrocrural celiac plexus block versus splanchnic nerve block, C-arm guided, for upper gastrointestinal tract tumors on pain relief and the quality of life at a six-month follow up. *Korean J Pain* 2015; 28:22-31.
- Pisheng Q, Wang Z, Huang LX, Zhen HG. Comparison of splanchnic nerves block and celiac plexus block for pain relief in patients with advanced pancreatic cancer. J Oncol 2009; 15:239-241.
- 26. Tewari S, Agarwal A, Dhiraaj S, et al. Comparative evaluation of retrocrural versus transaortic neurolytic celiac plexus block for pain relief in patients with upper abdominal malignancy: A retrospective observational study. *Indian J Palliat Care* 2016; 22:301-306.
- van den Beuken-van Everdingen MH, de Rijke JM, Kessels AG, Schouten HC, van Kleef M, Patijn J. Prevalence of pain in patients with cancer: A systematic review of the past 40 years Ann Oncol 2007; 18:1437-1449.
- Hearn J, Higginson IJ. Cancer pain epidemiology: A systematic review. In: Bruera ED, Portenoy RK. (eds). Cancer Pain: Assessment and Management. Cambridge University Press, London, UK, 2003, pp 19-37.
- 29. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2021; 71:209-249.
- Ashlock K. Celiac plexus block: Management of abdominal pain in patients with late-stage cancer. Clin J Oncol Nurs 2018; 22:663-665.
- Coveler AL, Mizrahi J, Eastman B, et al. Pancreas cancer-associated pain management. *Oncologist* 2021; 26:e971-e982.
- Dobosz Ł, Stefaniak T, Dobrzycka M, et al. Invasive treatment of pain associated with pancreatic cancer on different levels of WHO analgesic ladder. BMC Surg 2016; 16:20.
- Yasuda I, Wang HP. Endoscopic ultrasound-guided celiac plexus block and neurolysis. *Dig Endosc* 2017; 29:455-462.
- Gunaratnam NT, Sarma AV, Norton ID, Wiersema MJ. A prospective study of EUS-guided celiac plexus neurolysis for pancreatic cancer pain. Gastrointest

Endosc 2001; 54:316-324.

- Loukas M, Klaassen Z, Merbs W, Tubbs RS, Gielecki J, Zurada A. A review of the thoracic splanchnic nerves and celiac ganglia. *Clin Anat (New York, NY)* 2010; 23:512-522.
- Novy DM, Engle MP, Lai EA, et al. Effectiveness of splanchnic nerve neurolysis for targeting location of cancer pain: Using the pain drawing as an outcome variable. *Pain Physician* 2016; 19:397-403.
- Kapural L, Lee N, Badhey H, McRoberts WP, Jolly S. Splanchnic block at T11

provides a longer relief than celiac plexus block from nonmalignant, chronic abdominal pain. *Pain Manag* 2019; 9:115-121.

- Vanbutsele G, Pardon K, Van Belle S, et al. Effect of early and systematic integration of palliative care in patients with advanced cancer: A randomised controlled trial. *Lancet Oncol* 2018; 19:394-404.
- 39. Bakitas MA, Tosteson TD, Li Z, et al. Early versus delayed initiation of concurrent palliative oncology care: Patient outcomes in the ENABLE III

randomized controlled trial. *J Clin Oncol* 2015; 33:1438-1445.

- 40. Agarwal A, Gautam A, Rastogi S, Malviya D, Das PK, Harjai M. Effect of celiac plexus neurolysis for pain relief in patients with upper abdominal malignancy: A retrospective observational study and review of literature. Indian J Palliat Care 2020; 26:512-517.
- Comlek S. Pain control with splanchnic neurolysis in pancreatic cancer patients unresponsive to celiac plexus neurolysis. *J Pain Res* 2020; 13:2023-2031.

#### Appendix

Search via Pubmed database 1 Celiac plexus 2 Coeliac plexus 3 Celiac and plexus 4 1 or 2 or 3 5 Splanchnic 6 Splanchnic nerve 7 Splanchnicectomy 8 5 or 6 or 7 9 Retrocrural 10 Antecrural 11 9 or 10 12 Neurolysis 13 Block 14 12 or 13 15 4 and 8 16 4 and 11 17 (15 or 16) and 14 The term "cancer pain" was not used in the search strategy, instead we manually screened the titles and abstracts to identify more potentially relevant studies.