Percutaneous CT-Guided Cryoablation of the Celiac Plexus: A Retrospective Cohort Comparison with Ethanol

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ABSTRACT

Purpose: To retrospectively analyze and compare the incidence of diarrhea in patients who underwent cryoablation of the celiac plexus for intractable abdominal pain versus ethanol therapy over a 5-year period.

Materials and Methods: From June 2014 to August 2019, 83 patients were identified who underwent neurolysis of the celiac plexus for management of intractable abdominal pain by using either cryoablation (n = 39 [59% female; age range, 36–79 years old [average, 60 ± 11 years old]) or alcohol (n = 44 [48% female; age range, 29–76 years old [average, 60 ± 12 years old]). Pain scores and reports of procedure-related complications or side effects, with special attention to diarrhea and/or other gastrointestinal symptoms, were collected from follow-up visits at 1 week, 1 month, and 3 months post-intervention and were compared between groups.

Results: The mean time of follow-up was 17.7 days. Four patients who underwent cryoablation developed gastrointestinal symptoms consisting of 2 cases of nausea and vomiting and 2 cases of diarrhea (5.1%). Twelve patients who underwent ethanol ablation developed gastrointestinal symptoms, including 1 case of nausea, 3 cases of vomiting, and 9 cases of diarrhea (20.5%). There was a significantly higher incidence of both diarrhea (chi-squared likelihood ratio, $P = .03$) and overall gastrointestinal symptoms (chi-squared likelihood ratio, $P = .04$) in the ethanol group than in the cryoablation group.

Conclusions: Cryoablation of the celiac plexus may provide a new treatment option for intractable abdominal pain, and it appears to have a lower incidence of diarrhea and fewer gastrointestinal side effects than ablation using ethanol.

ABBREVIATIONS

VAS = visual analog scale

Transient diarrhea is a well-established adverse sequela of alcohol- or phenol-mediated celiac plexus neurolysis, occurring in approximately 44%–60% of cases (1,2). Chronic, debilitating diarrhea has also been associated with celiac plexus neurolysis but occurs in less than 1% of cases (3,4).

Cryoablation and cryoneurolysis are being used increasingly by interventional radiologists and interventional pain physicians for the management of acute and chronic pain (5–7), including targeting the celiac plexus for palliation of intractable abdominal pain (8–10). Computed tomography (CT)-guided percutaneous cryoablation of the celiac plexus affords operators several advantages compared to alcohol neurolysis, including direct visualization of the ablation zone, detailed knowledge of probe placement, predictable targeting, and improved safety profile (11–13)

The purpose of this study was to retrospectively analyze and compare the incidence of diarrhea in cohorts of patients who underwent CT-guided celiac plexus neurolysis with either alcohol or cryoablation for the management of intractable abdominal pain over a 5-year period.

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Table 1. Patient Demographics

	Cryoablation	Ethanol Ablation
Number of patients	39	44
Mean ± SD age, y (range)	60 ± 11 (36-79)	60 ± 12 (29- 76)
% Males/females	41/59	52/48
Indication		
Pancreatic cancer	26	30
Colon cancer	3	4
Pancreatitis	4	2
Gastric adenocarcinoma	2	1
Esophageal cancer	1	1
Cholangiocarcinoma	1	1
Ovarian cancer	-	2
Median arcuate ligament syndrome	2	-
Hepatocellular carcinoma	-	1
Persistent gastric ulceration	-	1
Bladder cancer	-	1

SD = standard deviation.

MATERIALS AND METHODS

This was a single-center retrospective review of all patients who underwent percutaneous CT-guided neurolysis of the celiac plexus between June 2014 and August 2019. The study was approved by the local Institutional Review Board and complied with the Health Insurance Portability and Accountability Act. Patients were identified through a medical record search using a search engine populated with radiology reports and associated metadata from the radiology information system. Reports and associated patients were identified using the strings "cryoneurolysis," "cryoablation," "celiac," "alcohol," and "ablation" over the time period June 1, 2014, to August 01, 2019 (Performance-Bridge Report Search, Philips, Amsterdam, The Netherlands]).

A total of 104 patients were identified using the search criteria described above. Of these patients, 83 had adequate follow-up documentation following neurolysis of the celiac plexus for management of intractable abdominal pain by using either cryoablation (n = 39 [59% female; age, 36 to 79 years old, average 60 ± 11 years old]) or alcohol (n = 44 [48% female; age, 29–76 years old; average, 60 ± 12 years old]). A total of 65 subjects had documented pain scores within a window of 48 hours before and after the procedures. Preprocedural and postprocedural pain scores and procedure-related complications were collected from all available inpatient and outpatient clinic records. Subjects were included for analysis when at least 3 documented visual analog scale (VAS) pain scores were available in the medical record within a period starting 48 hours before the procedure and ending 48 hours after the procedure. Pain scores and reports of procedure-related complications or side effects were also collected from follow-up visits at 1 week, 1 month, and 3 months postintervention, as available; therefore the range of follow-up was 90 days. Hospital progress notes, consultations, and follow-up clinic visit documentation records were reviewed specifically for any description of gastrointestinal symptoms, with special attention to diarrhea. Patient demographics and underlying indications for the procedures are delineated in Table 1.

For each cryoablation case, two 17-gauge cryoablation probes were advanced to the celiac plexus bilaterally (Fig 1). Two freeze cycles were undertaken that ranged from 8 to 10 minutes, separated by passive thaw cycles which lasted 3–5 minutes. For each alcohol case, two 22-gauge needles were advanced to the celiac plexus (one on each side) and injected with contrast to confirm extravascular location of the needle tips (Fig 2). A total of 40 mL of absolute alcohol was split between sides and injected. Needles were flushed before removal.

Likelihood ratio chi-squared tests were applied to compare the incidence of diarrhea and any other gastrointestinal symptoms postintervention between cryoablation and ethanol ablation (the primary outcome measurement). In addition, one-way ANOVA was used to compare preintervention pain scores after cryoablation with those after ethanol ablation and long-term follow-up postintervention pain scores from cryoablation with those from ethanol neurolysis. One-way ANOVA was also used to compare the differences between pre- and postintervention pain resulting from cryoablation with that from ethanol ablation. The 2-sample Wilcoxon ranked sum tests were used to compare postintervention scores between Cryoablation and ethanol neurolysis within 48 hours of the intervention (the secondary outcome measurements). A P value of $<.05$ indicated statistical significance.

RESULTS

Four patients who underwent cryoablation developed gastrointestinal symptoms, including 2 cases of nausea and vomiting and 2 cases of diarrhea (5.1%) which lasted 1.8 days and did not require treatment (SIR classification B) (see Table 2). A total of 32 subjects included in this group had pain scores recorded 48 hours before and 48 hours after the intervention. The average preintervention pain score was 5.9 ± 1.9 (range, 3–10). The average postintervention pain score was 3.1 ± 2.1 (range, 0–10) . Pain scores were available for 19 patients at 1 week (mean, 4.7 ± 2.4 [range, 0–8]), for 8 patients at 1 month (3.6 ± 2.4 [range, 0–7]), and for 1 patient at 3 months (2.9) (Table 3).

Twelve patients who underwent ethanol ablation developed gastrointestinal symptoms, including 1 case of nausea, 3 cases of vomiting, and 9 cases of diarrhea (20.5%) which lasted 3.4 days and did not require treatment (SIR classification B) (Table 3). A total of 33 subjects included in this group had pain scores recorded 48 hour before and 48

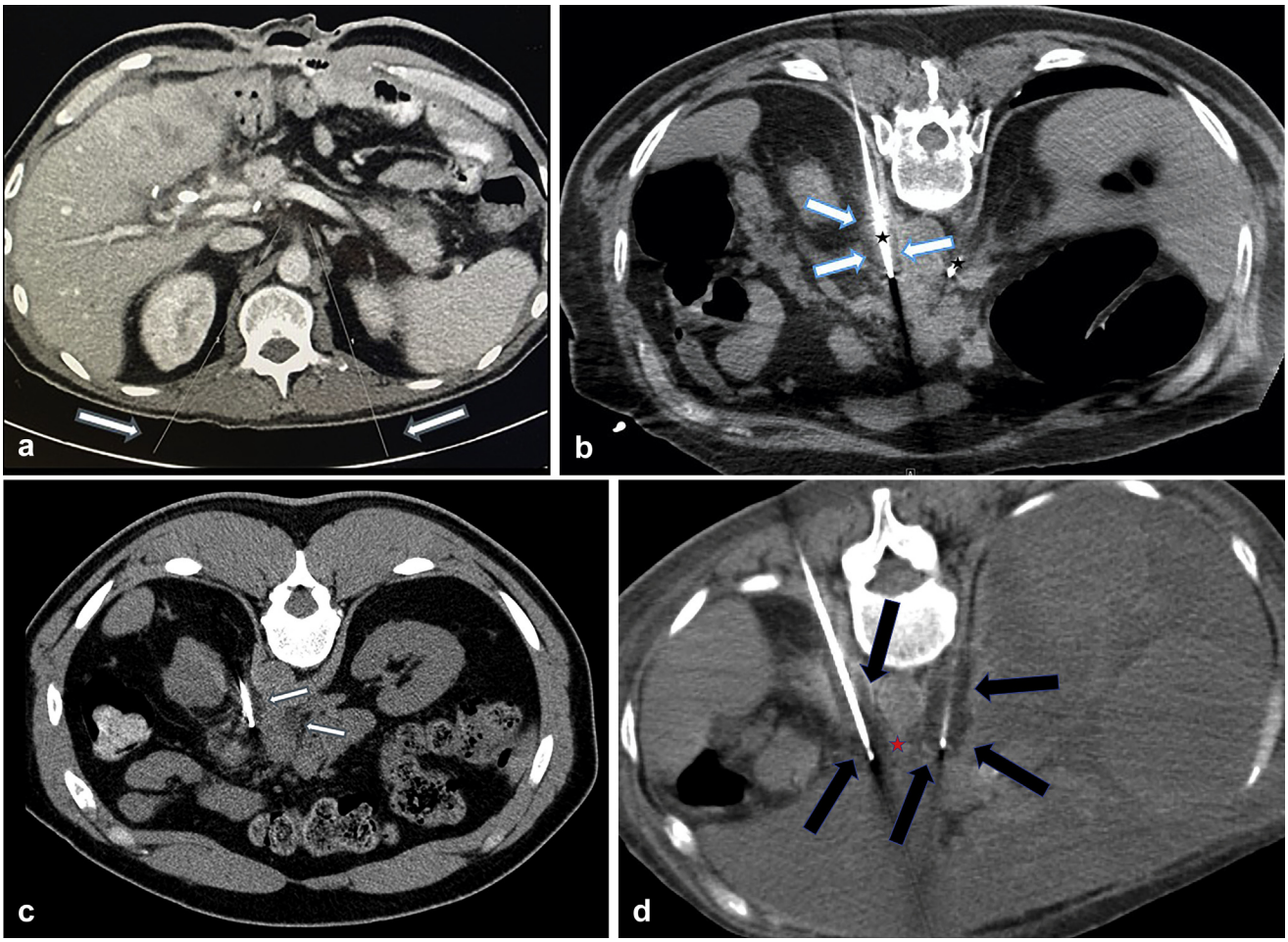

Figure 1. **(a)** Single axial contrast enhanced planning CT image demonstrates a typical approach to the celiac plexus, targeting the anterolateral aorta at the level of the celiac artery (arrows). **(b)** Single axial intraprocedural CT image at the level of T12 demonstrates two 17-gauge cryoablation probes (stars) advanced to the celiac plexus. The hypoattenuating ablation zone is outlined by arrows. **(c)** Second single axial CT image slightly above the level of the cryoprobes demonstrates the hypoattenuating ablation zone occupying the target region (**[a]** arrows). **(d)** Single axial intraprocedural image from a different patient at the level of the celiac artery (star) demonstrates coverage of the expected location of the celiac plexus network by hypoattenuating cryoablation zones bilaterally (arrows).

hours after the intervention. The average preintervention pain score was 5.0 ± 2.3 (range, 2–10). The average postintervention pain score was 3.7 ± 2.7 (range, 0–10). Pain scores were available for 14 patients at 1 week (3.9 ± 3.1 [range, 0–9]), for 5 patients at 1 month (2.6 ± 2.0 [range, 0–7]), and for 5 patients at 3 months (2.6 ± 2.5 [range, 0–7]) (Table 2).

There was a significantly higher incidence of both diarrhea (chi-squared likelihood ratio, $P = .03$) and overall gastrointestinal symptoms (chi-squared likelihood ratio, $P = .04$) in the ethanol group (27%) than in the cryoablation group (10%), although in both groups diarrhea was mild and self-limiting. The mean follow-up time was 17.7 days.

There were no significant statistical differences between the preintervention pain scores (one-way ANOVA, $P = .10$) and the postintervention pain scores in the cryoneurolysis group and those in the ethanol neurolysis group (2-sample Wilcoxon ranked sums of normal approximation, $P = .43$). There were significant differences in pain scores at the 48-hour postprocedure time point, such that those who underwent cryoablation reported significantly lower pain scores than those reported by the ethanol group (one-way ANOVA, $P = .02$). There were no significant differences among the follow-up pain scores at 1 week, 1 month, and 3 months between the cryoablation and the ethanol neurolysis groups (one-way ANOVA, $P = .74$).

DISCUSSION

The incidence of reported diarrhea and other gastrointestinal side effects (nausea, vomiting, reflux, bloating) for patients who underwent CT-guided ethanol neurolysis of the celiac plexus in this study was 20.5% and 27.3%, respectively. The incidence of diarrhea was 5.1% and 10.3% for other gastrointestinal side effects for patients who underwent CT-guided cryoneurolysis of the celiac plexus, which was significantly less than that in the ethanol group.

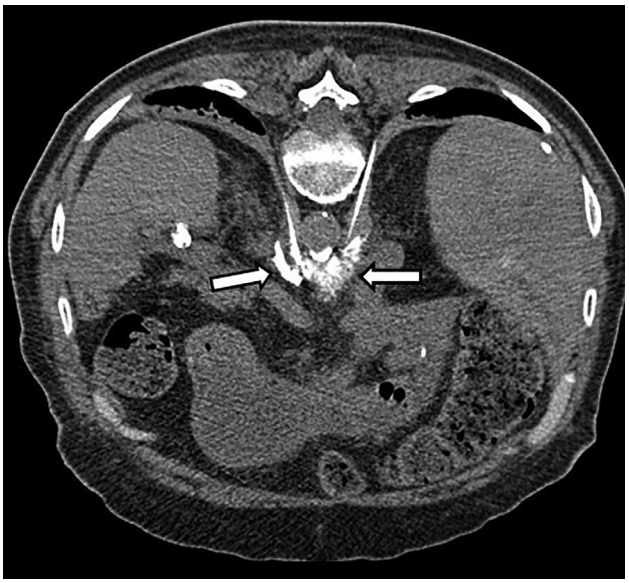

Figure 2. Single axial intraprocedural CT image demonstrates diffusion of contrast material around the celiac plexus just before ethanol injection (arrows).

Transient diarrhea is a well-known adverse sequela related to palliative celiac plexus neurolysis. Chronic and severe diarrhea have also been reported in this setting but are rare (1–4). The proposed mechanism for diarrhea is complete interruption of sympathetic efferent activity and may be dose-dependent when ethanol is used (14). Cryoablation of these nerves results in a predictable sequence of events beginning with conduction cessation and endoneural edema. Subsequent processes lead to Wallerian degeneration among an intact endoneurium and epineurium, which allows for axonal regeneration over time (15–17).

A number of studies have confirmed the efficacy of cryoablation in the setting of cancer pain, including a recent meta-analyses describing a significant decrease of requirements for opioid therapy in patients who underwent palliative cryoablation (18). Specific targeting of the celiac plexus with cryoablation was originally undertaken to offset the unpredictable diffusion of alcohol and/or bulky tumors directly invading neural tissue as part of a U.S. Food and Drug Administration-approved indication for use of existing cryoablation devices (neurology, cryoanalgesia) (8,9,19,20). The use of percutaneous cryoablation as an ablation modality or neurolytic for palliation under CT guidance also offers the unique advantages of precise targeting, direct ablation zone visualization, and less procedure-related pain than heat-mediated or chemical agent treatments (11,21).

Consistent with the proposed advantage of decreased procedure-related pain, there were significant differences in the improvement of pain scores at 48 hours after the intervention between the 2 groups in this study. The average pain scores of patients who underwent cryoablation decreased by 46.7%, whereas pain scores for patients who underwent ethanol neurolysis decreased by 26.6%. This occurrence is in line with previous reports of cryoablation for similar indications (21,22).

Table 2. GI Side-Effect Profile for Cryoablation and Ethanol Ablation with Onset 5 Days after the Procedure

	Diarrhea	Nausea and Vomiting	Nausea (No Vomiting)	All GI Side Effects
Cryoablation (n = 39)	2 (5.1%)	2 (5.1%)	0 (0%)	4 (10.3%)
Ethanol ablation (n = 44)	9 (20.5%)	3 (6.8%)	1 (2.3%)	12 (27.3%)

GI = gastrointestinal.

The study is limited by retrospective methodology, as well as by the lack of an objective method for measuring characteristics and severity of patients' diarrhea when present. Specifically, objective measurements such as the Visual Analogue Scale for Irritable Bowel Syndrome questionnaire (which evaluates abdominal pain, diarrhea, constipation; bloating and flatulence; vomiting and nausea; psychological well being; and the intestinal symptoms' influence on daily life; 23) were not used clinically, prospectively, and therefore were not available for review. It is possible that patients were not specifically asked about gastrointestinal symptoms clinically, which may lead to under-reporting or that symptoms recurred outside of the hospital system. Likewise, no prophylactic courses were implemented to protect against diarrhea, which may have lowered the documented rates of symptoms after the procedure. Finally, other potential side effects that may follow celiac plexus neurolysis or neuroablation, such as orthostatic hypotension or back pain, were not explored.

For purposes of minimizing variability in analyses, only subjects with quantitative data during the specified periprocedural time period were included. Although this approach limited the number of subjects available for inclusion and limits the amount of data available over time during follow-up, it is consistent with previous reports. For example, Eisenberg et al (2) performed a meta-analysis of studies describing alcohol or phenol neurolysis of the celiac plexus, including 21 studies and 1,145 subjects. They reported available data, including subjective descriptions of pain such as a "good" and "satisfactory" at a rate of 86% within 14 days, which dropped to 23% by 3 months, a pattern consistent with the present report.

Table 3. VAS Pain Scores for Cryoablation and Ethanol Ablation before and after Procedure

	48 h before	48 h after	1 Week	1 Month	3 Months
Cryoablation (n = 32)	5.8 ± 1.9 (n = 32)	3.1 ± 2.0 (n = 32)	4.7 ± 2.4 (n = 19)	3.7 ± 2.4 (n = 8)	2.9 (n = 1)
Ethanol ablation (n = 33)	5.0 ± 2.3 (n = 33)	3.7 ± 2.7 (n = 33)	3.9 ± 3.1 (n = 14)	2.5 ± 1.9 (n = 5)	2.6 ± 2.5 (n = 5)

VAS = visual analog scale.

Cryoablation of the celiac plexus may provide a new treatment option for intractable abdominal pain, and it appears to have a lower incidence of diarrhea and fewer gastrointestinal side effects than ablation using ethanol.

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