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ORIGINAL ARTICLE

The value of angio-CT system on splanchnic nerve neurolysis

Shinji Wada
Yasuaki Arai
Miyuki Sone
Shunsuke Sugawara
Chihiro Itou

PURPOSE
We aimed to evaluate the effectiveness and safety of splanchnic nerve neurolysis (SNN) with angio-CT, a hybrid system combining computed tomography (CT) with X-ray fluoroscopy.

METHODS
Thirty-three SNN procedures with angio-CT performed in 30 patients with severe epigastric cancer pain (11 males and 19 females; median age, 57 years; age range, 19–79 years) between January 2010 and July 2017 were retrospectively evaluated. The primary endpoints were the technical success and adverse event rates. The secondary endpoints included the clinical success rate, defined as a reduction in the numerical rating scale for pain score or a decrease in the consumption of analgesics on day 1 and at 1–2 weeks after the procedure; procedure time; the number of needle punctures; amount of ethanol required; and the distribution of contrast medium in the retrocrural space. These endpoints were compared with previous studies that did not employ the angio-CT system.

RESULTS
The technical success rate was 96.97%. There were two procedure-related adverse events (one retroperitoneal hemorrhage, one pneumothorax). The clinical success rates on day 1 and at 1–2 weeks after the procedure were 84.38% and 87.5%, respectively. The median procedure time was 60 minutes. The median number of needles used was 2. The median amount of ethanol used was 20 mL.

CONCLUSION
SNN under angio-CT is safe and effective, with excellent technical and clinical success rates and acceptable adverse event rates. These results are comparable with previous studies that did not involve angio-CT. However, the use of angio-CT allows for easier needle positioning and an earlier response to complications compared with conventional methods.

Splanchnic nerve neurolysis (SNN) has been established as an effective palliative treatment for intractable cancer pain in the upper abdomen (1–6). The splanchnic nerve is located in the retrocrural space, which is a narrow area surrounded by the crura of the diaphragm, vertebral bodies, and aorta (Fig. 1). This makes it difficult to access this space and achieve adequate local distribution of drugs. X-ray fluoroscopy, computed tomography (CT), and endoscopic ultrasonography (EUS) are the imaging modalities generally used for SNN; however, each of these alone cannot provide real-time, high spatial resolution images of the coronal, axial, and sagittal planes, or three-dimensional visualization. With angio-CT, X-ray fluoroscopy, conventional CT, and CT fluoroscopy images can be obtained on the same sliding table when needed. Therefore, the purpose of this retrospective study was to evaluate the usefulness of angio-CT in SNN.

Methods

Patients

The medical records of patients with severe epigastric pain treated by SNN with angio-CT from January 2010 to July 2017 were included in this retrospective, single-center observational study. Thirty-three SNN procedures were performed in 30 patients during the study

From the Department of Radiology (S.W. ✉ *shinjiwada@marianna-u.ac.jp*), St. Marianna University School of Medicine, Kanagawa, Japan; Department of Diagnostic Radiology (Y.A., M.S., S.S., C.I.), National Cancer Center Hospital, Tokyo, Japan.

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period; the procedure was repeated in 3 patients. The patient characteristics are shown in Table 1.

The study was approved by our institutional review board (2020-028), which waived the requirement for informed patient consent. Written informed consent for the SNN procedure itself was obtained from all patients. All patients had intractable upper abdominal pain due to insufficient analgesia with narcotics or side effects that precluded the use of adequate doses of narcotics. However, patients with a prothrombin time/international normalized ratio ≥1.5 or platelet count of ≤50 000 were excluded.

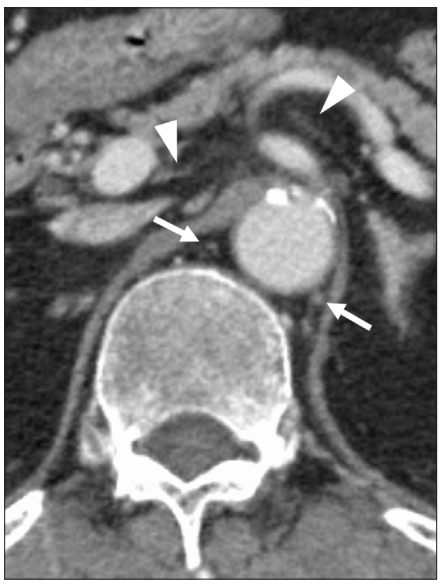

Figure 1. Axial CT image shows normal splanchnic and celiac ganglions. The splanchnic nerve is located in the retrocrural space, which is a narrow area surrounded by the crura of the diaphragm, vertebral bodies, and aorta *(arrows)*. However, the celiac plexus is located over the anterolateral surface of the aorta and around the origin of the celiac trunk *(arrowheads)*.

Procedures

All SNN procedures were performed by one or two radiologists, at least one of whom was a certificated interventional radiologist, in collaboration with an anesthesiologist. Vital signs and neurological deficits were monitored during treatment. First, the patient underwent a CT scan using a 16-slice angio-CT unit (Infinix-I 4DCT; AquilionLB, INFX-8000c; Canon Medical Systems Corp.) in the prone or lateral decubitus position, and the puncture route from the patient's back to the retrocrural space at T12-L1 was determined. After administration of local anesthesia, a 21-gauge disposable percutaneous transhepatic cholangiography needle (TOP Corp.) was used to puncture the retrocrural space. If the target could be reached with a needle via the paravertebral route, the puncture was performed under CT fluoroscopy. With access via the intervertebral disc, the needle was advanced under CT-fluoroscopy guidance until the intervertebral disc was reached, after which the needle was guided through the intervertebral space under X-ray fluoroscopy in the lateral view.

Next, approximately 10 mL of a 1:1 mixture of 2% xylocaine and nonionic contrast medium (240 mg iodine per mL) was slowly injected. The distribution of the mixture was observed in real time using X-ray fluoroscopy in the craniocaudal aspect. A CT scan was subsequently performed to assess the distribution of the mixture in the retrocrural space. If the spread of the contrast medium was inadequate, an additional needle puncture or re-positioning of the needle was performed. When monitoring of trajectory was difficult on CT cross-sections, we switched to guidance using lateral view X-ray fluoroscopy. Vital signs and symptoms were carefully monitored for 15 minutes to check for adverse events. After confirming that no adverse events had occurred, the same amount of absolute ethanol, as determined according to the spread of the contrast medium, was injected. The needle was withdrawn using the negative pressure technique. To complete the procedure, a CT scan was performed to rule out the occurrence of adverse events.

Endpoints

The primary endpoints were the technical success and adverse event rates. The procedure was deemed to be successful if the distribution of the contrast medium in the retrocrural space was confirmed in the craniocaudal direction bilaterally. Adverse events during and after the procedure were evaluated using the Common Terminology Criteria for Adverse Events, version 4.0. The secondary endpoints were the clinical success rates, number of needle punctures required, amount of ethanol, and the distribution of the contrast medium in the craniocaudal direction. Clinical success was defined as a 50% reduction in the numerical rating scale (NRS) pain score or a 50% reduction in the consumption of analgesics (opioids and nonsteroidal antiinflammatory

Main points

- The technical success rate of splanchnic nerve neurolysis was 96.97%. The clinical success rates on day 1 and 1–2 weeks after the procedure were 84.38% and 87.5%, respectively.
- By using angio-CT, it is easy to advance the needle to just before the intervertebral disc under CT or CT fluoroscopy; switching to X-ray fluoroscopic guidance in the intervertebral space facilitates puncture to the target and the distribution of the contrast materials can be confirmed in real time.
- These results are comparable to previous reports; however, with angio-CT, the procedure of splanchnic nerve neurolysis is thought to be easier than conventional methods due to accurate needle positioning and early response to complications.

Table 1. Patients characteristics

Age (years), median (min–max)	57 (19–79)
Male : female	11 : 19
ECOG performance status, n (%)	
0–1	14 (46.67)
2–3	16 (53.33)
Type of malignancy, n (%)	
Pancreatic cancer	18 (60)
Retroperitoneal lymph node (esophageal cancer, gastric cancer, cholangiocarcinoma, neuroendocrine tumor, lung cancer and carcinoma of unknown primary)	10 (33.33)
Others	2 (6.67)
Initial NRS, median (min–max)	4.5 (0–10)
Observation period (days), median (min–max)	90 (7–1490)

ECOG, Eastern Cooperative Oncology Group; NRS, numerical rating scale.

Table 2. Details of patients who underwent splanchnic nerve neurolysis with angio-CT

Technical success, n (%)	32 (96.97)
Clinical success, n (%)	
Day 1	27 (84.38)
1–2 weeks	28 (87.5)
Procedure time (min), median (min–max)	60 (40–150)
Number of needle punctures, median (min–max)	2 (1–3)
Amount of ethanol (mL), median (min–max)	20 (7.5–30)
Adverse events (CTCAE v4.0), n (%)	
Hypotension (grade 1)	10 (30.3)
Diarrhea (grade 1)	3 (9.09)
Retroperitoneal hematoma (grade 2)	1 (3.03)
Pneumothorax (grade 1)	1 (3.03)
Stroke (grade 4)	1 (3.03)

CTCAE, common terminology criteria for adverse events.

Table 3. Comparison between the clinical success and failure groups after splanchnic nerve neurolysis

	Success (n=28)	Failure (n=4)	*p*
Age (years), median (min–max)	57 (19–79)	55.5 (37–58)	0.494
Female, n (%)	19 (67.86)	2 (50)	0.593
ECOG performance status, median (min–max)	2 (1–3)	2 (1–3)	0.476
Initial NRS score, median (min–max)	4 (0–10)	4.5 (1–10)	0.752
Patients of pancreatic cancer, n (%)	16 (57.14)	3 (75)	0.629
Procedure time (min), median (min–max)	60 (40–150)	75 (60–110)	0.144
Number of needle punctures, median (min–max)	2 (1–3)	2 (2–2)	1.000
Amount of ethanol (mL), median (min–max)	20 (10–20)	20 (7.5–30)	0.926
Distribution of ethanol (cranio-caudal direction)			
In the range of 3 vertebral bodies, n (%)	11 (39.29)	4 (100)	0.038
In the range of 4 or 5 vertebral bodies, n (%)	17 (60.71)	0 (0)	

ECOG, Eastern Cooperative Oncology Group; NRS, numerical rating scale.

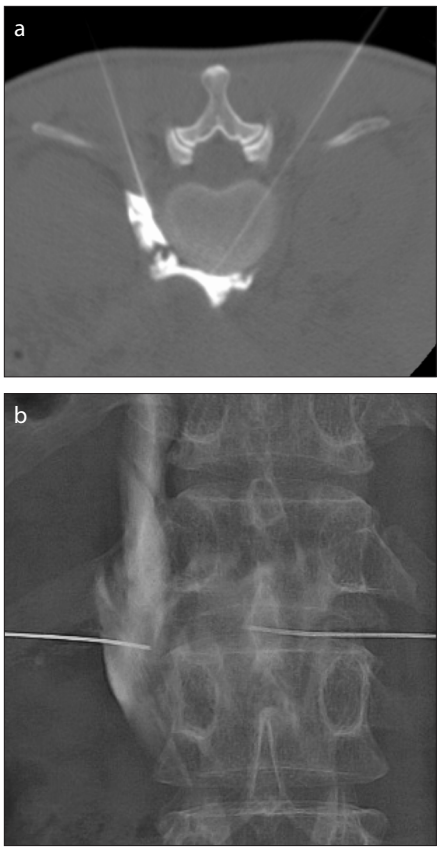

Figure 2. a, b. Images of a man in his 50s with pancreatic cancer who underwent splanchnic nerve neurolysis. Axial CT image **(a)** shows the bilateral distribution of contrast medium in the retrocrural space. Right-sided puncture is often performed via the intervertebral disc. In image **(b)**, the distribution of contrast medium in the craniocaudal direction is easily observed with X-ray fluoroscopy. In this case, the contrast medium was distributed within the range of 3 vertebral bodies.

drugs) on the day following the procedure and 1–2 weeks later.

The results were subsequently reviewed and SNN using angio-CT was compared to the conventional approaches.

Statistical analysis

Factors potentially influencing the clinical success of SNN were determined via univariate analysis. Shapiro–Wilk test was used for normality. Fisher's exact test was used to compare categorical variables and the Wilcoxon rank sum test was used as a nonparametric test for continuous variables that were not normally distributed. Descriptive statistics of the data are presented either as n (%) or median (min–max) for non-normalized variables. A p value < 0.05 was considered statistically significant. The statistical analysis was performed using JMP software (version 14.2.0; SAS Institute Inc.).

Results

The technical success rate was 96.97% (32 of 33 procedures). The procedure was terminated in one patient because of retrocrural hemorrhage. SNN was subsequently performed successfully 2 weeks later after absorption of the hematoma. There were 16 complications (grade 1 hypotension, n=10; grade 1 diarrhea, n=3; grade 1 retroperitoneal hematoma, n=1; grade 1 pneumothorax, n=1; and grade 4 stroke, n=1). Procedure-related adverse events included one case of retroperitoneal hemorrhage and one case of pneumothorax. Although not directly related to the procedure, stroke on the day following SNN occurred in one patient. The clinical success rates on the day after the procedure and 1–2 weeks later were 84.38% and 87.5%, respectively. The median procedure time was 60 minutes (40–150 min), the median number of needle punctures was 2 (1–3), and the median volume of ethanol used was 20 mL (5–30 mL) (Table 2).

Spread of contrast medium within the range of 3 and 4-5 vertebral bodies was observed in 15 and 17 cases, respectively. In 4 patients in whom SNN was considered a clinical failure, the contrast medium had spread within the range of 3 vertebral bodies. There was a significant difference (p = 0.038) in the clinical success rate and distribution of contrast medium between the 2 levels, but not in the patient characteristics or procedures (Table 3).

Table 4. Literature review of "splanchnic nerve neurolysis" or "splanchnic nerve block"

Reference	No. of patients	Technique	Clinical success, time after procedure	Severe complications
Ahmed et al., 2017 (14)	21	Fluoroscopy, 6 mL of 50% alcohol in 0.25% bupivacaine on each side	92%, 1–2 weeks	No
Koyyalagunta et al., 2016 (13)	93	Fluoroscopy, ultrasound, endoscopic, or CT guidance, alcohol (98% dehydrated ethanol), phenol (10% phenol in 20% glycerin)	64%, 1 month	No
Novy et al., 2016 (12)	60	Fluoroscopy, 8 mL of 6% phenol or 98% alcohol on each side	80%, 1 month	Not reported
Shwita et al., 2015 (7)	79	Fluoroscopy SNN: 10 mL of 70% alcohol on each side CPN: 20 mL of 70% alcohol	Comparison of results between groups	No
Chen et al., 2015 (11)	24	Fluoroscopy, 6 mL of 95% alcohol on each side	All patients who had ≥50% pain relief after diagnostic nerve block	No
Plancarte et al., 2010 (10)	109	CT, 8–10 mL of 10% aqueous phenol	98%, 1 week	Transient paraparesis occurred in 1 patient
Süleyman Ozyalçin et al., 2004 (6)	39	Fluoroscopy SNN: 6 mL of 75% alcohol on each side CPN: 40 mL of 75% alcohol on left side	All patients who had ≥50% pain relief after diagnostic nerve block	No
Fields, 1996 (9)	10	CT, 5–15 mL of 96% alcohol	80%, not uniform	No
Fujita, 1993 (8)	27	CT, 15 mL of 93% alcohol on each side	95%, 3–5 days	No

CT, computed tomography; CPN, celiac plexus neurolysis; SNN, splanchnic nerve neurolysis.

Discussion

Numerous studies, including randomized controlled trials, have demonstrated that SNN is an effective palliative therapy for severe upper abdominal pain; however, none has investigated the use of angio-CT during SNN (1–14). Delineating the precise anatomical structure of the abdomen using conventional fluoroscopic guidance is challenging. Furthermore, it is difficult to puncture through the intervertebral disc and confirm the distribution of drugs in the craniocaudal direction in real time using CT guidance. In recent years, EUS-guided procedures have been performed, but the results depend on the operator's skill and there is an associated risk of pancreatitis (15). It is often difficult to avoid needle puncture through the intervertebral disc when employing the posterior approach to SNN. Angio-CT allows the operator to easily advance the needle to a point immediately before the intervertebral disc under CT or CT fluoroscopic guidance. Furthermore, switching to X-ray fluoroscopic guidance in the intervertebral space facilitates puncture of the target, and allows the distribution of the contrast medium to be monitored in real time (Fig. 2).

A PubMed search for studies on "splanchnic nerve neurolysis or block" for intractable abdominal cancer pain (excluding case reports) published over the past 30 years revealed that the most common underlying disease was pancreatic cancer. Most SNN procedures were performed using the posterior approach and the reported clinical effectiveness was 64%–98% (Table 4) (6–14). However, few reports mention technical success; only one report by Fujita et al. (7) reported a technical success rate of 83%. Considering that half of the procedures in this study were performed by operators with experience of less than 5 cases, the 96.97% technical success rate achieved is notable.

The clinical success (i.e., pain relief) rates were 84.38% on the day after treatment and 87.5% 1–2 weeks later, which were comparable to those of previous reports. In celiac plexus neurolysis, it is more effective to distribute the drug around the celiac artery bilaterally than unilaterally (6, 16). Using angio-CT to confirm bilateral distribution of the drug in the retrocrural space in three dimensions may have helped achieve the high clinical success rate. When the spread of contrast agent in the craniocaudal direction was greater than the range of 4 vertebral bodies, the clinical results were significantly better than when it was within the range of 3 vertebral bodies ($p = 0.038$). In fact, in the 4 cases that were considered failures, the drug distribution was within the range of 3 vertebral bodies.

In terms of adverse events, diarrhea and hypotension were common, both of which have been previously reported and are considered to be clinically acceptable. Cerebral infarction occurred in one case and was not considered to be directly related to the procedure; however, the stroke may have been triggered by hypotension as a result of the SNN. In addition, in one case, the procedure was temporarily stopped due to the development of hematoma in the retrocrural space. In this case, since the spread of the contrast medium was poor after puncture under X-ray fluoroscopy, the procedure was discontinued because hematoma was immediately confirmed by CT. The procedure was subsequently performed at a later date and was clinically successful. Therefore, angio-CT is considered to have been useful in quickly recognizing such adverse events and facilitating quick clinical decisions.

This study shows that with angio-CT, SNN, which was previously considered a difficult procedure, can be performed with high technical success rates (even by a non-specialist), clinical effectiveness, and acceptable safety. The ability to immediately evaluate drug distribution and complications are also considered to be advantages of angio-CT. These benefits are similar to those obtained using cone-beam CT, but angio-CT seems to offer superior CT image

quality while allowing quick switching between X-ray fluoroscopy and CT (17).

However, some limitations to this study should be noted. First, the method presented here was not compared with conventional methods. Second, this was a retrospective study involving a small number of cases. Third, the post-procedure follow-up period was short; therefore, we cannot comment on the long-term clinical effectiveness of SNN with angio-CT. Further evaluation with a prospective study involving a larger number of cases is warranted.

In conclusion, SNN under angio-CT demonstrated high technical success and clinical effectiveness rates with acceptable adverse event rates. In addition, performing SNN using angio-CT may be technically easier and safer, allowing for early detection, and rapid judgment and response to adverse events.

Financial disclosure

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Conflict of interest disclosure

Dr. Arai has received personal fees from Guerbet Japan, Kyorin Pharma, Canon Medical Systems, Fuji Pharma, Sumitomo Bakelite, and Japan Lifeline, none of which have any bearing on the submitted work. The other authors have nothing to disclose.

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