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Ultrasound-guided alcoholization of celiac plexus for pain control in oncology

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Abstract
Background: Treatment of inoperable pancreatic cancer pain is of paramount importance. The ineffectiveness of pharmacological agents has led many investigators to recommend chemical neurolysis of the celiac ganglions for pain control. This procedure may be performed under either fluoroscopic or computed tomography (CT) guidance, or it may accompany laparotomy. The authors describe a modified sonographically (ultrasound—US)-guided technique for alcoholization of the celiac ganglions.
Methods: Twelve patients underwent the neurolytic procedure. Nine of 12 suffered from pancreatic cancer. The remaining three were affected by inoperable hepatic, gastric, or colon cancer, respectively, with multiple hepatic metastases. US-guided alcohol neurolysis was performed by an anterior approach. In the last four patients, PIA (percutaneous injection alcohol) needles, modified by the authors, replaced the spinal needles employed in the first eight patients to inject the alcohol. Pain and pain relief were rated according to a Simple Descriptive Scale (SDS), and treatment success was gauged by declining opiate doses and need for pharmacological therapy. Results after treatment performed using different needles were compared.
Results: Procedure-related mortality was zero. Complications of the neurolytic procedure included left pleural effusion in one patient and mild diarrhea in two other patients. Positive, negative, and indeterminant results were noted in nine (75%, $p < 0.001$), two, and one patient(s), respectively.
Conclusions: The neurolytic technique, although far from being considered a routine procedure, appears to provide patients with safe and effective pain relief for pain unresponsive to conventional medical treatment.

Key words: Pain-relieving procedures — Alcoholization of celiac plexus — Ultrasound-guided — Inoperable pancreatic cancer

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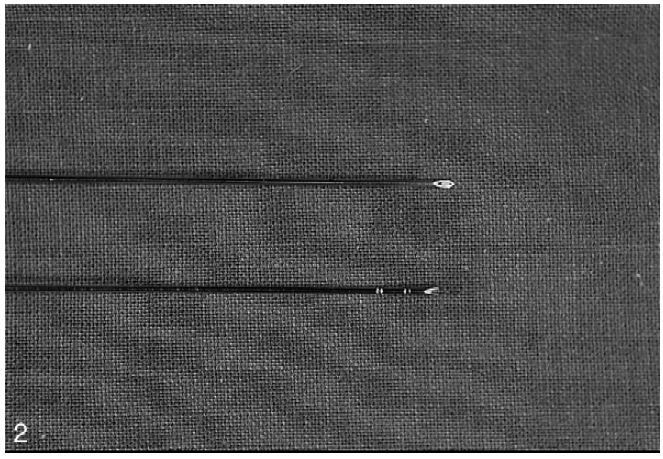
Malignant tumors of the pancreas, particularly those arising from the exocrine part, are extremely difficult to treat surgically, and 5-year mortality rates of up to 99% have been reported [22]. The incidence of pancreatic neoplasms has tripled over the last 40 years, and survival after demolitive procedures, when possible, is of very short duration [9, 22].

Extremely severe pain usually arises from invasion of nervous structures by the expanding neoplastic mass [8]. Pain relief, therefore, has become an issue of paramount importance, and the search for effective analgesic agents continues. Studies of variably increasing doses of different types of drugs, such as nonsteroidal antiinflammatory drugs (NSAIDs) and major and minor opioids, conducted along lines proposed by the World Health Organization (W.H.O.), have yielded poor or inconclusive results. Chemical neurolysis of celiac ganglions is currently an extremely effective procedure to block transmission and achieve significant or complete alleviation of deep visceral pain, which is responsible for a marked reduction of survival in 85% of patients with pancreatic neoplasms. The technique is common, has been described extensively [2, 4, 10, 11, 13, 15, 17], and may be performed by an anterior or posterior approach employing either laparotomy or fluoroscopic, computerized tomographic (CT), or sonographic (US) guidance.

In 1990, Sharfman and Walsh [20] presented a 15-year retrospective study of 480 cases of successful chemical neurolysis. Nonetheless, widespread consensus for the procedure has not been forthcoming, and it has been performed in only a small number of patients affected by acute pain. Relative ignorance of its advantages, fear of therapeutic ineffectiveness, and possible complications due to erroneous performance of it have negatively influenced universal acceptance of the procedure among practitioners. Variability of results and difficulty in localizing the right celiac plexus have also been cited [13].

Recently, radiologic guidance has been shown to be fundamental in improving the quality and reproducibility of the neurolytic procedure and in making it safer and more effective. Serial computed tomography (CT) concomitant with chemical neurolysis has been proposed.



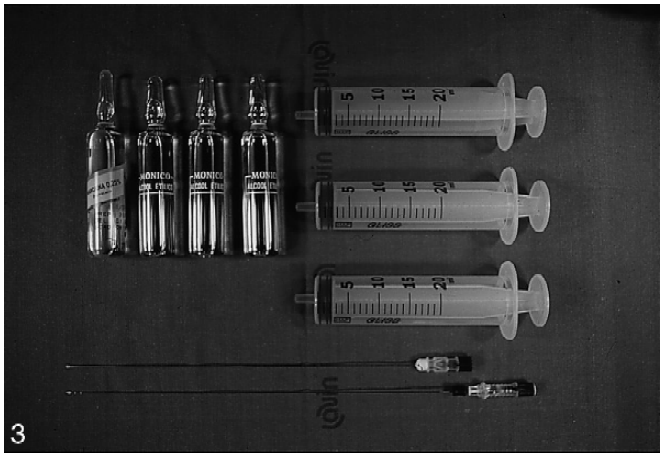


Fig. 1. The 3.5-MHz convex probe with mounted biopsy kit.

Fig. 2. The 22-gauge spinal needle with Chiba tip **(upper figure)** and the modified 22-gauge PIA bore tip needle with multiple lateral holes **(lower figure).** *PIA* = percutaneous injection alcohol.

Fig. 3. Disposable parts composing the US-guided alcoholization kit. US = ultrasound.

Montero Matamala et al. [17] have described both an anterior and posterior approach in which a 21- or 22-gauge needle is inserted laterally to the celiac trunk from the right or left side of the patient. The procedure is then repeated on the opposite side to produce the desired neurolysis of both celiac ganglions, and consequent maximal analgesia.

Recently, Montero Matamala et al. employed ultrasound (US) guidance to perform celiac ganglion alcoholization by anterior approach [18]. Precise needle placement in the retroperitoneum posed a problem, however, as ultrasound reflection from the needle tip was poorly visible in the hyperechoic retroperitoneal tissue.

For that reason, a variant of the original anteriorly executed, US-guided, celiac plexus alcoholization procedure first described by Montero Matamala et al. [18] has been proposed by the authors and described in this paper [3, 16].

Materials and methods

Between January 1991 and May 1995, a study population of 12 patients (eight women and four men) with a mean age of 57.2 years (range 48–67) was evaluated at the 4th Department of Surgery and the Department of Anesthesiology (Palliative Care Unit) of the University of Rome (Italy) ''La Sapienza'' School of Medicine. Nine patients were affected by pancreatic cancer, one by gastric cancer with hepatic metastases, one by colon cancer with multiple hepatic metastases, and one by multifocal hepatocellular carcinoma.

Three of nine pancreatic cancer patients had undergone prior resection of the pancreatic head by Whipple procedure and were subsequently deemed candidates for celiac plexus alcoholization either 3, 4, or 6 months, respectively, after surgery. The remaining six pancreatic carcinoma patients had been considered inoperable due to vascular encasement or obstruction, distant metastases, or significant expansion of neoplastic mass.

Also, prior total gastrectomy had been performed on the patient affected by gastric cancer.

Moderate-to-severe dull, sore, or burning pain, localized in the abdomen, was noted in all patients, and became shooting and intolerable as it radiated to the back. Pain radiated to the right shoulder in the patient affected by hepatocellular carcinoma, and in one case of cancer of the pancreatic head with metastatic pleural effusion, radiation to the left hemithorax was observed.

Pain was resistant to high oral doses of morphine in all patients and to continuous subcutaneous infusion of morphine in four patients. Administration of steroids or NSAIDs was without effect in all cases.

All patients underwent US-guided celiac plexus neurolysis by anterior approach. Real-time two-dimensional US guidance was performed employing either an Aloka SSD 650 (Aloka, Mitaka-shi, Tokyo, Japan) scanner or an EsaOte 560 (EsaOte Biomedica, Genoa, Italy) scanner, both equipped with a 3.5-MHz convex transducer (Fig. 1). Percutaneous introduction of the needle by linear puncture probe, angled at 30°, followed. Enhanced precision of plexus localization and rapidity of execution over the free-hand technique were characteristic of this procedure protocol.

Two types of needles were used: (1) a 22-gauge spinal needle (Becton & Dickinson, Madrid, Spain) 17.8 cm long, with internal stylet incorporated, in eight patients; and (2) a modified 22-gauge PIA (Percutaneous Injection Alcohol) needle (Sterylab, Rho, Italy) 20 cm long, possessing both internal stylet and 0.5-mm-diameter lateral holes located 8 mm from the tip, in the remaining patients (Figs. 2, 3). The PIA needle was specifically modified by the authors to meet procedural needs, with a Chiba bore tip substituting for the usual conical tip.

Although all patients were in the terminal phase of their diseases and extremely emaciated due to neoplastic cachexia and nutritional decline, when the alcoholization procedure was attempted, needle lengths >17 cm

Table 1. Score of the Simple Descriptive Scale (SDS)

5 Terrible pain
4 Severe pain
3 Moderate pain
2 Mild pain
1 No pain

were nonetheless required to reach the target area in the retroperitoneum; needle shafts had to traverse the entire abdomen in the anterior approach, and 5–6 cm of needle length remained incorporated in the puncture kit.

In order to better evaluate treatment results, each patient was asked to judge the intensity of preprocedure pain, according to a Simple Descriptive Scale (SDS) of five categories, from grade 1 (no pain) up to grade 5 (terrible pain) (Table 1).

The procedure was performed in an operating room with electrocardiogram (ECG) and blood pressure monitored by an anesthesiologist. Sedation was initiated by a 7 μg/kg IV dose of fentanyl (Fentanest, Carlo Erba, Milan, Italy), followed by 2 mg/kg of propofol (Diprivan, Zeneca, Basiglio, Italy) to prevent unintentional movements during the procedure. A 10 ml/kg IV infusion of dextran (MW 40,000) in water was administered to expand blood volume and prevent a hypotensive reaction to sudden opening of splanchnic arterial shunts [3], a possible consequence of celiac plexus destruction.

Patient position on the operating table was supine, and serial transverse sonographic scans were made to define the common celiac trunk at its origin from the aorta and at its division into splenic and gastrohepatic branches.

Optimal ventilation was assured by the anesthesiologist, through hyperextension and forward displacement of the mandible and use of a ventilation bag.

A spinal needle was inserted via anterior approach and advanced along a pathway lying perpendicular to the common celiac trunk. Contrary to the opinions expressed by other authors [18], the anterior lateral wall of the aorta was punctured to allow entrance of the needle tip into the vascular lumen (Fig. 4). As precise placement of the needle is crucial to the success of neurolysis, this variant of the usual procedure made that possible by permitting clear identification of the needle tip and its unequivocal demarcation from the surrounding hyperechoic retroperitoneal adipose tissue.

Subsequently, the distance between needle tip and celiac ganglion was estimated visually on a video monitor, and the needle tip was then withdrawn from the aortic lumen and positioned exactly 1 cm from the anterior lateral aortic wall (Fig. 5). The stylet was then removed, and, after careful suction to exclude needle presence within a vascular lumen, 6 ml of 0.25% bupivacaine (Marcaine, Astra Farmaceutici, Milan, Italy) was injected. Injection of local anesthetic must always precede that of alcohol to reduce the pain of either ganglion neurolysis or retroperitoneal tissue necrosis. Shortly after bupivacaine injection and additional suction, 15 ml of 48% sterile alcohol was injected under US guidance (Fig. 6).

The entire procedure was then repeated on the opposite side [3, 16] (Figs. 7–9), and careful monitorization of ECG, heart rate, blood pressure, serum amylase, and coagulation tests for the first 24 h postop followed in the Intensive Care Unit (ICU).

Tolerance to pain classified by SDS was evaluated every 12 h for 2 days and then every 30 days. The results achieved after the treatments performed using spinal needles and specially modified PIA needles were compared.

Results

Neither mortality nor major complications followed the transaortic approach to celiac ganglion block, although one patient did die 2 days after the procedure as a result of chronic restrictive cardiomyopathy and heart failure, as confirmed by autopsy. Minor complications included an increase of preexisting left pleural effusion of neoplastic origin in one patient, caused by alcohol dispersion along the left diaphragmatic crus, resulting in pleural inflammation. Evacuative thoracentesis was resolutive in that case. Two patients experienced mild diarrhea (4–8 bowel movements/day), which resolved with medical treatment. Severe falls in blood pressure and orthostatic hypotension were not observed.

Tolerance to pain, classified by SDS, was optimal in nine patients (75%, $p < 0.001$), who received only NSAIDs or cortisone until their deaths (2–6 months after the procedure).

The puncture site in the patient who had succumbed on the 2nd postoperative day was examined at autopsy, and no procedure-related injury to the aortic wall was found. Although many intimal atherosclerotic plaques were evident in the aorta, with thrombi and ulcers at the aortic bifurcation, only a mild and relatively irrelevant adventitial hemorrhagic suffusion was found at the puncture site.

The pharmacological therapy administered before and after celiac plexus alcohol neurolysis is reported in Table 2, with a net reduction in opiate administration evident. In only two patients was it necessary to prolong oral analgesic therapy with half doses (60 mg/day) of timed-delay morphine (MS Contin, Chinoin, Milan, Italy).

When the modified PIA needle was employed in the last four cases to inject the alcohol, both radial distribution of alcohol in the retroperitoneum and patient reaction to treatment improved. Because of the limited number of patients treated, the success rate of alcoholization when the modified PIA needle was used (100%) was not significantly higher than that (75%) when a conventional spinal needle was employed ($p = 0.38$) (Fig. 10).

Discussion

The reported positive results of celiac plexus chemical neurolysis have been rather variable, ranging from 60% to 85% of cases. The average postoperative pain-free interval has varied from 2 to 240 days [11, 14]. For those reasons, this procedure has been performed only when other medical treatments have failed to alleviate pain; and even then, universal consensus for the procedure has not been forthcoming [11].

Recent improvements in the procedure, such as its performance under fluoroscopic or CT guidance [17], have increased the percentages of positive results obtained in different studies, although nonuniformity of techniques has led to variability of those results [13].

Chemical neurolysis performed under US guidance offers many advantages over the other procedures proposed. First of all, it allows observation of the entire procedure on a video monitor in real time, with a clear and unobstructed view of needle puncture and needle insertion into the aortic lumen, precise localization of the needle on both sides of the celiac plexus, and demonstration of direction of alcohol diffusion in the retroperitoneal tissue. The latter permits correction of the diffusion pathway, when anatomic and structural alterations resulting from neoplastic expansion cause alcohol to diffuse in the wrong direction.

Second, the US-guided procedure exposes neither patient nor physician to unnecessary radiation, and is also less time-consuming than either fluoroscopic or CT-guided procedures, which require serial scanning to precisely localize the needle before injection of alcohol can be initiated. Preparation, sedation, and alcoholization of both celiac gan-

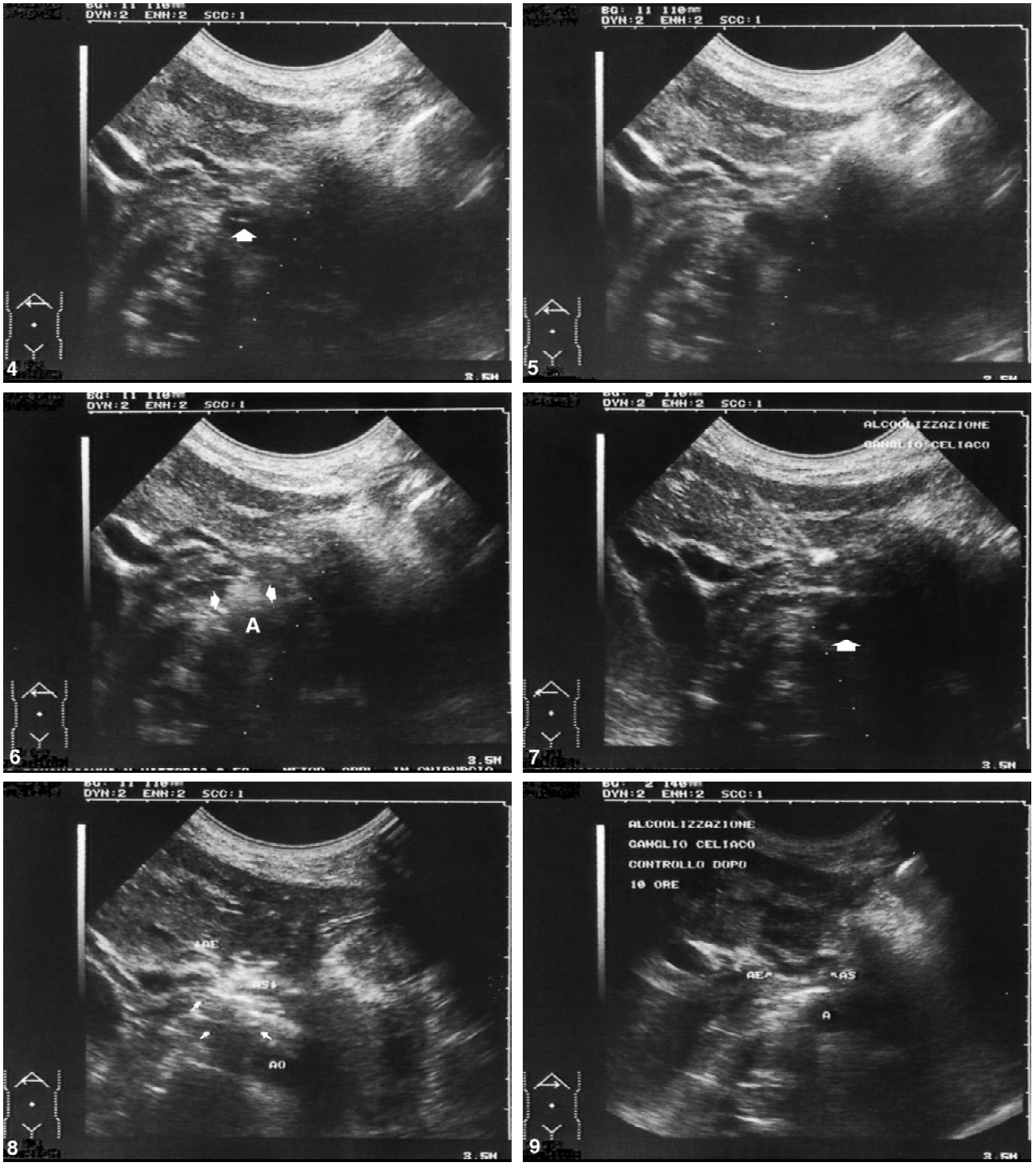


Fig. 4. Transverse scan at celiac trunk level. The *arrow* indicates the needle tip within the aortic lumen. Left approach.

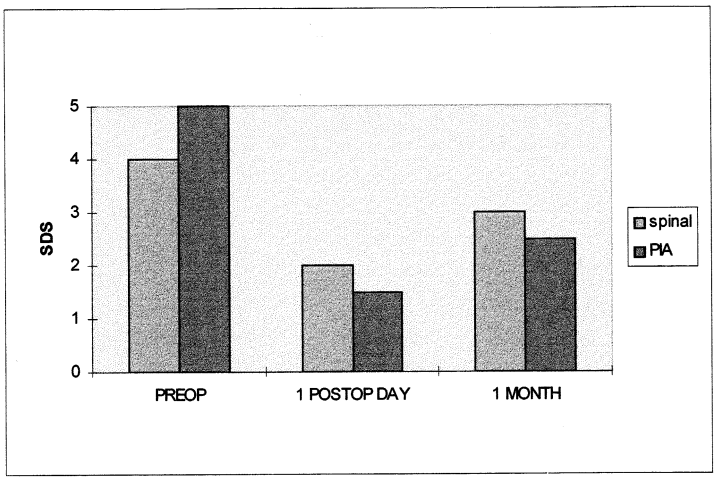
Fig. 5. The needle is withdrawn 2 cm and repositioned anterior to the vessel. The *arrow* indicates the needle tip in the retroperitoneal space.

Fig. 6. *Arrowheads* indicate alcohol diffusion along the aorta after injection. *A* = aorta.

Fig. 7. The *white arrow* indicates needle penetration to the aorta. Right approach.

Fig. 8. Hyperechoic area (*arrows*) of alcohol diffusion anterior to the aorta. *AO* = aorta; *AE* = hepatic artery; *AS* = splenic artery.

Fig. 9. Sonographic control 10 h after treatment. Hyperechoic halo of alcohol-induced necrosis surrounds the celiac trunk. *A* = aorta; *AE* = hepatic artery; *AS* = splenic artery.



	SDS		
	PREOP (min-max)	*1 POSTOP DAY (min-max)*	*1 MONTH (min-max)*
Spinal	4 - 5	1 - 3	2 - 5
PIA	4 - 5	1 - 2	1 - 3

Fig. 10. Diagram of pain decrease as median SDS value at 1-day and 1-month after treatments performed employing conventional spinal needles and specially modified PIA needles. The enclosed table shows the min and max SDS values before treatment, and at 1 day and 1 month after treatment.

Table 2. Therapetucial results and variations of SDS

Before alcoholization						After alcoholization				
NSAID	Corticoids	Morphine	SDS	Patient	Needle	NSAID	Corticoids	Morphine	SDS 1 day	SDS 1 month
Y	Y	Y	4	1	Spinal	N	Y	N	1	2
N	Y	Y	4	2	Spinal	Y	Y	N	2	3
Y	Y	Y	5	3	Spinal	N	Y	N	2	2
Y	Y	Y	5	4	Spinal	Y	Y	Y	3	5
N	Y	Y	4	5	Spinal	N	Y	N	1	2
Y	Y	Y	4	6	Spinal	Y	Y	N	2	3
Y	Y	Y	5	7	Spinal	Y	Y	Y	2	4
N	Y	Y	4	8	Modified PIA	Y	Y	N	1	2
Y	Y	Y	5	9	Modified PIA	Y	Y	N	2	3
Y	Y	Y	5	10	Modified PIA	Y	Y	N	2	3
Y	Y	Y	4	11	Spinal	Y	Y	N	1	–
Y	Y	Y	5	12	Modified PIA	N	Y	N	1	1

glions under US guidance require a mere 30–40 min to perform.

Third, US-guided alcohol neurolysis is less expensive than the other techniques mentioned, and sonographic equipment is more readily available than CT units. Furthermore, the US-guided procedure is more cost-effective for an average hospital and frees the CT unit, which might otherwise be monopolized for up to 90 min per procedure.

One final advantage of US-guided ganglion neurolysis is that it can be performed with the patient in a supine position, which is much more comfortable for pancreatic cancer patients than the prone position required for the posterior approach; this also eliminates the risk of accidents known to occur during a conventional posterior approach [1, 5–7, 12, 18, 21], such as cephalad diffusion of alcohol, posterior to sympathetic chain and lumbar plexus, along the aorta and diaphragmatic crura. Actually, the last few years have seen the posterior approach replaced by the anterior technique in the majority of cases, even in those performed under CT guidance [17]; and Montero Matamala chose the anterior approach for the US-guided technique he described [18].

The only side effect of alcohol neurolysis was an increase of preexisting left pleural effusion in one patient. Hiccups, a sign of chemical irritation of the phrenic nerve, accompanied the neurolytic procedure in the same patient. Diarrhea of 3 days' duration, with multiple bowel movements, was noted in two other patients; it resolved with medical treatment and should be considered a consequence of celiac plexus block, rather than a true complication [19].

Patient sedation, to avoid inconvenient and dangerous reflex reactions, and aortic perforation, to provide a constant and unequivocal landmark even in an anatomic field altered by neoplastic expansion or surgery, may be considered disadvantages of the neurolytic procedure. Aortic perforation, however, is not a limitation of the procedure, as demonstrated in the autopsied patient who died 2 days after celiac ganglion neurolysis for reasons unrelated to aortic perforation with a 22-gauge needle, and subsequent needle withdrawal.

Conventional PIA needles have a conical tip which excludes their use, when major arterial walls must be traversed, due to the risk of hemorrhage. For that reason, a new open-ended Chiba-like tip has been designed in order to guarantee safe introduction into the aortic lumen. When the newly designed, multiperforated, Chiba bore tip needle was employed in the last four patients treated by chemical neurolysis, significantly better alcohol diffusion in the retroperitoneum (as monitored by US guidance) seemed to lead to improved therapeutic results. Although definitive conclusions cannot be drawn due to the small size of the study population in which the multiperforated needle was em-

ployed, and the improvement of therapeutic results is not statistically significant, the observed relative improvement of the medium-term results in the last four patients can be theoretically attributed to radial alcohol diffusion from the multiperforated needle vs a less-effective 90° diffusion pattern produced by spinal needles in the other patients.

The anterior approach to US-guided celiac ganglion neurolysis has been presented as a cheap, easy to perform, time-saving, safe procedure whose therapeutic efficacy equals, if not exceeds, that of the posterior approach and those of the fluoroscopic and CT-guided procedures.

Far from a routine technique to relieve upper abdominal pain, alcoholization of the celiac plexus must, on the contrary, be considered an extraordinary measure to manage pain unresponsive to conventional medical treatment.

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