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A Retrospective Evaluation

Pulsed Radiofrequency of the Dorsal Root Ganglia is Superior to Pharmacotherapy or Pulsed Radiofrequency of the Intercostal Nerves in the Treatment of Chronic Postsurgical Thoracic Pain

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Background: Chronic postsurgical thoracic pain (CPTP) represents a major therapeutic challenge characterized by an absence of clinical studies to guide treatment. Recently, the implementation of pulsed radiofrequency (RF) has generated intense interest in the medical community as a safe and potentially effective treatment for neuropathic pain. To date, there are no studies comparing pulsed RF to more conventional therapeutic modalities for any pain condition.

Objectives: To compare treatment outcomes between pharmacotherapy, pulsed RF of the intercostal nerves (ICN) and pulsed RF of the dorsal root ganglia (DRG) in CPTP.

Methods: Retrospective data analysis involving 49 patients.

Results: At 6-week follow-up, 61.5% of the pulsed RF DRG group reported ≥ 50% pain relief vs. 27.3% in the medical management (MM) group and 21.4% in the ICN group (P=0.12). At 3-month follow-up, 53.8% in the DRG group continued to report ≥ 50% pain relief vs. 19.9% in the MM and 6.7% in the ICN groups, respectively (P=0.02). Among the pulsed RF patients who did report a successful outcome, the mean duration of pain relief was 2.87 months in the ICN group and 4.74 months in the DRG group (P=0.01).

Conclusions: Pulsed RF of the DRG was a superior treatment to pharmacotherapy and pulsed RF of the ICN in patients with CPTP. Prospective studies are needed to confirm these results and identify the best candidates for this treatment.

Key words: Dorsal root ganglion, intercostal nerve block, postmastectomy pain, postthoracotomy pain, poststernotomy pain, pulsed radiofrequency

Chronic postsurgical thoracic pain (CPTP) is one of the most challenging conditions confronting physicians. Even the definition of CPTP pain is ambiguous, with some authors citing 12 weeks as the delineation between "acute" and "chronic" postsurgical pain (1), others quoting 2 months as the cutoff (2), and still other investigators utilizing one year after surgery as the threshold for diagnosis (3). Thus, the transition between acute and chronic postoperative pain is probably best viewed as a continuum, or as the International Association for the Study of Pain defines it, "pain that persists beyond the normal time of healing."

The prevalence rate of CPTP is equally contentious, although thoracic incisions are generally acknowledged to be a major cause of chronic postoperative pain. For postthoracotomy pain, the reported incidence of chronic pain ranges between 22% and 67%, depending on the surgical approach (4,5). With regards to poststernotomy pain, the most widely quoted study cites an incidence of 25% (6). The reported prevalence of pain following breast surgery also varies greatly, from less than 10% to upwards of 60% in some women (7,8).

Compounding the high incidence of CPTP and its refractoriness to treatment is the paucity of clinical studies used to guide treatment. To illustrate, a recent literature search revealed only one case series evaluating trigger point injections for chronic postthoracotomy pain (9), and one clinical study assessing topical capsaicin for postmastectomy pain (10). There are anecdotal reports touting beneficial effects for cryoanalgesia with intercostal neuralgia (11) and controlled studies demonstrating efficacy for acute postthoracotomy pain (12), but none examining its role exclusively in CPTP. No studies were found for chronic poststernotomy pain.

In recent years the use of pulsed radiofrequency (RF) to treat chronic pain conditions has generated intense interest in the pain community. Percutaneous RF denervation has been used for more than 3 decades to treat pain of spinal origin (13-15) and other etiologies (16-19). However, since the use of RF ablation involves the thermal destruction of surrounding tissue, there is a concomitant risk of damage to adjacent nervous tissue. In some cases, this can lead to sensory loss or motor dysfunction.

Recently, a safer alternative to percutaneous RF neurotomy has emerged in the medical literature whereby the targeted neural tissue is subjected to

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high frequency (300-500-kHz), relatively low voltage (around 40-60 volts) RF pulses rather than coagulation by continuous, high temperature RF current. The main advantage of pulsed RF is that unlike continuous thermal RF, it does not result in significant tissue injury. In a study comparing the cellular effects of conventional RF current at 67° C and pulsed RF current at 42° C on dorsal root ganglion (DRG) morphology in rabbits, Erdine et al (20) found that animals subjected to both RF modes had increased cytoplasmic vacuolization and enlarged endoplasmic reticulum compared to sham RF and control groups 2 weeks after lesioning on electron microscopic analysis of spinal cord and DRG. However unlike cells in the continuous RF group, no mitochondrial degeneration or structural pathology in cell or nuclear membranes occurred in response to pulsed RF current.

The mode of action of pulsed RF is not understood, but may include inhibition of excitatory C-fiber responses by repetitive, burst-like stimulation of A-delta fibers (21,22), global reduction of evoked synaptic activity (23), and minor structural changes in nerve tissue elicited by alterations in the function of the blood-nerve barrier, fibroblast activation and collagen deposition (24). Which, if any, of these effects plays the dominant role in analgesia is not known.

There are currently no studies comparing pulsed RF to any other treatment modality, although clinical case series and anecdotal reports have shown pulsed RF to be effective in spinal pain (25,26), groin pain (27), extremity pain (28), and facial neuralgias (29,30) (illustrated in Table 1). The notion of a minimally invasive, relatively nondestructive technique that shows is effective in the treatment of chronic pain without the inherent risks associated with damage to neural tissue is conceptually appealing. This allure is especially compelling in neuropathic conditions, whereby the etiology of pain is believed to derive from neuronal injury. In a recent review on postthoracotomy pain, Gottschalk et al (32) recommended the use of pulsed RF to treat persistent pain in patients who failed conservative therapy based solely on anecdotal evidence.

In this study, we compare medical management (MM) with anticonvulsants and tricyclic antidepressants (TCA) to pulsed RF of intercostal nerves (ICN) and dorsal root ganglia (DRG) in 49 patients with CPTP.

Methods

Permission to conduct this study was obtained from the Internal Review Boards at 2 academic teaching hospitals. Inclusion criteria were age ≥ 18 years, duration of pain ≥ 3 months, visual analogue scale pain score ≥ 5 on a

Table 1. *Clinical series evaluating the efficacy of pulsed radiofrequency in painful conditions.*

Publication	Patients Treated	Treatment	Results
Munglani, 1999 (31)	4 patients with neuropathic pain including 3 patients with failed back surgery syndrome and 1 with postthoracotomy pain.	2 pts had pulsed RF of the L5 DRG, one of the L5 DRG and S1 nerve root and the pt with postthoracotomy pain had the T2-4 nerve roots treated.	All 4 pts obtained a dramatic reduction in neuropathic symptoms. One FBSS pt obtained relief of leg pain but not back pain, and another developed a new disc protrusion requiring re-operation. Follow-up ranged between 2 and 7 mos.
Cohen and Foster, 2003 (27)	3 patients with postsurgical groin pain or orchialgia.	1 pt had pulsed RF of the genitofemoral n, one had the ilioinguinal n treated and the 3rd had the iliohypogastric n lesioned.	All patients obtained > 90% pain relief at 6-month follow-up.
Van Zundert et al, 2003 (29)	5 patients with idiopathic trigeminal neuralgia affecting V1 (n=1), V2 (n=3) and V3 (n=2).	1 pt had pulsed RF on V1, 2 on V2, 1 on V3 and the last on V2 &3.	4 pts obtained > 90% pain relief at follow-ups ranging from 10 to 22 mos. One required a 2nd treatment after 15 mos. The last pt obtained > 75% pain relief which lasted between 1 and 5 mos, and underwent microvascular decompression.
Mikeladze et al, 2003 (26)	114 patients with chronic lumbar (n=83) and cervical (n=31) facet arthropathy.	All underwent pulsed RF of their medial branches after a positive response to diagnostic local anesthetic blocks.	60% of pts achieved > 50% pain relief, with the average duration lasting 3.9 +/- 1.9 mos. 18 pts had a repeat procedure with the same duration of pain relief initially obtained.
Pevzner et al, 2005 (25)	28 patients with lumbar (n=20) and cervical (n=8) radiculopathy.	All underwent pulsed RF of the DRG at the affected level(s).	At 3 mos, 7% obtained excellent and 43% good results. After 6 mos, 7% had excellent and 25% good results. At 12-mo. follow-up, 7% and 21% cont'd to have excellent and good results, respectively.
Gurbert et al, 2005 (28)	8 patients with chronic shoulder pain secondary to rotator cuff tears.	All underwent pulsed RF of the suprascapular nerve.	At the 4 and 8-wk follow-up, 100% and 75% obtained > 50% pain relief, respectively. Mean VAS pain scores at baseline, 4-wks& 8-wks postprocedure were 8.0, 1.75 & 3.25, respectively.

Case reports not included. DRG – dorsal root ganglion Pts – patients RF – radiofrequency VAS – visual analogue scale

Table 2. *Patient Characteristics by Pain Intervention*

	DRG (n=13)	ICN (n=15)	MM (n=21)	P Value *
Age	45.8±4.7	50.8±4.0	48.6±2.4	0.66
Sex				1.0
Male (n=22)	6 (27.3%)	7 (31.8%)	9 (40.9%)	
Female (n=27)	7 (25.9%)	8 (29.6%)	12 (44.4%)	
Surgical Procedure				0.32
Thoracotomy (n=31)	8 (25.8%)	10 (32.2%)	13 (41.9%)	
Sternotomy (n=5)	0	2 (40%)	3 (60%)	
Mastectomy (n=9)	2 (22.2%)	2 (22.2%)	5 (55.6%)	
Other (n=4)	3 (75%)	1 (25%)	0	
Opioid use				<0.01
Yes (n=26)	12 (46.2%)	9 (34.6%)	5 (19.2%)	
No (n=23)	1 (4.3%)	6 (26.1%)	16 (69.6%)	
Duration of symptoms, mean (SE), y	4.2 (1.9)	2.6 (0.5)	3.1 (0.5)	0.58

DRG = Dorsal root ganglion, ICN = Intercostal nerve, MM = Medical management
Data are presented as number (percent) unless otherwise specified.
* Age and duration of symptoms were compared with ANOVA; other data were compared with Fisher's exact test.

0-10 scale, and CPTP deemed to be of neuropathic origin based on history and physical examination. Exclusion criteria included the presence of pathology that could account for a majority of persistent symptoms (e.g. recurrent cancer), untreated coagulopathy for procedure patients, and unstable medical or psychiatric condition. Data on 28 consecutive pulsed RF patients were collected and stored in databases designed for research purposes. This was then compared with data collected retrospectively on a cohort of 21 consecutive patients who were pharmacologically treated for CPTP because of either patient preference or lack of pulsed RF capability. In accordance with our standard practice, no medication changes were made after pulsed RF treatment until the first follow-up.

Procedures

All pulsed RF procedures were performed in hospital outpatient ambulatory care setting using local anesthesia and conscious sedation as necessary, with fluoroscopic guidance to facilitate needle placement. The segmental spinal levels treated were selected based on the patients' pain referral pattern as determined by historical and physical examination findings. Pulsed RF ICN was performed with the patient in the prone position and the fluoroscopy beam positioned in an antero-posterior (AP) direction. A 10 cm electrode with a 5 mm active tip (PMC22-100-5, Baylis Medical, Montreal, Quebec, Canada) was then inserted at a slightly cephalad angle until it contacted the bottom of the rib just lateral to the vertebral body, at which point it was walked off caudally for sensory testing. For DRG procedures, the image intensifier was rotated in a cephalo-caudad direction until the endplates of the adjacent thoracic intervertebral discs were lined up and the transverse processes became discernable from the ribs. The electrodes were then inserted in a slightly medial-cephalad direction under the transverse processes, and using lateral fluoroscopic imaging, incrementally walked into the thoracic intervertebral foramen (Figs. 1 and 2).

Once correct needle position was confirmed, test stimulation was performed at 50 Hz, during which time the needles were slightly redirected to optimize stimulation. Since neural tissue cannot be seen on plain radiographs and the DRG may vary with respect to its spatial relationship with the intervertebral foramen (33), the point of maximum stimulation was designated to be the location of the DRG. Injection of contrast revealed epidural uptake for all DRG procedures. For all ICN procedures, concordant stimulation was obtained at ≤ 0.4 volts; with all DRG procedures, concordant stimulation was obtained at ≤ 0.2 volts. To prevent possible procedure-related discomfort, 1 ml of lidocaine 1% was injected prior to lesioning.

Pulsed RF was performed with a radiofrequency generator (PMG-115-TD, V2.0A, Baylis Medical) containing a voltage output in the 40 to 60-V range using the following settings: 2-Hz frequency, 20-ms pulses in a 1 second cycle, 120 second duration, and 42°C temperature. Impedance ranged between 150 and 400 Ohms at all levels. For each pulsed RF application, the procedure was repeated 4 times, for a total duration of 8 minutes.

Pharmacotherapy

Pharmacotherapy consisted of either treatment with a secondary amine TCA (nortriptyline (n=9) or desipramine (n=2)) or anticonvulsant (gabapentin (n=8) or oxcarbazepine (n=2)) titrated to efficacy and side effects. For TCA treatment, dosing was initiated at either 10 mg or 25 mg po qhs, and titrated to efficacy and side effects up to 100 mg po qhs. Gabapentin treatment was started at either 100 or 300 mg po qhs, and increased up to 3600 mg/d in TID dosing, as tolerated. Oxcarbazepine treatment was commenced at 150 mg po qhs and titrated up to 1800 mg/d in divided doses.

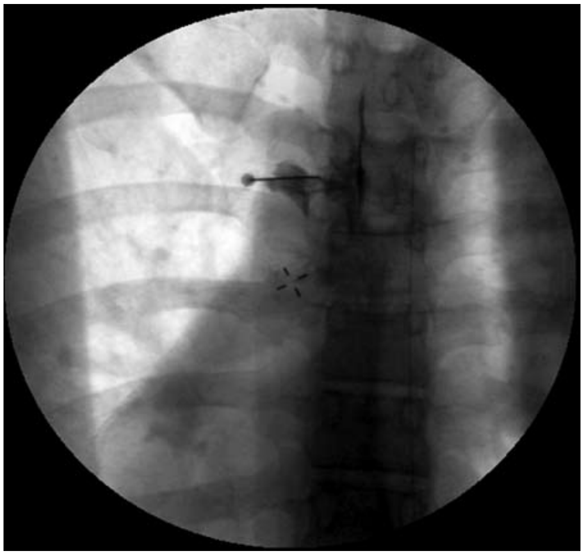

Fig 1. *Antero-posterior fluoroscopic image showing needle placement for thoracic dorsal root ganglion pulsed radiofrequency. The contrast spread in the vertical direction indicates epidural uptake.*

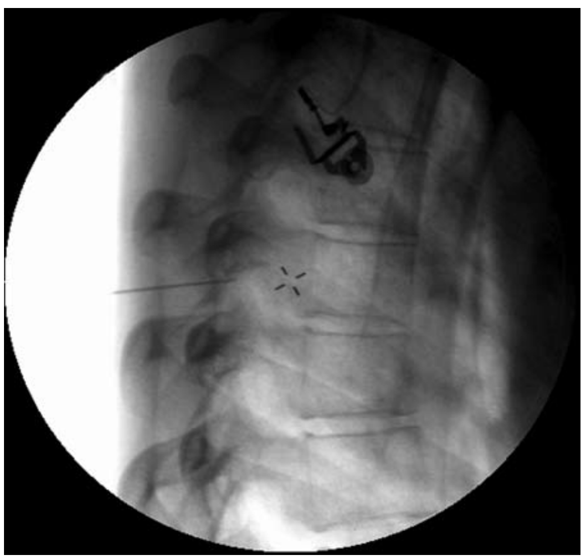

Fig 2. *Lateral fluoroscopic image showing needle placement for thoracic dorsal root ganglion pulsed radiofrequency in a patient with postthoracotomy*

Outcomes and Statistical Analysis

Treatment outcomes were categorically divided into "success" and "failure," and assessed at 6-week and 3-month follow-up visits. A successful treatment was defined as ≥ 50% pain reduction on a 0-10 visual analogue scale, and affirmative answers to 2 questions evaluating patient satisfaction and functional improvement. These questions were:

1. I am satisfied with the treatment I received and would recommend it to others.
2. The treatment I received significantly improved my ability to perform activities of daily living.

The inciting surgical procedure was coded by name with the exception of those procedures lacking replicates. These were coded as "other," and included transhiatal esophagectomy, nephrostomy tube placement, nephrectomy, and spinal surgery. Statistical analyses were performed using STATA version 9.1 (Statcorp, College Station, TX). The distribution of categorical variables in each group was compared using Fisher's exact test and logistic regression. Continuous variables were compared with analysis of variance (ANOVA) and linear regression. Post-hoc tests were performed on significant main effects with the above tests using Bonferroni correction of the P value. Categorical data are reported by number of subjects and percentage. Continuous data are reported as mean and standard error unless otherwise indicated. A P value < 0.05 was considered statistically significant.

Results

Data were analyzed on 49 patients with chronic thoracic pain following thoracotomy, sternotomy, mastectomy or other surgical procedures. The category "other" included patients who underwent nephrostomy tube placement (n=1), nephrectomy (n=1), spinal surgery (n=1) and transhiatal esophagectomy (n=1). All patients received either pulsed RF ICN (n=15), pulsed RF DRG (n=13) or pharmacotherapy (MM; n=21) for their pain treatment. Morphometric, demographic and clinical characteristics were similar among the 3 treatment groups except that a greater number of patients receiving DRG or ICN pulsed RF treatments were being treated with opioids (Table 2). Age, sex, duration of symptoms or type of surgical procedure were not different between treatment groups in either univariate analysis, or when all covariates were controlled for using multivariate logistic regression. The mean number of levels treated was 2.6 (SD 1.1, range 1-5) in the DRG group and 2.5 (SD 1.0, range 1-5) in the ICN group. There was no association between successful outcome and the number of levels treated in either of the pulsed RF groups.

Success was defined as ≥ 50% relief of symptoms by patient report at 6-week and 3-month follow-up visits, and positive responses to the 2 questions evaluating satisfaction and functional improvement. At 6 weeks, patients in the DRG, ICN and MM groups had success rates of 61.5%, 28.6% and 27.3%, respectively. Despite the trend towards improved outcomes in the DRG group, this effect did not reach statistical significance (P=0.12; Table 3). At 3 months, success rates between groups were significantly different (P=0.02). In subgroup analysis, the success rate for patients in the DRG group (53.8%) was significantly greater than for those patients treated with pulsed RF ICN (6.7 %; P=0.01), and approached significance when compared with MM (19.9%) (P=0.06). The difference between ICN and MM groups did not approach statistical significance (P=0.38).

One patient who underwent pulsed RF DRG for postmastectomy pain died after her 3-month follow-up visit from metastatic spread of her cancer. She reported > 90% pain relief at her latest follow-up. Three patients in the DRG group who had a successful outcome at 3 months had the procedure repeated, along with one patient in the ICN group who had a successful outcome at 6 weeks but a return of his pain at 3 months. All obtained results comparable to their initial procedure after pulsed RF was repeated. In the pulsed RF patients who did have a successful outcome, the mean duration of pain relief was 11.5 weeks (range 6-26 weeks, SD 9.7) in the ICN group and 4.74 months (range 2.5-12 months, SD 3.2; P=0.01) in the DRG group.

Among the 31 patients who reported < 50% pain relief at their first follow-up visit, 6 patients responded positively to the 2 questions assessing satisfaction and functional improvement. These were comprised of 2 patients in the DRG group (40%), one patient in the ICN group (9%) and 3 patients in

Table 3. *Patient Outcome at 6-Week and 3-Month Follow-ups*

Time	Pain Intervention	Positive Outcome	Negative Outcome	P Value*
6 Weeks				0.12
	DRG (n=13)	8 (61.5%)	5 (38.5%)	
	ICN (n=15)	4 (21.4%)	11 (78.6%)	
	MM (n=21)	6 (27.3%)	15 (72.7%)	
3 Months				0.02
	DRG (n=13)	7 (53.8%)	6 (46.2%)	
	ICN (n=15)	1 (6.7%)	14 (96.3%)	
	MM (n=21)	4 (19.9%)	17 (80.1%)	
	DRG vs. ICN			0.01
	DRG vs. MM			0.06
	ICN vs. MM			0.38

Data are presented as number (percent).
* Fisher's exact test with Bonferroni correction when appropriate.

Table 4. *Patient Characteristics*

Time	Demographic Variables		Positive Outcome	Negative Outcome	P Value*
6 weeks	Number of Subjects		n=18	n=31	
	Age, mean (SE), y		47.6 (3.6)	49.1 (2.4)	0.73
	Sex				0.77
		Male (n=22)	9 (40.9%)	13 (59.1%)	
		Female (n=27)	9 (33.3%)	18 (66.7%)	
	Surgical Procedure				0.89
		Thoracotomy (n=31)	12 (38.7%)	19 (61.3%)	
		Sternotomy (n=5)	1 (20%)	4 (80%)	
		Mastectomy (n=9)	4 (44.4%)	5 (55.6%)	
		Other (n=4)	1 (25%)	3 (75%)	
	Opioid Use				0.55
		Yes (n=26)	11 (42.3%)	15 (57.7%)	
		No (n=23)	7 (30.4%)	16 (69.6%)	
	Duration of symptoms, mean (SE), y		2.2 (0.3)	3.8 (0.9)	0.15
3 months	Number of Subjects		n=12	n=37	
	Age, mean (SE), y		47.1 (2.4)	49.0 (2.2)	0.17
	Sex				0.75
		Male (n=22)	6 (27.7%)	16 (72.3%)	
		Female (n=27)	6 (22.2%)	21 (77.8%)	
	Surgical Procedure				0.94
		Thoracotomy (n=31)	7 (22.6%)	24 (77.4%)	
		Sternotomy (n=5)	1 (20%)	4 (80%)	
		Mastectomy (n=9)	3 (33.3%)	6 (66.7%)	
		Other (n=4)	1 (25%)	3 (75%)	
	Opioid Use				0.33
		Yes (n=26)	8 (30.8%)	18 (69.2%)	
		No (n=23)	4 (17.4%)	19 (82.6%)	
	Duration of symptoms, mean (SE), y		2.0 (0.3)	3.6 (0.5)	0.24

Data are presented as number (percent) unless otherwise specified.
* Age and duration of symptoms were compared with ANOVA; other data were compared using Fisher's exact test.
y = years

the MM group (20%). No patient who reported ≥ 50% pain relief at either follow-up responded negatively to the 2 questions.

Analysis of demographic and non-interventional clinical factors, including age, sex, type of surgical procedure, opioid use and duration of symptoms, revealed no significant effect on patient outcome at 6-week and 3-month follow-up visits when compared across treatment groups (Table 4) or analyzed by individual treatment group (data not shown). Additionally, none of these variables predicted outcomes at any time frame when analyzed by linear and logistic regression.

Separate treatment analysis of the largest subset of patients, those presenting with chronic postthoracotomy pain (n=31), mirrored that of the whole study group. At 6-week follow-up, 23% (3 of 13) of postthoracotomy pain patients treated medically had a successful treatment vs. 40% in the ICN group (4 of 10) and 62% (5 of 8) in the DRG group (p=0.22). At their 3-month follow-up visit, 2 of 13 (15%) in the MM group continued to have a positive outcome, compared to 10% (1 of 10) in the ICN group and half the patients in the DRG group (4 of 8). However, the small numbers involved precluded the P value from reaching statistical significance (P=0.12).

Complications

Seven patients (33%) in the medical management group experienced adverse side effects. These included two cases of sedation with gabapentin, one instance of tremors with gabapentin, two cases of sedation with nortriptyline, one patient who experienced both dizziness and urinary retention with nortriptyline, and one report of persistent nightmares with desipramine. In the pulsed RF treatment groups, two pneumothoraxes occurred. In the first, a patient in the ICN group required placement of a chest tube and hospitalization for two days. In the second case, a small incidental pneumothorax was found during a routine scan of the lung fields after pulsed RF DRG. This patient was not symptomatic and was treated conservatively with observation.

Discussion

Faced with a burgeoning geriatric population and improved cancer survival rates, the recognition and treatment of CPTP has become a major challenge modern medicine cannot afford to lose. In the quest for a safe, reliable treatment devoid of major side effects, pulsed RF has become a prime candidate for the treatment of chronic postoperative pain (27). The results of this study support recently published data suggesting that the application of short bursts of radiofrequency energy to nervous tissue can result in intermediate to long-term pain relief, with minimal risk of aggravating neural pathology. Despite these statistics, this is the first comparative study evaluating the use of pulsed RF for pain, and one of very few studies evaluating any type of treatment for CPTP.

The main finding in this study is that patients who underwent pulsed RF of the DRG had improved treatment outcomes 3 months postprocedure compared to patients who underwent treatment with medications alone or pulsed RF ICN. This finding occurred despite the fact that the trend for patients in the DRG treatment group showed that they experienced symptoms for a longer duration of time than patients in the other 2 groups. Previous studies evaluating procedural interventions for pain control have shown duration of symptoms to negatively correlate with success rates (34-36). Further evidence for the efficacy of DRG pulsed RF lies in the observation that several patients who did obtain significant, intermediate-term pain relief after the procedure failed previous trials with neuropathic medications (n=2) and ICN pulsed RF (n=1).

Although there was a trend for pulsed RF DRG patients to have improved outcomes at 6-week follow-up visits, these differences fell shy of statistical significance. Accounting for the differences in treatment outcomes at 6 weeks and 3 months was the observation that 2 patients in the pharmacotherapy group and 3 in the pulsed RF ICN group experienced a diminution in pain relief between the 2 visits. This finding is consistent with previous studies demonstrating that the beneficial effects of anticonvulsants, tricyclic antidepressants and pulsed RF of peripheral nerves tend to diminish with time (26,37,38).

The two principal questions that arise from our findings are how does pulsed RF exert its analgesic effects, and why is the duration of these effects longer when the procedure is performed on the DRG rather than a peripheral nerve? The work of several investigators who conducted animal studies evaluating the effect of pulsed and continuous RF help elucidate these dilemmas. In a study by Higuchi et al (39), the investigators exposed rat DRG to continuous RF, pulsed RF and sham lesioning. In both groups, the treated tissue was heated to a temperature of 38° for 2 minutes. When the animals were humanely killed 3 hours after lesioning, the authors found increased c-Fos expression in laminae I and II of the dorsal horn after pulsed, but not continuous RF application.

In a later study, Van Zundert et al (22) performed sham RF, continuous RF at 67° C for 60 seconds, or pulsed RF for either 120 seconds or 8 minutes on 19 rats who underwent cervical laminectomies. The animals were then humanely killed 7 days post-intervention and their spinal cords prepared for c-Fos labeling. Unlike the findings by Higuchi et al, the authors of this study found increased numbers of c-Fos immunoreactive cells in the dorsal horn of animals subjected to all 3 RF groups compared to those who underwent sham lesioning, with no differences noted between groups. No c-Fos immunoreactive cells were observed in the ventral or intermediate gray matter zones of the spinal cord. The presence of transcription factor c-Fos suggests that pulsed RF impulses may be involved in the long-term changes in gene expression that underlie neuronal plasticity.

Animal studies also provide a framework for why the antinociceptive effects of performing pulsed RF on the DRG outlast the beneficial effects of pulsing peripheral nerves (i.e. ICN). Podhajsky et al (24) conducted a histologic study examining the effects of pulsed and continuous RF on 118 rat DRG and sciatic nerves. In the 42º C pulsed RF group, subclinical changes characterized by fibroblast activation, collagen deposition and endoneurial edema secondary to alterations in the blood-nerve barrier occurred, returning to normal by 7 days in sciatic nerve and 21 days in DRG specimens. In the 80º C continuous RF group, tissue specimens showed consistent evidence of Wallerian degeneration. Of note, rats treated with pulsed RF or continuous RF at 42º C exhibited no signs of sensory deficits or paralysis, whereas rat sciatic nerves subjected to continuous RF at 80º C demonstrated immediate foot drop and later developed ulcerative lesions on their feet.

Finally, in a study by Hamann et al (40), the investigators delivered pulsed RF to either the sciatic nerve or the L4 ventral primary ramus just distal to the intervertebral foramen in adult rats. On tissue examination 14 days postprocedure, the authors found an upregulation in activating transcription factor 3, an indicator of cellular stress, in L4 DRG cell bodies. In the sciatic nerve RF group, no cellular changes were apparent in either the treated nerve or the L4 DRG. These findings indicate that pulsed RF selectively targets neurons whose axons are composed of small diameter A delta and C fibers, which are intimately involved in nociception. It may also explain the strong trend towards greater improvement at 6-week follow-up in the pulsed RF DRG compared to the ICN group. In the only clinical study evaluating pulsed RF of the DRG, Pevzner et al (25) followed 28 patients with lumbar or cervical radiculopathy for 12 months after a single round of treatment. At their 3-month follow-up, 50% of patients rated their pain relief as either good or excellent. At their 6 and 12-month follow-up visits, these percentages declined to 32% and 29%, respectively.

Whereas our adverse events were all self-limited and transient, the potential exists for more serious, even catastrophic complications to occur with pulsed RF of the DRG. In the thoracic region, intercostal arteries from the posterior aorta give rise to radicular arteries comprising the major blood supply to the spinal cord. The upper thoracic cord may be supplied by only one small radiculomedullary artery and is considered a watershed area. In the lower thoracic region, the large, unpaired artery of Adamkiewicz almost exclusively supplies the spinal cord, making this area particularly vulnerable to ischemic injury (41). The artery of Adamkiewicz arises in 85% of people between T9 and L2, usually on the left. For both cervical and lumbar transforaminal epidural steroid injections, spinal cord infarcts leading to paraplegia and even death have been reported. Although depot steroid injection into small radicular arteries have been implicated in most of these cases (42), catastrophic events have also been attributed to vascular injury from needle placement (43, 44). In addition, the authors are aware of at least one case of paraplegia following a left lower thoracic transforaminal epidural steroid injection (45). Thus, besides the typical risks associated with transforaminal and RF procedures such as bleeding, infection, nerve injury and burns, extreme caution must be exercised to avoid damaging the precarious blood supply to the thoracic spinal cord. Injecting steroid prior to RF lesioning, as some authors advocate to reduce the incidence of neuritis (46), further increases the potential risks.

There are several limitations of this study that need to be addressed in order to better evaluate our findings. First, because this was a retrospective study the patients were not randomized and treatment protocols not standardized. Second, there are multiple etiologies for postsurgical chest pain besides classical neuropathic pain, including myofascial pain (9) and phantom pain. Although the postsurgical pain treated in this study was deemed by clinicians to be neuropathic in nature, no validated tests such as quantitative sensory testing were used to make this distinction. Third, since some clinicians reported their outcomes in terms of percent pain relief, visual analogue or numerical scale pain scores were not tabulated. In clinical practice, a patient's reported percent reduction in pain does not always correspond precisely with their change in numerical pain rating. However if visual analogue pain scores were analyzed, it is possible our findings at 6 weeks would have reached clinical significance. Fourth, unlike the two pulsed RF groups, the MM group did not receive a homogeneous treatment, with patients receiving varying dosages of either a TCA or membrane stabilizer, titrated to effect. Yet these 2 drug classes have been shown in numerous reviews to be of comparable efficacy, and are generally considered to be the most effective medical treatments for an assortment of neuropathic pain conditions (47). Since there are no published data on any pharmacological agent in CPTP despite their widespread use, we felt the inclusion of these patients as a comparison group was appropriate. Finally, although two self-explanatory and apparently self-evident questions were used to assess patient satisfaction and change in function, neither has been validated in formal outcome studies. Any future studies should include validated outcome measures assessing not only pain, but mood, function and quality of life. In spite of these limitations, our findings merit serious consideration in view of the absence of comparative studies for both pulsed RF and CPTP.

Taken in context, our findings suggest that pulsed RF of the DRG is superior to both medical management and pulsed RF of the ICN in the treatment of patients suffering from chronic postsurgical chest pain. However, given the inherent risk of performing thoracic interventional procedures, we cannot recommend it as a first line treatment based on the results of one study. Rather, we believe it should be reserved for those patients refractory to pharmacotherapy, and if implemented, done so only as part of a multidimensional treatment approach that includes medical management, rehabilitation and psychological counseling, as indicated. Future prospective, randomized studies are needed to confirm our findings and identify the best candidates for pulsed RF procedures.

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