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Lumbar Sympathetic Plexus Radiofrequency Ablation for Chronic Non-Cancer Pain: A Brief Review and Two Case Reports

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Background: Lumbar sympathetic plexus (LSP) has been described as a target for managing chronic pain with a sympathetic component in the lower limbs such as complex regional pain syndrome (CRPS) or pain of ischemic origin. LSP neurolysis with phenol or ethanol has been applied; more recently, radiofrequency (RF) lesioning has been proposed as an alternative. RF denervation has the advantage of avoiding the complications associated with ethanol/phenol spread.

Case Report: We describe 2 cases in which RF denervation of LSP was performed in patients suffering from chronic pain from CRPS and chronic ischemic disease of the lower limb.

Conclusion: RF denervation of LSP could be considered as a treatment for CRPS and chronic ischemic pain when conventional medical therapy fails. Compared to chemical neurolysis, RF denervation carries less risk for postprocedural deafferentation pain.

Key words: Complex regional pain syndrome; ischemic pain; lumbar sympathetic plexus; neurolysis; radiofrequency; sympathetically maintained pain

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BACKGROUND

Lumbar sympathetic plexus (LSP) has been described as a target for managing chronic pain with a sympathetic component in the lower limbs.

Complex regional pain syndrome (CRPS) and vascular insufficiency are 2 conditions in which LSP blocks or neurolysis have shown positive results in managing the patient's pain.

Radiofrequency (RF) ablation has been proposed as a safer alternative to chemical neurolysis; however, data are limited and its efficacy uncertain.

The purpose of this study was to review the published reports and data on LSP RF neurolysis and to add our experience with 2 case reports.

Anatomical Overview

The sympathetic fibers responsible for lower limb innervation originate from cell bodies located in the lower 3 thoracic and first 3 lumbar segments. Those fibers exit the spinal cord through their segmental nerves and travel as white rami communicantes to the sympathetic chain located on the anterolateral side of the lumbar column (1,2). Sympathetic fibers for the lower limbs synapse in the ganglia of the LSP, which is located between the L2 and L4 vertebral levels (3). The LSP usually contains a variable number of 2 to 5 interconnected ganglia usually located between the second and the fourth lumbar vertebrae (3).

These ganglia are located at the anterolateral side of the lumbar vertebrae and they can be reached by a fluoroscopically guided approach (3,4). Postganglionic gray rami leave the ganglia joining segmental nerves to the lower limbs.

Lumbar Sympathetic Plexus Neurolysis: Applications and Side Effects

Sympathetic fibers of the LSP are responsible for vasomotor, pilomotor, and sudomotor functions; blocking or destroying those fibers with either anesthetic blocks, neurolysis, or RF lesioning has been proposed as a treatment for CRPS of the lower limbs as well as for pain of ischemic origin (3-14). Anesthetic blocks were applied in one small case series on postamputation pain with a good outcome at 3 months' follow-up (17). Chemical neurolysis uses 50% to 100% ethanol or 5% to 10 % phenol to obtain Wallerian degeneration of Schwann cells of sympathetic fibers (16), and has been used for treating lower limbs with vascular insufficiency or pain caused by pelvic malignancies (16,17). This approach has the risk of creating postprocedural deafferentation pain; moreover, the diffusion of the neurolytic agent could damage adjacent structures (18).

A rare but devastating complication is the accidental spread of the neurolytic agent to the posterior side of the aorta, where the spinal segmental arteries originate, leading to spasm and spinal cord ischemia resulting in paraplegia (18). LSP neurolysis has the potential of injuring the genitofemoral nerve, with secondary pain in the groin and thigh and, less frequently, the lateral cutaneous femoral nerve (20). Lesions of the bowel, kidney, and ureter are other severe complications related to needle placement (18).

Radiofrequency Technique

RF lesioning requires positioning a RF probe near the target nerve and applying a high-frequency electrical current (usually 400-500 kHz) (21). The RF current flows into tissues through the active tip of the electrode (which is uninsulated), heating tissues with coagulation necrosis as the end result (22). Tissue temperature must be raised over 50°C to enable coagulation necrosis. Besides the aforementioned RF (which is usually referred to as continuous RF), a different modality of RF has been developed, called pulsed radiofrequency (PRF) (23-25). During PRF treatment, short bursts (pulses) of electrical current are delivered and the generated heat dissipates between these bursts of treatment. PRF applies high-voltage, fluctuating electrical fields without electrode tip temperature exceeding the temperature of 42°C, preventing damage to the target nerve. The PRF action mechanism is not completely understood, but it involves structural rearrangement of axonal membrane proteins, modification of gene expression, and modulation of inflammatory response (23-25). RF lesioning requires a multilevel approach placing a RF probe at the L2, L3, and L4 levels in order to destroy most sympathetic fibers (3,4).

Theoretically, using a multilevel approach gives the advantage of creating a large lesion with fewer risks than injecting a large volume of neurolytic agent in a single location, but it is unclear if RF efficacy is comparable to phenol or alcohol injection (3,10-16). Prior to RF denervation, once the needle is in place, a sensory stimulation at 50 Hz is performed to elicit paresthesia or pain in the target area and a motor stimulation at 2 Hz is done to avoid proximity of the needle to motor fibers. Those stimulations ensure more precise positioning of the RF probe close to the target nerve and increase the

safety of the procedure, while chemical neurolysis relies only on fluoroscopic positioning without any further measures to increase precision and safety.

Lumbar Sympathetic Plexus Radiofrequency: Review of Published Data

The PubMed, Scopus, and ISI Web of Science databases were systematically searched to find articles related to LSP RF denervation; the latest search was performed in June 2019.

We found only 10 articles: 3 randomized controlled trials (12,13,15), 2 case series (10,14), 2 narrative reviews (3,24), 2 case reports (11,16), and one Cochrane systematic review (8).

Overall, RF was applied only in 51 patients (9-16); none of these studies compared RF to sham.

All studies applied RF in patients who had been diagnosed with CRPS; RF application in patients with vascular ischemic pain has not been reported.

Regarding the modality of RF treatment, multilevel PRF was compared with anesthetic sympathetic blocks in a randomized clinical trial of 40 patients. Both groups showed a significant decrease in pain scores and functional improvement at 6 months' follow-up, without differences and without significant procedure-related side effects (13). PRF was also used in 2 case-series (10,14) with favorable outcomes at 4 and 12 months' follow-up, respectively. Continuous RF was used by Noe et al (10) in 8 patients with sympathetically maintained pain in the lower extremities; they obtained a significant reduction of pain in 75% of patients at 8 weeks' follow-up. The author reported a transient sympathetic neuralgia in 50% of patients which spontaneously resolved without sequelae. Continuous RF of the LSP at the L2-L4 sympathetic ganglia was compared with phenol neurolysis in a small randomized study of 20 patients; both groups showed a comparable reduction of pain scores without significant side effects, except for one patient in the phenol group who suffered from a postsympathectomy neuralgia (12).

Haynsworth et al (15) randomized 17 patients with sympathetically mediated pain to receive RF (n = 8) or phenol (n = 9) neurolysis. Better results were observed in the phenol group, with 89% of patients showing a persistent reduction in sympathetic activity at 8 weeks' follow-up compared to 12% of patients in the RF group.

A case report involved a patient with CRPS related to spinal cord injury (11). The patient received PRF and reported significant pain relief that persisted 4 months after the procedure; signs of sympathetic dysfunction in his lower limbs (edema, color changes) disappeared as well.

CASE REPORTS

We describe 2 cases in which RF denervation of LSP was performed in patients suffering from chronic pain from CRPS and chronic ischemic disease of the lower limb.

Written informed consent for the procedure and for using personal data for research purposes was obtained from both patients.

Case 1

A 69-year-old man who suffered a severe gunshot injury to his leg 6 years earlier was referred to our department in 2017. He underwent multiple orthopedic (Fig. 1) and plastic surgeries; his rehabilitation was complicated by wound infection that required additional surgical treatment. During all of his postsurgical and rehabilitative process, the patient complained about chronic pain that was not well-controlled with nonsteroidal anti-inflammatory drugs (NSAIDs) and opioids. At the time of our first evaluation, the lower left limb was edematous from mid-thigh to his foot, all cutaneous annexes were missing (hair, nails), and the affected limb was hypothermic compared to the uninjured one. Thermic and tactile hypoesthesia was reported all over the leg. The patient reported that the edema was variable over time and unrelated to postural changes and walking. We diagnosed a type 1 CRPS according to the Budapest criteria (24). The patient complained of severe pain with a Numeric Rating Scale (NRS-11) score of 8 out of 10 with a continuous stabbing sensation. Pain interfered with the patient's sleep and reduced his working ability. We proposed the patient undergo RF denervation of the LSP without a preliminary test block because the patient lived far from our institution and refused to make the trip twice to be injected (one injection for the test block and one for the RF). The RF procedure was performed under fluoroscopic guidance with the patient in prone position as described by Van Eijs (4). Fluoroscopy was positioned in order to obtain a left oblique view. After sterile draping and local anesthesia with lidocaine 2%, a 20-gauge 150-mm RF needle with an active tip of 10 mm was positioned at the level of the lower portion of the L2 vertebral body with left paravertebral access. A lateral view was obtained to confirm needle positioning at the anterior end of the L2

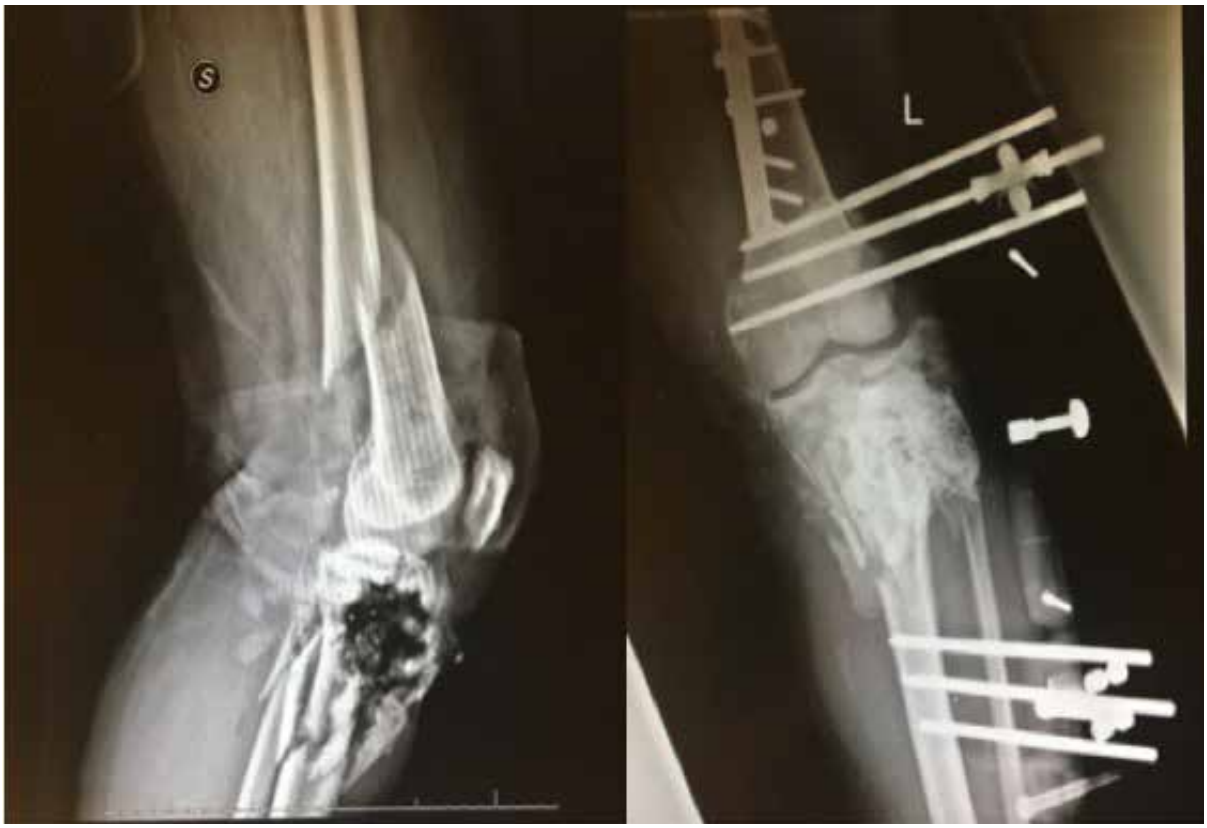

Fig. 1. X-rays showing patient's leg injury after gunshot (left) and bone fixing after first surgery.

vertebral body. Contrast medium (iopamidol 300 mOsm) was injected and correct spread of the contrast medium along the sympathetic chain was obtained (Fig. 2). Motor and sensory stimulation at 2 Hz and 50 Hz showed no muscle contractions and no painful sensation along the lower limbs or testicles. RF denervation was performed at 80°C for 90 seconds; at the end of the procedure, 4 mL of ropivacaine 0.1% with 4 mg of dexamethasone were given through the needle to reduce postprocedural pain and the risk of neuritis. The procedure was repeated at the level of the L3 and L4 vertebral bodies. The patient was discharged after 8 hours of monitoring without any change in his vital parameters and any neurological deficit. The patient returned one month after the procedure, his NRS-11 score dropped to one without any episode of breakthrough pain, the left lower limb was normothermic compared to the contralateral one, edema was significantly reduced, and allodynia was not reported. The patient reported a crampy sensation in his leg at night that did not interfere with his sleep; a supplementation with oral magnesium was prescribed. After 6 months, the patient was completely satisfied with the procedure. He did not report any significant episode of pain with NRS-11 score > 1; he also reported that the crampy sensation had disappeared and that he had resumed his normal life and work. We had our last telephone contact with the patient 8 months after the procedure and he reported that his conditions were stable.

Case 2

A 58-year-old man suffering from severe chronic vascular pain in his lower left leg was evaluated in our department in 2017. He reported severe persistent pain (NRS-11 score 8 out of 10) described as burning and stabbing in his left leg, and physical examination showed signs of ulcerations in his foot and ankle, which were being treated with repeated medications. He was taking 20 mg/10 mg of oxycodone/naloxone twice a day and 150 mg of pregabalin twice a day without benefit.

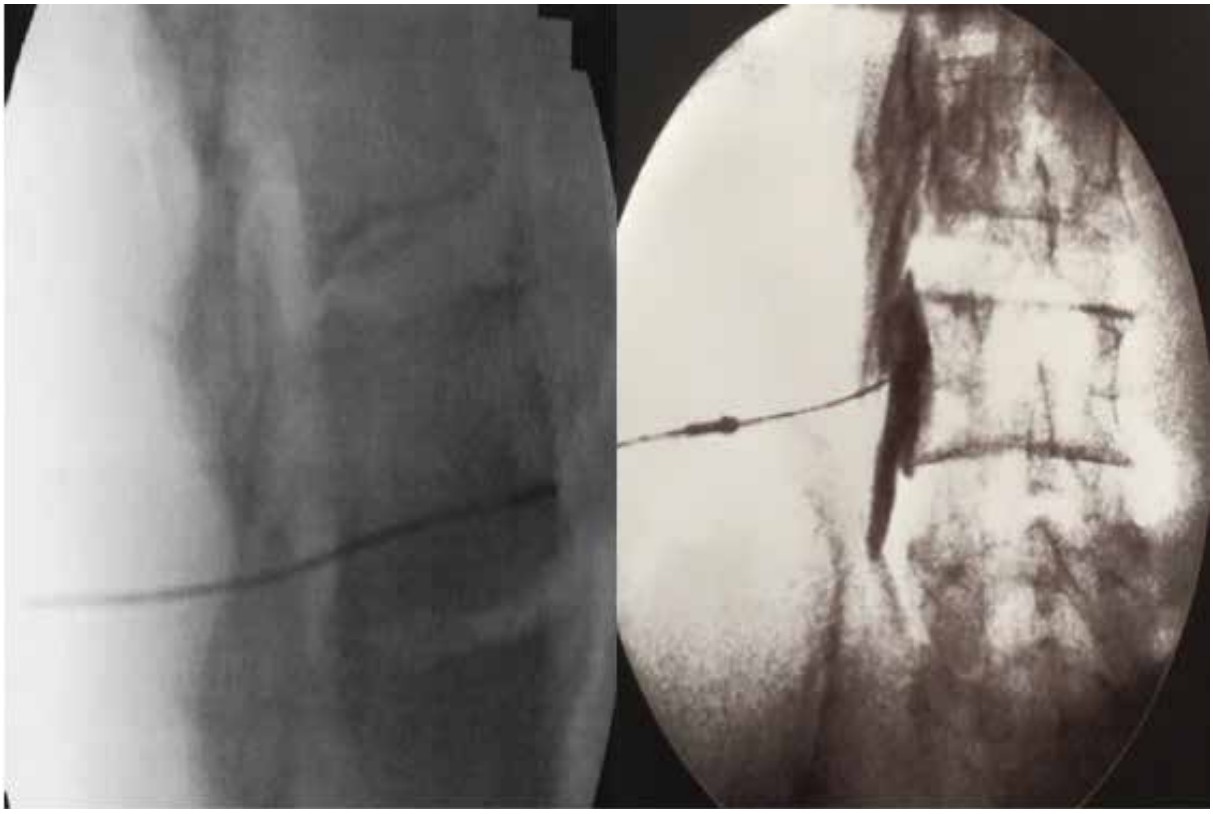

Fig. 2. Fluoroscopic image showing the final needle position for LSP denervation on lateral (left) AP view (right). Contrast medium spread is visible in AP view image.

Sublingual fentanyl (200 mcg) was given to him 20 minutes before every medication of his ulcers.

He was also on oral anticoagulants; for his case, vascular surgery was considered out of therapeutic possibility unless for limb amputation. We proposed a RF denervation of LSP without a prior test block to avoid a prolonged suspension of anticoagulants. The procedure was carried out with the same technique as described before, targeting the LSP at L3 and L4 on the left side. L2 denervation was not performed because sensory stimulation at 50 Hz elicited pain and paresthesia in his left testicle and we were not able to avoid this sensation despite needle repositioning.

At one month's follow-up, the patient reported good pain relief with an NRS-11 score of 4. He was still taking sublingual fentanyl for his medications and we proposed a deescalation of his chronic therapy with oxycodone/naloxone. At 6 months' follow-up, he was still reporting adequate pain control with an NRS-11 score of 3, and he had suspended opioids both for chronic pain control and for medications (his ulcers were healing, and surgical medications were no longer needed). We had our last contact with the patient one year after the procedure and he was still reporting good clinical conditions.

DISCUSSION

Our case reports represent typical indications for LSP neurolysis. In fact, the majority of reports regarding this technique describe patients suffering with CRPS or ischemic pain, 2 conditions in which the sympathetic system plays a major role in sustaining pain. In these conditions, when medical management fails, there is no strong recommendation for which treatment should be proposed to the patient. Chemical neurolysis has been used on LSP to treat lower limb pain related to CRPS, chronic ischemia, and post amputation.

RF is a more recent development and, in published works, has been applied to LSP only in patients with

CRPS, with an extremely small number of patients treated and with low-quality evidence.

Even with these limitations, RF treatment appears to be safe and effective; however, it is unclear if its results can be compared to those observed with alcohol or phenol. The only 2 studies that compared these 2 neurolytic techniques were conducted on a very small number of patients with different outcome measurements and showed conflicting results (12,15).

Another limitation of published studies of RF and chemical neurolysis is the short-term follow-up reported in all of the aforementioned studies; only one paper reported 12 months of follow-up (14).

Spinal cord stimulation (SCS) and, more recently, dorsal root ganglion (DRG) stimulation, are neuromodulation techniques that have shown impressive results for ischemic pain and CRPS (28,30-34). However, these techniques have some downsides: high costs, the patient must be educated on managing an implantable device, risk of infection, catheter displacement, pocket hematoma, and neurological damage to the spinal cord or nerve roots. Moreover, long-term results are lacking since data usually report a follow-up between 6 and 24 months (27,28,30-34). Sympathetic neurolysis is a relatively easy treatment that is less invasive and expensive than SCS or DRG stimulation and has shown good results in published reports (even if with low-quality evidence). In our pain management unit, we reserve chemical neurolysis with alcohol for patients with cancer-related pain when life expectancy is short and the possible severe side-effects of alcohol are acceptable, in particular deafferentation pain which usually takes months to develop. For patients with nonmalignant pain, we use RF as a first choice since it is considerably safer. One argument against RF is that the lesion is smaller compared with the larger amount of tissue that can be destroyed with chemical neurolysis.

However, using a multilevel approach and applying sensory stimulation prior to lesioning ensures good precision and an acceptable lesion size for creating the desired effect. In our cases, patients reported excellent pain relief lasting for almost one year after the procedure without any side effects or complications.

Patient 1 reported a crampy sensation after the procedure; even though we have no clear explanation for this phenomenon, we hypothesize that it could be related to a transient neuritis of sympathetic fibers resulting in these symptoms. Kabbara et al (35) reported 2 cases of LSP RF lesioning in which patients reported paresthesias with a dermatomal distribution in their lower limbs during sensory stimulation at 50 Hz and less than 0.8 V. They suggested that sympathetic fibers could be connected with DRG cells via anatomical or pathological synapses, which are responsible for the patient's sensory experience.

CONCLUSION

RF denervation of LSP could be considered as a treatment for CRPS and chronic ischemic pain when conventional medical therapy fails. Compared to chemical neurolysis, RF denervation has fewer risks for postprocedural deafferentation pain and it is considerably cheaper than DRG or SCS. Larger studies are needed to assess the efficacy of LSP RF denervation and to compare it with chemical lysis and, eventually, with SCS and DRG stimulation. In our opinion, even from a cost-effectiveness perspective, an LSP RF neurolysis could be considered as a second-line treatment (after conservative therapy fails) for sympathetically mediated pain in the lower limbs, reserving SCS and DRG stimulation as a third line treatment.

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Each author certifies that he or she, or a member of his or her immediate family, has no commercial association that might pose a conflict of interest in connection with the submitted manuscript.

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