

Operating on patients with complex regional pain syndrome

by Ryon Wiska DPM^{1*}, Lawrence Fallat DPM FACFAS²

The Foot and Ankle Online Journal 11 (2): 3

Complex regional pain syndrome (CRPS) is a debilitating disorder characterized by widespread, chronic pain. While elective procedures should be held until acute CRPS flare ups have subsided, certain scenarios require immediate surgical care. Surgical management of patients with CRPS requires a team approach with several other specialties including pain management and anesthesiology. In this article, we outline a pre-operative and post-operative management course for lower extremity surgery of patients with diagnosed CRPS. We also present several case reports where this protocol was utilized.

Keywords: Causalgia, Complex Regional Pain Syndrome, CRPS, Pain, Reflex Sympathetic Dystrophy, RSD, Surgical Management

This is an Open Access article distributed under the terms of the Creative Commons Attribution License. It permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. ©The Foot and Ankle Online Journal (www.faoj.org), 2018. All rights reserved.

Physicians have been documenting disorders of chronic pain for centuries, with earliest documentation spanning back to Ambroise Pare's description of chronic pain with King Charles IX in the 17th century [1]. Mitchell and colleagues documented cases of chronic pain in soldiers secondary to gunshot wounds and injuries of peripheral nerves during the Civil War [2]. Complex regional pain syndrome (CRPS) has historically been known by multiple names including reflex sympathetic dystrophy, causalgia, Sudeck's atrophy, and shoulder-hand syndrome. Most experts now abide by terminology introduced by the International Association for Study of Pain (IASP) in 1994, which subdivided CRPS into type 1 and type 2, with type 2 having an inciting nerve injury [3].

The diagnosis of CRPS is based on clinical findings. The original IASP diagnostic criteria for CRPS

includes: 1) The presence of an initiating noxious event or a cause of immobilization. 2) Continuing pain, allodynia, or hyperalgesia with which the pain is disproportionate to any inciting event. 3) Evidence at some time of edema, changes in skin blood flow, or abnormal sudomotor activity in the region of pain. 4) This diagnosis is excluded by the existence of conditions that would otherwise account for the degree of pain and dysfunction [4]. More recent literature from the Reflex Sympathetic Dystrophy Association unveiled a clinical diagnostic criteria update, which reflects systemic findings that can be documented during patient visits (Table 1)[5]. Current management for active CRPS includes physical therapy, antidepressant agents, gabapentin, corticosteroids, topical analgesics, opioids, sympathetic blocks, somatic blocks, and neuromodulation [6-10].

1 - Second year podiatric surgery resident at Beaumont Hospital, Wayne.

2 - Program director for podiatric surgery at Beaumont Hospital, Wayne.

* - Corresponding author: rwiska@gmail.com

<ol style="list-style-type: none"> 1. Continuing pain, which is disproportionate to any inciting event 2. Must report at least one symptom in <i>three of the four</i> following categories Sensory: Reports of hyperalgesia and/or allodynia <ol style="list-style-type: none"> a. Vasomotor: Reports of temperature asymmetry and/or skin color changes and/or skin color asymmetry b. Sudomotor/Edema: Reports of edema and/or sweating changes and/or sweating asymmetry c. Motor/Trophic: Reports of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin) 3. Must display at least one sign* at time of evaluation in <i>two or more</i> of the following categories <ol style="list-style-type: none"> a. Sensory: Evidence of hyperalgesia (to pinprick) and/or allodynia (to light touch and/or deep somatic pressure and/or joint movement) b. Vasomotor: Evidence of temperature asymmetry and/or skin color changes and/or asymmetry c. Sudomotor/Edema: Evidence of edema and/or sweating changes and/or sweating asymmetry Motor/Trophic: Evidence of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin) 4. There is no other diagnosis that better explains the signs and symptoms <p>* A sign is counted only if it is observed at time of diagnosis</p>

Table 1 Clinical diagnostic criteria for complex regional pain syndrome.

In recent pain management literature, low dose naltrexone (LDN) has been shown to be efficacious in treating patients with CRPS [11]. LDN refers to doses approximately 50-fold lower than doses of naltrexone typically given to patients addicted to opioids [12]. It has been shown that LDN antagonizes the Toll-like receptor 4 (TLR 4) pathway and attenuate microglia. TLR 4 in both CNS neurons and microglia augments the production of pro-inflammatory cytokines via the nuclear factor kappa-light-chain-enhancer of activated B cells (NF- κ B) pathway, which acts as a mediator for neuropathic pain [13]. In a double blind study of 30 women with chronic pain, twice daily administrations of 4.5 mg of Naltrexone resulted in 57% of the participants exhibiting a significant reduction in pain when compared to placebo [14].

The current paradigm of surgeons has been to avoid operating on patients with CRPS because symptoms could either recur or worsen. In 6-10% of patients, surgical intervention is warranted and should not be delayed. These conditions include painful deformity, displacement of fixation, fracture, trauma, tumors, and soft tissue masses [15]. Surgical management of patients with CRPS has been documented in

orthopedic literature, with several papers discussing surgical intervention of the upper extremity and the knee [16,17]. Previous recommendations in the knee included waiting 5 months, with ranges from 2 months to 1 year. Prolonging surgery allows for subsidence of acute pain, as well as allowing time for treatment such as sympathetic blocks and physical therapy [16,17]. The purpose of this article is to outline a surgical management approach preoperatively and postoperatively for patients with active CRPS to provide the podiatric surgeon with management options, as well as review three cases in which this protocol was used.

Preoperative Management

Surgical management of patients with CRPS requires a team approach. It is imperative to coordinate with the physician who is actively managing the patient's CRPS. If a patient does not have an active pain management specialist, consultation with a pain management specialist should be sought prior to operating. The surgeon should coordinate with the pain management physician as well as anesthesiologist regarding patient's operative management course with

clear understanding of preoperative and postoperative treatment.

Recent literature has found that low dose naltrexone (LDN) has been shown to be efficacious in treating patients with CRPS through its endorphin releasing and anti-inflammatory properties. However, it should be held at least 24-36 hours before surgery to ensure that opiate medication administered from anesthesia is able to reach full efficacy.

Anesthesia choice is critical in ensuring that CRPS flare-ups or increase in symptoms of active CRPS do not occur. Either epidural or spinal anesthesia should be utilized in patients with CRPS. This practice has been documented in orthopedic literature with studies showing recurrence rates of CRPS falling from 72% to 10% with the use of a preoperative spinal or epidural block [16]. It is believed that this may provide a clinical advantage by blocking the potential barrage of nociceptive afferent signals in the central nervous system during surgery [18].

When trying to evaluate whether epidural or spinal anesthesia should be performed, several variables should be considered such as time from start of induction to achievement of anesthesia, time for resolution of anesthesia, and possible side effects. In spinal anesthesia, the average time from intrathecal injection of local anesthetic to achievement of surgical anesthesia is 13 minutes in conventional spinal and 16 minutes in unilateral spinal [19]. In epidural anesthesia with insertion of catheter, the average time to achieve induction was noted to be 40 minutes [20]. When performing spinal anesthesia with 5 mg hypobaric bupivacaine, Ben-David reported two segment regression after 53 minutes and discharge after 180-190 minutes, with newer studies stating average PACU time following completion of procedure ranging between 65-98 minutes [21, 22]. Mulroy noted average PACU time for patients who received epidural prior to knee surgery as 92 ± 18 minutes [23].

Epidural allows for the titration of short term local anesthetic which may lead to quicker discharge times following outpatient procedure, while still providing blockade to prevent CRPS flare-ups. In patients with CRPS, epidural catheter allows the option for

continuous titration of anesthetic, which may be beneficial following the procedure, whereas spinal anesthesia employs a single dosage of anesthetic.

Common side effects noted in both spinal and epidural anesthesia are hypotension, bradycardia, post-dural puncture headaches, nausea, and vomiting. In more severe side effects, prolonged neurological complications have been observed. In epidural anesthesia, urinary retention is also a common side effect, which may require catheterization and hospitalization.

Postoperative Management

Following the surgical procedure, patients are admitted for 24-48 hours of IV pain medication administration. Patients are given take-home oral analgesic medication for pain relief until acute surgical pain has subsided. Typical examples of oral medications include Percocet 10 mg/325 mg, 1-2 tablets by mouth every 4-6 hours, or Hydromorphone 2-4 mg, 1 tablet by mouth every 4-6 hours. If patients were previously taking LDN, they are to resume daily LDN when surgical pain is controlled and after 7 days have elapsed. We recommend early range of motion and aggressive physical therapy following procedure once the surgical site is stable. If symptoms of CRPS appear to be exacerbated following surgery, we recommend patients undergo intravenous Ketamine infusion therapy, under the management of their pain specialist.

Case Report No. 1

A 38-year-old male presented to our clinic one month after injuring his right foot when a 1000-pound roll of vinyl fell onto his foot. The patient was initially referred to our clinic for care of a nondisplaced fracture of the fifth metatarsal; however, radiographs and bone scan failed to reveal signs of fracture and a diagnosis of contusion to the right foot was made. The patient had been immobilized in a nonweightbearing below knee cast for one month and had subsequently developed increased pain out of proportion to injury as well as exhibited mottling of skin to dorsum of right foot in relation to left. The patient also began to exhibit rigid contractures of the right tibialis anterior, extensor digitorum longus, and

extensor hallucis longus. The patient was referred to a pain management specialist where the diagnosis of CRPS to the right lower extremity was made. The patient reported that since date of injury, the pain had progressively increased and at time of initial presentation, was so severe that even light touch to the right lower extremity was excruciatingly painful. On evaluation it was determined that the patient exhibited two distinct types of pain, a generalized CRPS pain to the affected lower extremity as well as a muscular pain secondary to rigid contractures. The patient was treated in our office monthly for peripheral nerve blocks at the level of the ankle joint consisting of 0.5% Marcaine plain, which the patient reported provided several hours of relief of contractures and pain before pain and contractures returned. At the same time, he underwent 22 sympathetic blockades over the course of 3 years from 4 different pain clinics, but had no relief, despite multiple pain management treatment modality attempts including a spinal cord stimulator. The patient was treated noninvasively by pain management specialists as well as our clinic for approximately 3 years, at which time it was determined that pain level had plateaued and was not improving with the treatment.

The patient underwent three different manipulations of the right foot under epidural anesthesia. The extensor tendons were stretched for a period of 20 minutes, until relaxation of rigidly contracted muscles were noted. The patient was then placed in an anterior splint following the procedures. No acute flare up of CRPS was seen immediately after the procedure; however, the patient exhibited return of rigid contractures and pain 48 hours following each procedure and was unable to tolerate the anterior splint. No increase in CRPS pain was seen following procedures.

The patient then underwent a series of botox injections that provided some pain relief and reduction of contracture to right foot and ankle that lasted for approximately two to three weeks before the muscles returned to rigid clonus.

Surgical intervention to the right foot was discussed with the patient. The patient was offered procedures

that included manipulation of the right foot under anesthesia, capsulotomy of the right first metatarsophalangeal joint, lengthening of the tibialis anterior, extensor hallucis longus, and extensor digitorum longus tendons, and sectioning of extensor hallucis brevis, all of the right foot. The patient was advised that procedure may exacerbate symptoms of CRPS and that no guarantees were given or implied. The patient met with his pain management specialist prior to the procedure and was given provisions for oral analgesics following the procedure.

On the day of the procedure, anesthesia was obtained with spinal anesthesia. The patient was placed on the operating table in the supine position. Manipulation of the foot was first performed where attention was made to manually plantarflex the right ankle joint as well as toes 1-5, which were noted to be rigidly contracted in a dorsiflexed position. Following manipulation, the foot was noted to held in a plantarflexed position. Standard z-lengthening procedures were then performed to the extensor digitorum longus, extensor hallucis longus, and tibialis anterior tendons. The extensor hallucis brevis tendon was identified and then sectioned proximal to its insertion. Attention was then directed to the first metatarsophalangeal joint where a dorsal and lateral capsulotomy was then performed and contracture of the first metatarsophalangeal joint was noted to be decreased. Closure was completed using a combination of dissolving and nondissolving suture. A postoperative block was then infiltrated around the incision sites consisting of 9 mL of 0.5% Marcaine plain and 2 mL of dexamethasone.

Following the procedure, the patient was admitted for 48-hour pain management. The patient reported a relief in pain following the procedure and was able to tolerate weight bearing to the right lower extremity without the use of an assistive device for the first time since the injury. Ultimately, the patient reported return of CRPS pain and contractures 2 weeks following the procedure; however, no increase in CRPS pain was noted. In addition, the patient noted that contractures to the right lower extremity were not as rigid or painful.

Case Report No. 2

A 31-year-old female with history of CRPS type 1 after sustaining multiple injuries from a motor vehicle accident presented to our clinic with complaints of right ankle pain. The patient had history of multiple surgeries to her right ankle with internal fixation after suffering a comminuted open right ankle fracture. The patient's pain was actively cared for by a pain management specialist who had maintained the patient's pain in a tolerable level with the use of LDN as well as IV Ketamine infusion therapy. The patient presented to our office with complaints of a painful right ankle, which had subsequently developed a severe valgus alignment of the right heel, subtalar joint arthritis, a nonunion of a right fibular fracture, as well as pain along course of retained hardware. Despite active pain management therapy, the patient admitted to 10/10 pain to the right ankle. The patient related that pain to her right ankle was becoming debilitating to the point that she was unable to ambulate. Initial attempts were made to treat the patient conservatively with the use of padding, bracing, and offloading with patient reporting no relief of pain. When conservative treatment options were exhausted, the patient was advised of surgical correction. The patient was made aware that surgical correction risked the possibility of a CRPS flare-up. She was fully aware of this and wished to proceed with procedure. Prior to boarding procedure, multiple conversations were had with patient's pain management specialist as well as anesthesia team at our institution with preoperative, perioperative, and postoperative management discussed at length. It was determined that prior to procedure, patient was to hold LDN. The day of the procedure, patient was to obtain a popliteal block prior to induction and then undergo general anesthesia. The patient was then to be admitted for extended stay pain monitoring.

Twenty-four hours prior to procedure, patient's LDN was held. On the day of the procedure, the patient was to undergo a popliteal block prior to induction; however, she did not receive the block prior to procedure. The patient was brought to the operating room and placed on the hospital table in the supine position where general anesthesia was obtained. The patient then underwent removal of painful retained

bone screws and plates of the ankle, open reduction and internal fixation of right fibular nonunion, resection of synostosis of right ankle, excision of scar tissue of right ankle, medial transpositional calcaneal osteotomy with internal fixation of right foot, as well as arthrotomy of right ankle. The patient was then placed in a well-padded cast and was instructed to be non-weight bearing to the right lower extremity with the use of crutches.

Following the procedure, the patient awoke from anesthesia in intense pain to the surgical limb. An epidural was placed and pain was controlled. The patient was converted to 48 hour full admit due to epidural. After 24 hours, she related that epidural was starting to wear off and was admitting to increased pain to surgical limb. The patient was maintained on IV Dilaudid and oral Percocet, 10 mg. After 4 days postoperatively, her pain was maintained on oral Percocet and patient was discharged home. The patient went on to achieve surgical union of fibular fracture, but continued to admit to CRPS pain to the surgical limb, which limited activities of daily living. The patient related to no increase in CRPS pain. Six months following her procedure, the patient successfully underwent a spinal cord stimulator trial. Following insertion of the stimulator, the patient was able to stand and walk around a department store, which she had been unable to do following the initial accident. Although the patient still relates to CRPS pain, the pain related to her foot and ankle condition has subsided and no increase in CRPS pain has been noted.

Case Report No. 3

A 65-year-old female presented to our office with history of CRPS, which she developed following a third intermetatarsal space neurectomy to the left foot. On clinical exam, the patient exhibited symptoms of a neuroma to the second intermetatarsal space to the left foot as well as a stump neuroma to the third intermetatarsal space of the left foot and admitted to 10/10 left pain with maximal tenderness to the forefoot. The patient admitted that pain to the left foot was so intense that her ability to ambulate was becoming limited. Conservative treatment was attempted with offloading, padding, and local steroid

injections to the affected intermetatarsal spaces, which provided little to no relief. Once conservative options had failed, surgical intervention was discussed with the patient. The patient was advised that the proposed procedures would be an excision of neuroma to second and third intermetatarsal space of the left foot. The patient was made aware that CRPS symptoms could be exacerbated by the procedure and that clear pain management goals were outlined with her pain management physician.

On the day of the surgery, anesthesia was obtained with spinal anesthesia as well as a local anesthetic block to the second and third intermetatarsal spaces of the left foot. Anatomic dissection was carried down to the level of the neuroma and nerve was tracked proximally until healthy nerve tissue was observed. Inflamed nerve was then resected from the second and third intermetatarsal space. A 4 cm x 2 cm x 0.5 cm nerve specimen was excised from the second intermetatarsal space and a 2 cm x 1.5 cm x 0.3 cm nerve specimen was excised from the third interspace. Closure was then performed with a combination of dissolving and non-dissolving suture and a postoperative block was infiltrated to the incision site consisting of 9 mL of 0.5% Marcaine plain and 4 mL of dexamethasone. The patient was given Norco 7.5 mg/325 mg for pain control postoperatively and was partial weight bearing to the left heel in a surgical shoe. The patient declined postoperative observation for pain management and was discharged home once cleared by anesthesia.

Following the procedure, the patient reported no increased exacerbation of CRPS and admitted to decreased pain to the neuroma site on the left foot. While the patient still reports CRPS pain to the left lower extremity, she is now able to pursue activities of daily living and maintains a tolerable level of pain to the left lower extremity.

In conclusion, our outlined pre-operative and post-operative management course for lower extremity surgery of patients with diagnosed CRPS has proven effective in preventing flare-ups of CRPS and preventing increase of active CRPS pain.

Funding Declarations

No funding was used.

Conflict of Interest

None

References

1. Pare A. Of the cure of wounds of the nervous parts. In *The Collected Works of Ambrose Pare*, book 10, pp 400-402, translated by T Johnson, Milford House, Pound Ridge, NY, 1634.
2. Mitchell SW; Morehouse GR, Kenn WW. Gunshot Wounds and Other Injuries of Nerves, pp 148-157, JB Lippincott, Philadelphia, 1864.
3. Stanton-Hicks M, Baron R, Boss R, et al. Complex regional pain syndrome: guidelines for therapy. *Clin J Pain*. 1998; 14:155-166.
4. Merskey H, Bogduk N. Classification of Chronic Pain: Descriptions of Chronic Pain Syndromes and Definitions of Pain Terms, 2nd edition. Seattle, WA: IASP Press; 1994.
5. Harden, R. N., Oaklander, A. L., Burton, A. W., Perez, R. S. G. M., Richardson, K., Swan, M., Barthel, J., Costa, B., Graciosa, J. R. and Bruehl, S. (2013), Complex Regional Pain Syndrome: Practical Diagnostic and Treatment Guidelines, 4th Edition. *Pain Med*, 14: 180–229. doi:10.1111/pme.12033
6. Rho RH, Brewer RP, Lamar TJ, Wilson PR. Complex regional pain syndrome. *Mayo Found Med Educ Res* 77: 174-180, 2002.
7. Oerlemans HM, Oostendorp RA, de Boo T, van der Laan L, Severens JL, Goris JA. Adjuvant physical therapy versus occupational therapy in patients with reflex sympathetic dystrophy/complex regional pain syndrome type I. *Arch Phys Med Rehabil*. 2000; 81:49-56.
8. Kingery WS. A critical review of neuropathic pain: antidepressants and opioids. *Clin J Pain*. 2000; 16 (2, suppl):S49-S55.
9. Kemler MA, Barends GAM, van Kleef M, et al. Spinal cord stimulation in patients with chronic reflex sympathetic dystrophy. *N Engl J Med*. 2000; 343:618-624.
10. Van Hilten BJ, van de Beek W-JT, Hoff JI, Voormolen JHC, Delhaas EM. Intrathecal baclofen for the treatment of dystonia in patients with reflex sympathetic dystrophy. *N Engl J Med*. 2000; 343: 625-630.
11. Chopra P, Cooper M. Treatment of complex regional pain syndrome using low dose naltrexone. *J neuroimmune pharmacol*. 2013; 8:470-476.
12. Rea F, Bell JR, Young MR, Mattick RP. A randomized controlled trial of low dose naltrexone for the treatment of opioid dependence. *Drug Alcohol Depend*. 2004; 75:79-88.

13. Milligan ED, Watkins LR. Pathological and protective roles of glia in chronic pain. *Nat Rev Neurosci*. 2009; 10:23-26.
14. Younger J, Noor N, McCue R, Mackey S (2013) Low-dose naltrexone for the treatment of fibromyalgia: findings of a small, randomized, double-blind, placebo-controlled, counterbalanced, crossover trial assessing daily pain levels. *Arthritis Rheum*, 2013; 65(2):529–538
15. Moesker A: Complex regional pain syndrome, formerly called Reflex sympathetic dystrophy, treated with Ketanserin and Carnitine (thesis). Rotterdam, Erasmus University Rotterdam, 2000, pp 1-147.
16. Reuben S, Rosenthal E, Steinberg R. Surgery of the affected upper extremity of patients with a history of complex regional pain syndrome: a retrospective study of 100 patients. *J of Hand Surgery*. 2000; 6:147-151.
17. Katz MM, Hungerford DS: Reflex Sympathetic Dystrophy Affecting the knee. *J Bone Joint Surg*. 1987; 69: 797 – 803.
18. R. Norman Harden, MD, Stephen Bruehl, PhD, Michael Stanton-Hicks, MB, BS, DMSc, FRCA, ABPM, Peter R. Wilson, MB, BS; Proposed New Diagnostic Criteria for Complex Regional Pain Syndrome. *Pain Med* 2007; 8 (4): 326-331.
19. Fanelli, G, Borghi, B, Casati A, et al. Unilateral bupivacaine spinal anesthesia for outpatient knee arthroscopy. *Can J Anesth* 2000; 47 (8):746-751.
20. Koenig T, Neumann C, Ocker T, Kramer S, et al. Estimating the time needed for induction of anesthesia and its importance in balancing anaesthetists' and surgeons' waiting times around the start of surgery. *Anaesthesia* 2011; 66:556-562.
21. Ben-David B, Levin H, Solomon E, Admoni H, Vaida S. Spinal bupivacaine in ambulatory surgery: the effect of saline dilution. *Anesth Analg* 1996; 83: 716–20.
22. Valanne J, Korhonen AM, Jokela R, Ravaska P. Selective spinal anesthesia: A comparison of hyperbaric bupivacaine 4 mg versus 6 mg for outpatient knee arthroscopy. *Anesth Analg* 2001; 93: 1377-9.
23. Mulroy M, Larkin K, Hodgson P, et al. A comparison of spinal, epidural, and general anesthesia for outpatient knee arthroscopy. *Anesth Analg* 2000; 91:860-4.