Neurotherapeutics (2019) 16:9–25
https://doi.org/10.1007/s13311-018-00695-z

REVIEW

The Role of the Peripheral Nerve Surgeon in the Treatment of Pain

Louis H. Poppler[1] · Susan E. Mackinnon[2]

Published online: 12 December 2018
© The American Society for Experimental NeuroTherapeutics, Inc. 2018

Abstract
Pain is a frequent cause of physician visits. Many physicians find these patients challenging because they often have complicated histories, emotional comorbidities, confusing examinations, difficult problems to fix, and the possibility of factitious complaints for attention or narcotic pain medications. As a result, many patients are lumped into the category of chronic, centralized pain and relegated to pain management. However, recent literature suggests that surgical management of carefully diagnosed generators of pain can greatly reduce patients' pain and narcotic requirements. This article reviews recent literature on surgical management of pain and four specific sources of chronic pain amenable to surgical treatment: painful neuroma, nerve compression, myofascial/musculoskeletal pain, and complex regional pain syndrome type II.

Keywords Neuralgia · Chronic pain · Hyperalgesia · Neuroma · Nerve compression · Complex regional pain syndromes · Causalgia · Reflex sympathetic dystrophy · Myofascial pain syndromes · Peripheral nerve injury · Surgery · Plastic surgery · Neurosurgery · Orthopedic surgery

Introduction

Severe pain and chronic pain are frequent chief complaints among patients presenting for care. According to the Institute of Medicine, chronic pain affects over 100 million Americans and the socioeconomic costs of pain in the USA are estimated at over $500 billion per year. This means pain affects more patients than diabetes, cancer, and heart disease combined [1]. Beyond socioeconomic costs, the degree of morbidity and human suffering is immeasurable. Pain also has costs within our own clinics, particularly time, difficult and emotionally taxing patients, fear of bad outcomes, fear of lawsuits, and difficulty discerning drug-seeking patients from patients with real pain. Although pain is a common reason for healthcare visits, most health profession education programs provide minimal pain evaluation and management education, and unsurprisingly, many physicians feel unprepared to properly evaluate and treat these patients [2].

✉ Louis H. Poppler
louispoppler@gmail.com

[1] Department of Orthopedic Surgery, Mayo Clinic, Rochester, MN, USA

[2] Division of Plastic and Reconstructive Surgery, Washington University in St. Louis, St. Louis, MO, USA

Within the medical community, a dogma that operating for pain will only cause more pain has led many pain specialists and primary care physicians to avoid referring patients with severe or chronic pain to surgeons [3, 4]. In many ways, surgeons share the guilt for perpetrating this dogma as many surgeons do not know how they can help or they do not want to take the time to thoroughly interview and examine these challenging patients. Consequently, many patients with pain caused by surgically manageable conditions are forced to either take chronic pain medications for life and deal with their side effects, or suffer. Recent literature indicates that surgical management of carefully diagnosed underlying pain generators results in pain improvement in 70–80% patients [5–7]. Regardless of surgery type, 10–30% of patients go on to have chronic pain and this pain is usually neuropathic [8, 9]. Understanding who is at risk for developing persistent pain, why, and how to prevent or treat it is an active area of research in many surgical specialties.

Therefore, the role of surgeons who treat peripheral nerve lesions and musculoskeletal complaints must be re-examined. We believe that the diagnosis of intractable, chronic, centralized pain should be a diagnosis of exclusion made only after ruling out treatable conditions of the peripheral nerves, bones, joints, muscles, and tendons. After all, patients with chronic pain frequently have or develop painful conditions amenable to treatment, like carpal tunnel, osteoarthritis, or peripheral neuropathy. The purpose of this paper is to highlight diagnosis

and management of conditions that cause persistent, chronic, or severe pain and are amenable to surgical treatment. We also review the pathophysiology of pain and its implications on surgical management so that surgeons can be more active participants in a multidisciplinary pain team and non-surgeons understand what conditions might merit surgical referral. Many of the surgical techniques described in this paper are not new; however, growing understanding of the nature of pain, the frequency of neuropathic origins, and growing comfort with intraneural anatomy and dissection facilitated by the growing field of nerve transfers allows for better outcomes than in the past.

Pain Definitions and Biology

Pain is a physiologic response to a noxious stimulus intended to trigger protective behaviors and limit tissue damage [10]. The International Association for Study of Pain defines pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage. Perception of pain requires actualization of three stages: activation of nociceptive receptors, relay of the message to and through to the central nervous system, and pain response [11]. Unfortunately, like any finely tuned system, pain perception can become dysregulated. This process is known as central sensitization [12, 13]. The focus of this paper will be on identifying and stopping sources of nociceptive activation in the periphery, recognizing that modulation and perception of pain signals within the central nervous system also play an important role in pain experience and management. Methods to modify pain modulation (sympathetic blocks, neuroleptic medications, spinal cord, dorsal root ganglion, and peripheral nerve stimulation) and perception (relaxation, cognitive behavior therapy, psychotherapy, pharmacologic treatment of depression, anxiety, pain catastrophizing) will also briefly be discussed but only in the context of team-based care, multimodal therapy, pre-optimizing patients for surgery, and peri-operative pain management.

Peripheral nociceptive pain can result from injuries or inflammation of the musculoskeletal system or the peripheral nerves. Pain derived from injury or inflammation of the nerves is called neuropathic pain and often much more severe and distressing. Sustained input from the peripheral nervous system can lead to central sensitization, which results in amplification of pain signals and response within the central nervous system and manifests as more severe pain, often in response to non-painful stimuli and beyond the anatomic territory of injury. Physiologic and psychologic factors can predispose patients to central sensitization and heightened experience of pain. Therefore, it is important for all severe or chronic pain patients to have each of the three stages of pain be treated with the cooperation of specialists in the pharmacologic management of pain (pain medicine doctors), psychologic management of pain (psychiatrists, psychologists, and case managers), and management of musculoskeletal and nerve disorders (surgeons, physical medicine and rehabilitation doctors, physical and occupational therapists). This is ideally done within a team setting that facilitates close communication and coordination between various team members. At a minimum, the patient should be established with a pain management physician who will manage their pain medications and take over care when healing from surgery is complete. Surgeons should not serve as patient's sole, or primary, pain management physicians.

The role of the surgeon within the pain team is to identify peripheral nociceptive and neuropathic sources of pain and eliminate or minimize them. These sources of pain fall into three categories: nerve compression, nerve injury (neuroma), and musculoskeletal injury/inflammation. Complex regional pain syndrome (CRPS) is a runaway pain syndrome with prominent physiologic changes frequently associated with nerve compression or neuroma that requires special attention. When seeing a patient with CRPS, nerve compression or neuroma should be suspected. A thorough discussion of sources of musculoskeletal pain is beyond the scope of this paper and not relevant to most readers of this journal. However, it is important to remember that musculoskeletal conditions are common and frequently co-exist with nerve injuries. Many of the same mechanisms that cause neuropathic pain such as swelling, inflammation, and muscle imbalance can also cause tendinitis, bursitis, or arthritis. It is typical for painful nerve injuries to result in postural modifications that then themselves generate secondary nerve compression. Consequently, the role of physical therapy to evaluate and treat posture-related extremity pain is critical and physicians that treat pain should not hesitate to refer patients with pain to physical and/or occupational therapy. Additionally, joint denervation is one treatment option in the algorithm for the management of arthritic pain [14–19].

Compression of a nerve can occur at any point along its trajectory from the spinal cord or dorsal root ganglion to its terminal end. There are more than 25 common points of nerve compression distal to the nerve roots, which can themselves be compressed as they exit the spine, in the upper and lower extremities and many more in the head, neck, and trunk (Table 1) [20–24]. Carpal tunnel is the most well-known and studied nerve compression syndrome. While anesthesia, dysesthesia, or pain are prominent symptoms of carpal tunnel, other compressions may present primarily with weakness or be subtler [25]. The physiology of nerve compression is the same at other points of compression [26, 27]. Changes from injury or compression at one point cause intraneural changes and edema along the nerve's entire course, predisposing it to compression at other known points of compression. This is known as the double/multiple crush phenomenon [28–30].

Table 1 Common points of nerve compression in the upper and lower extremities resulting in pain

Nerve(s)	Point(s) of compression	Prominent symptoms
Brachial plexus	- Nerve roots - Middle scalene muscles	- Upper extremity pain - Parascapular pain
Suprascapular nerve	- Supraspinous notch	- Shoulder pain
Axillary	- Quadrangular space	- Shoulder pain
Radial	- Spiral groove of the humerus - Radial tunnel - Brachioradialis/extensor carpi radialis longus	- Pain or dysesthesia along the dorsal radial arm, forearm, and hand
Ulnar	- Struther's ligament - Cubital tunnel - Osborne's ligament - Guyon's canal	- Pain or dysesthesia along the ulnar border of the forearm and hand
Median	- Pronator teres - Leading edge of deep flexor muscles in forearm - Carpal tunnel	- Pain or dysesthesia along the forearm, palm, and thumb, index, and long fingers
Sciatic	- Piriformis muscle	- Pain in the hip and buttock - Sciatica
Common peroneal	- Fibular head - Anterior, innominate, and posterior intermuscular septi	
Superficial peroneal	- Investing fascia of lateral compartment and lateral intermuscular septum - Extensor digitorum brevis	- Pain in anterior and lateral compartments - Pain, dysesthesia of dorsal foot
Tibial	- Leading edge of soleus muscle - Tarsal tunnel	- Pain, cramping of intrinsic foot muscles and calf - Pain and dysesthesia on plantar aspect of foot
Saphenous	- Adductor canal	- Pain along the medial thigh, knee, and foot
Lateral femoral cutaneous	- Inguinal ligament	- Burning, pain along the lateral thigh - Meralgia paresthetica

Painful neuromas usually develop following trauma or surgery and affect 2–60% of patients with nerve injury [31–34]. Neuromas form after all nerve injuries. Why some patients develop painful neuromas and others do not is an active area of research and is incompletely understood. Neuromas can also have associated nerve compressions due to the double crush phenomenon. There are certain nerves that are commonly injured in different surgeries; physicians treating pain should be familiar with these and have a high index of suspicion for them if a patient presents with extreme pain that began shortly following an operation (Table 2).

CRPS is a characteristic runaway pain syndrome with prominent features of pain out of proportion to degree of tissue injury and physiologic changes that include edema, erythema, warmth, skin and nail atrophy, and abnormal sweating [6]. In the acute phase, these typically improve with sympathetic blockade although this response diminishes as the disorder becomes chronic. CRPS is divided into three categories: type I involves trauma but no identifiable nerve injury, type II has a neuropathic source, and type III has no apparent traumatic cause. Types I and III are rare [35]. Both neuroma and nerve compression can be causes of CRPS. CRPS is often caused by trauma, which can include surgery or simple immobilization. The role of the surgeon who typically is managing these patients at the time CRPS develops is to (1) diagnose it quickly; (2) refer the patient for sympathetic blocks, physical therapy, and pharmacologic pain management; and (3) correct any underlying musculoskeletal injury, nerve compression, or neuroma. Delaying treatment must be avoided as CRPS that persists beyond 1 year rarely resolves [36].

A diagnosis of CRPS is made according to the Refined Budapest Criteria (Table 3). Review of the diagnostic criteria reveals that CRPS has multiple underlying pathologies that are incompletely understood. These include changes in the sympathetic nervous system, neurogenic inflammation, autoimmunity, and changes within the central nervous system [37]. As such, multimodal team management is even more important for patients with CRPS. Notably, postural response to the pain of CRPS may cause or exacerbate nerve compression, including edema, and dystonia. This can further exacerbate and reinforce the pain response. For example, the characteristic protective position in which patients with CRPS guard their arm increase pressure on the nerves in the arm (Fig. 1).

Examination of the Patient with Pain

The importance of careful and correct diagnosis when considering surgical intervention for pain cannot be overemphasized as the surgical management of nerve compression, neuroma, myofascial/muscle imbalance, or musculoskeletal pain are very different. In our experience, misdiagnosis and

Table 2 Sensory nerves at risk for painful neuroma after common surgeries

Operation(s)	Nerve affected
- Carpal tunnel release	- Palmar cutaneous branch of median - 3rd webspace branch of median
- Wrist operations	- Sensory branch of radial - Lateral antebrachial cutaneous - Dorsal cutaneous branch of the ulnar
- Cubital tunnel release/ulnar nerve transposition	- Medial antebrachial cutaneous - Medial brachial cutaneous
- Elbow operations	
- Humerus fractures	- Radial
- Shoulder arthroscopy	- Axillary
- Axillary dissection	- Intercosto-brachial
- Neck surgery	- Suprascapular - Greater auricular
- Breast surgery	- Intercostal neuroma
- Inguinal hernia repair	- Lateral femoral cutaneous
- Abdominoplasty	- Ilioinguinal
- Abdominal/pelvic surgeries	- Iliohypogastric - Genitofemoral
- Knee surgery	- Saphenous nerve infrapatellar branches - Lateral and medial femoral retinacular nerves - Medial femoral cutaneous nerve of thigh
- Ankle surgery	- Saphenous - Deep and superficial peroneal - Tibial nerve branches - Sural

subsequent mismanagement can make a patient's pain much worse. Patients with chronic pain often have a history of major

Table 3 Refined International Association for the Study of Pain Budapest Diagnostic Criteria for complex regional pain syndrome [38]

1. Continuing pain that is disproportionate to any inciting event
2. Must report at least one symptom in 3 of the following categories:
- Sensory: report of hyperesthesia and/or allodynia
- Vasomotor: reports of temperature asymmetry between limbs, skin color changes, or skin color asymmetry
- Sudomotor/edema: reports of edema, sweating changes, or sweating asymmetry
- Motor/trophic: evidence of decreased range of motion or motor dysfunction (weakness, tremor, dystonia) or trophic changes (hair, nails, skin)
3. Must display at least one sign at the time of evaluation in two or more of the following categories:
- Sensory: hyperalgesia to pinprick, allodynia to light touch, deep somatic pressure, or joint movement
- Vasomotor: evidence of temperature asymmetry or skin color asymmetry
- Sudomotor/edema: evidence of asymmetric edema or sweating
- Motor/trophic: evidence of decreased range of motion, motor dysfunction, or trophic changes
4. There is no diagnosis that better explains the signs and symptoms.

Fig. 1 This patient demonstrates the typical guarded posture of complex regional pain syndrome (CRPS). Note that the shoulder is adducted and forward flexed causing muscle imbalance, shoulder pain, and traction on the brachial plexus at the middle scalene and axillary at the quadrangular space. The elbow is flexed compressing the ulnar nerve at the cubital tunnel. The forearm is pronated compressing the radial and median nerves at the supinator and pronator. The wrist is also flexed compressing the median nerve. Also note that the metacarpal–phalangeal joints are extended, not flexed in a clenched fist position. The authors thank Dr. Catherine Curtin, MD for allowing us to use this photograph.

trauma or multiple surgeries, or both. It is not uncommon for them to have multiple sources of pain. Therefore, a systematic approach to diagnosis is essential.

Standardized assessment tools that include a subjective assessment of patients' pain level, quality, and location, as well as its impact on their function and psychological wellbeing, are very helpful. We like to use a form that we have customized which includes numerous visual analogue scales that are specific to each side, elaborates various time frames, includes an avatar for patients to mark the location of their pain, pain descriptors, questions about various factors that may intensify pain, and asks impact on their function (Fig. 2). Inspection of these forms often allows the physician to instantly identify the likely source of a patient's pain. Neuropathic pain will frequently be drawn in a dermatomal distribution or along the course of a nerve, while musculoskeletal pain will be more localized. Numerous other validated measures are available for use (Table 4). We suggest pairing a simple assessment of pain, like the visual analogue scale with a more detailed pain and function questionnaire the DASH or PROMIS [39, 40]. Serial assessment with these forms facilitates tracking progress that is sometimes not apparent to the patients themselves.

History

A thorough history and timeline of patients' pain is essential. Despite the subjective and individual experience of pain, different underlying pathologies will have typical histories and presentations (Table 5). It is important to take time to really

BARNES-JEWISH Hospital BJC HealthCare | Washington University in St. Louis Physicians

Susan E. Mackinnon, M.D.

Pain Questionnaire

Name _____ Date ___/___/___

Age____ Sex: ☐ Male ☐ Female Dominant Hand: ☐ Right ☐ Left Diagnosis _____

1. **Pain is difficult to describe. Check the words that best describe your symptoms:**

☐ Burning	☐ Throbbing	☐ Aching	☐ Stabbing	☐ Tingling	☐ Twisting	☐ Squeezing
☐ Cramping	☐ Cutting	☐ Shooting	☐ Numbing	☐ Vague	☐ Stinging	☐ Indescribable
☐ Pulling	☐ Smarting	☐ Pressure	☐ Coldness	☐ Dull	☐ Other_____	

LEVEL OF SYMPTOMS

Check to indicate the level of your pain, with zero being no pain and 10 the most severe pain you can imagine having.

2. **Mark your average level of pain in the last month:**

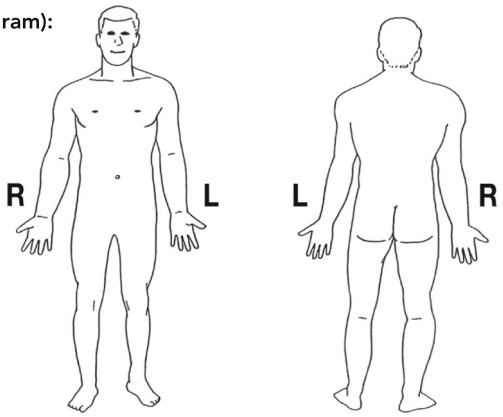
No Pain **Most Severe Pain**

3. **Mark your worst level of pain in the last week:**

Right **No Pain** **Most Severe Pain**

Left **No Pain** **Most Severe Pain**

4. **Where is your pain? (Draw on diagram):**



5. **Mark on this scale how your pain has affected your quality of life:**

0% (Not at All) **100% (A Large Amount)**

6. **Mark on this scale how sad you are:**

0% (Not at All) **100% (A Large Amount)**

7. **Mark on this scale how depressed you currently feel:**

0% (Not at All) **100% (A Large Amount)**

8. **Mark on this scale how frustrated you currently feel:**

0% (Not at All) **100% (A Large Amount)**

9. **Mark on this scale how angry you currently feel:**

0% (Not at All) **100% (A Large Amount)**

WUP PLAS SEM PAIN QUE A NL (Rev 10/17)

Fig. 2 Our preferred pain evaluation form includes multiple visual analogue scales of pain, depression, anxiety, and anger. It also includes an avatar for patients to mark their pain location(s) and numerous questions about relevant comorbidities

10. Mark on this scale how hopeful you are:

0% (Not at All) 100% (A Large Amount)

11. Mark your average level of stress in the last month:

At Home 0 10

At Work 0 10

12. How well are you able to cope with that stress:

At Home Very Well Not at All

At Work Very Well Not at All

13. How did the pain that you are now experiencing occur?
- ☐ a. Sudden onset with accident or definable event
- ☐ b. Slow progressive onset
- ☐ c. Slow progressive onset with acute exacerbation without an accident or definable event
- ☐ d. A sudden onset without an accident or definable event

14. How many surgical procedures have you had in order to try to eliminate the cause of your pain?
- ☐ a. None or one
- ☐ b. Two surgical procedures
- ☐ c. Three or four surgical procedures
- ☐ d. Greater than four surgical procedures

15. Does movement have any effect on your pain?
- ☐ a. The pain is always worsened by use or movement
- ☐ b. The pain is usually worsened by use and movement
- ☐ c. The pain is not altered by use and movement

16. Does weather have any effect on your pain?
- ☐ a. The pain is usually worse with damp or cold weather.
- ☐ b. The pain is occasionally worse with damp or cold weather.
- ☐ c. Damp or cold weather has no effect on the pain.

17. Do you ever have trouble falling asleep or awaken from sleep?
- ☐ a. No - ***Proceed to Question 19***
- ☐ b. Yes - ***Proceed to 18A & 18B***

18A. How often do you have trouble falling asleep?
- ☐ a. Trouble falling asleep every night due to pain
- ☐ b. Trouble falling asleep due to pain most nights of the week
- ☐ c. Occasionally having difficulty falling asleep due to pain
- ☐ d. No trouble falling asleep due to pain
- ☐ e. Trouble falling asleep which is not related to pain

18B. How often do you awaken from sleep?
- ☐ a. Awakened by pain every night
- ☐ b. Awakened from sleep by pain more than 3 times per week
- ☐ c. Not usually awakened from sleep by pain
- ☐ d. Restless sleep or early morning awakening with or without being able to return to sleep, both unrelated to pain

19. Has your pain affected your intimate personal relationships?

☐ a. No ☐ b. Yes

20. Are you involved in any legal action regarding your physical complaint?

☐ a. No ☐ b. Yes

WUP PLAS SEM PAIN QUE B NL (Rev 10/17)

Fig. 2 (continued)

understand the patients' pain quality, trajectory, alleviating and aggravating factors, and specific distribution. Physicians should ask about when and how the pain started, the type of pain the patient is experiencing, how this has changed over time, and any event that caused that to change. Often, patients will present with a history of pain for which they had surgery, and that pain resolved but was replaced with much worse pain immediately after surgery. This should raise suspicion for

21. Is this a Workers' Compensation case?
☐ a. No ☐ b. Yes

22. Are you presently receiving or have you ever received psychiatric/psychological treatment?
☐ a. No ☐ b. Presently receiving psychiatric treatment ☐ c. Previous psychiatric treatment

23. Have you ever thought of suicide?
☐ a. No ☐ b. Yes ☐ c. Previous suicide attempts

24. Were you a victim of childhood trauma– emotional or physical?
☐ a. No ☐ b. Yes ☐ c. No comment

25. Are you a victim of emotional abuse?
☐ a. No ☐ b. Yes ☐ c. No comment

26. Are you a victim of physical abuse?
☐ a. No ☐ b. Yes ☐ c. No comment

27. Are you a victim of sexual abuse?
☐ a. No ☐ b. Yes ☐ c. No comment

28. Are you presently a victim of abuse?
☐ a. No ☐ b. Yes ☐ c. No comment

29. Are you currently: (Check all that apply)

Employed for wages	☐ No	☐ Yes
On medical leave	☐ No	☐ Yes
A homemaker	☐ No	☐ Yes
Self-employed	☐ No	☐ Yes
Student	☐ No	☐ Yes
Retired	☐ No	☐ Yes
Volunteer	☐ No	☐ Yes
None of the above	☐ No	☐ Yes

30. If you are still working, do you?
☐ a. Work every day at the same pre-pain job.
☐ b. Work every day but the job is not the same as the pre-pain job with reduced responsibility or physical activity.
☐ c. Work occasionally.

31. Are you able to do your household chores?
☐ a. Do same level of household activities without discomfort.
☐ b. Do same level of household chores with discomfort.
☐ c. Do a reduced amount of household chores.
☐ d. Most household chores are now performed by others.

32. What pain medications have you used in the past month?
☐ a. No medications
☐ b. List medications:_____

_____

_____

c. Are you presently receiving or have you ever received narcotic/opioid medication(s)?
☐ No
☐ Previously → if so, when was last prescription? _____
☐ Presently → if so, who is your prescribing physician? _____

33. If you had three wishes for anything in the world, what would you wish for?

1. _____
2. _____
3. _____

From: Hendler N, Viernstein M, Gucer P, Long D: A preoperative screening test for chronic back pain patients. Psychosomatics 1979;20:801-808.
Mackinnon SE & Dellon AL: Surgery of the Peripheral Nerve, Thieme Medical Publishers, 1988
Melzack R: The McGill pain questionnaire: major properties and scoring methods. Pain 1975;1:277-299.
Modified by 1/5/2010 WUP PLAS SEM PAIN QUE C NL (Rev 10/17)

Fig. 2 (continued)

iatrogenic nerve injury and subsequent neuroma. Symptoms that progress more gradually may indicate nerve compression or musculoskeletal pathology and are typically less painful than neurotmetic injuries (Fig. 3). Whenever available, previous imaging, electrodiagnostic studies, and operative reports must be thoroughly reviewed.

Pain adjectives and associated descriptions can also help identify sources of pain. Electrical, burning, zapping,

Table 4 Common validated pain assessment scales

Assessment tool	Advantages	Disadvantages
Visual Analogue Scale (VAS) [41]	- Easy to administer - Easy to score - Previously validated in multiple languages and populations, and for various topics (pain, depression, anxiety)	- Difficult for the elderly or those unfamiliar with fractions
Faces Pain Scale [42]	- Faces give reference of pain degree, improving comparability between patients - Appropriate for use in children	- Relatively few choices
Short Form–36 (SF-36) [43]	- Provides a global assessment of function, and asks about pain - Not specific to the hand/upper extremity	- 36 questions long - No questions about related anxiety, depression, catastrophizing
McGill Short Form Pain Questionnaire [44]	- Provides pain characteristics and overall intensity - Only 15 questions long	- No questions about function - No questions about related anxiety, depression, catastrophizing
Australian/Canadian Osteoarthritis Hand Index (AUSCAN) [45]	- 3 subscales: pain, stiffness, function - Pain assessed at rest and during activities - Only 15 questions long	- Hand/upper extremity specific - No questions about related anxiety, depression, catastrophizing
Michigan Hand Questionnaire [46]	- 6 subscales: overall hand function, activities of daily living (ADLs), pain, work performance, esthetics, patient satisfaction with function - Assesses function in multiple ways	- Hand/upper extremity specific - 37 questions long - No questions about related anxiety, depression, catastrophizing
Disabilities of the Arm, Shoulder, and Hand (DASH) [40]	- 30-item survey assesses ADLs, global function, work function, pain, qualitative symptoms - Optional work and recreation modules	- Hand/upper extremity specific - 30–38 questions long - No questions about related anxiety, depression, catastrophizing
QuickDASH [47]	- 11-item survey assesses ADLs, global function, work function, pain, qualitative symptoms - Optional work and recreation modules	- Hand/upper extremity specific - No questions about related anxiety, depression, catastrophizing
Patient-Rated Wrist and Hand Evaluation (PRWHE) [48]	- 15-item survey assess pain and function in the wrist and hand	- Hand/upper extremity specific - No questions about related anxiety, depression, catastrophizing
PROMIS [39]	- Validated surveys available for multiple dimensions including global health, pain behavior, pain interference, pain intensity, pain quality, physical function (global and/or upper extremity specific), depression, anxiety, anger, self-efficacy - Short and long forms available - Computer adaptive testing available—only asks relevant questions based on prior response	- Number of questions can rapidly add up - Requires computer systems to administer

numbing, swelling and radiating, and stabbing are classically thought of as neuropathic symptoms while aching, pulling, smarting, deep pain is more often thought of as musculoskeletal. However, neuromas can also present as an aching, deep pain [35]. If patients describe multiple adjectives, we suggest asking them which ones are the most bothersome and working your way down the list from there to determine if the source of pain is likely neuropathic, or something else. In general, the more adjectives used, the more serious their pain response. Following surgery, the number of adjectives reported decreases [49]. Typically, pain from compression neuropathy is not as painful as that from neurotomy and surgery to treat a compression neuropathy is reliably successful.

Arthritic pain is usually worst in the morning and improves throughout the day, while neuropathic pain usually gets worse throughout the day. Allodynia is pain caused by a normally non-painful stimulus confined to a certain dermatomal or autonomous distribution. Dysesthesia is an unpleasant, abnormal sensation. Hyperpathia is an abnormally painful reaction to a stimulus that progresses slowly and beyond the distribution of any one dermatome. Allodynia, dysesthesia, or hyperpathia should raise suspicion of a neuropathic source of pain [6].

Patients' complaints will rarely fit neatly into just one diagnosis. Cutaneous nerve distributions often overlap and plexus formation between nerves is common [50, 51]. One must bear in mind the distinct possibility of the double crush phenomenon with proximal nerve compression and distal nerve injury or vice versa [28–30]. It is also possible for patients with chronic pain to develop muscle imbalances, contractures, or arthritis due to altered and use movement patterns. Therefore, asking about activities, how a patient uses the affected extremity, and how the patient holds the extremity can be insightful. For example, we recently examined a patient after a bike accident who underwent

Table 5 Common sources of chronic pain and their characteristic presentation

Problem	Characteristic history	Key examination findings	Helpful diagnostic tools
- Neurogenic			
neuroma	- Extreme pain immediately worse following trauma or surgery - Persistent pain after time of expected tissue healing - Allodynia, dysesthesia, and/or anesthesia distal to point of injury, though this may resolve with time	- Anatomical distribution of numbness - Pain may extend beyond distribution of affected nerve - (+) Tinel's sign a few cm proximal to neuroma/scar	- Diagnostic block(s) - Ultrasound - MR neurography if available
Entrapment neuropathy	- Gradual progression of symptoms - Dysesthesia - Hypoesthesia - Weakness - Aching ± radiating pain at/from point of compression - Pain typically less severe than neuroma or nerve root avulsion	- Anatomical distribution of dysesthesia, hypesthesia - Weakness/soreness of muscles innervated by affected nerve distal to compression point - (+) Tinel's or pressure provocation at point of compression - Scratch Collapse Test can help identify proximal compressions and distinguish point of maximum compression	- Electromyography and nerve conduction studies (can be falsely negative as C and A pain fibers are not picked up) - Ultrasound - MR neurography if available
Nerve root avulsion or radiculopathy	- Major trauma with associated anesthesia and weakness initially - Burning, electrical pain radiating from the neck/spine outward often in a dermatomal pattern - Area of pain can expand with time - Allodynia and hypesthesia can develop with time	- Areas of anesthesia will correspond with nerve root dermatomes - Weak muscles will correlate with nerve root myotomes	- Electromyography and nerve conduction studies - Pre-ganglionic injuries will have intact sensory nerve action potentials in setting of anesthesia - CT encephalogram - MRI of neck or spine
Complex regional pain syndrome (CRPS)	- Usually occurs following trauma but can occur following immobilization - Pain out of proportion to trauma - Burning pain that awakens patients from sleep - Allodynia - Hypesthesia	- Sympathetic changes are characteristic in early CRPS - Swelling - Erythema - Warmth - Hair loss - Nail changes - Skin atrophy or hyperkeratosis - Joint stiffness - Arm held in protective position: shoulder adducted and forward flexed, arm internally rotated, elbow flexed, forearm pronated, wrist and MCPs extended - Carefully examine for points of nerve compression or neuroma as pain generators	- Sympathetic block often improves symptoms - Radiographs assess osteopenia - 3-phase bone scan shows delayed uptake, followed by increased pooling and increased peri-articular uptake - MR neurography - Ultrasound - Musculoskeletal imaging as indicated
- Non-neurogenic			
Arthritis	- Joint pain/stiffness typically worst in morning and improved with activity - May have remote history of trauma to the joint - Rheumatoid/inflammatory arthritis often better in morning then worsens	- Pain with movement of joint - Crepitus with movement of joint - Swelling/effusion over joint - Joint disfiguration or malalignment	- Radiographs show loss of joint space, osteophytes, sclerosis, subchondral cysts - CT scan

Table 5 (continued)

Problem	Characteristic history	Key examination findings	Helpful diagnostic tools
Tendinitis, tendon rupture	- May have history of injury or can develop due to overuse, repetitive movements - Pain exacerbated by certain movements or activities - Pain usually localized but can radiate - Pain can be dull/aching, or sharp stabbing	- Point tenderness over tendon origin or insertion - Pain with stretch or loading of tendon - Weakness of involved muscle - Focal pain does not radiate in dermatomal distribution - No Tinel's - No allodynia, dysesthesia, anesthesia, hypesthesia	- Positive response to steroid injection at sites of tendinitis - MRI
Muscle imbalance	- History of posturing back, shoulders, or limb in fixed positions for prolonged periods of time - History of frequent computer work, leaning, or slouching - Aching pain in affected muscles - May be associated with nerve compressions exacerbated by shortened/tight tendons over nerves (e.g., neurogenic thoracic outlet with slouch, cubital tunnel with elbow flexion, carpal tunnel with prolonged wrist flexion, or frequent holding wrists extended at keyboard)	- Poor posture - Limb held in fixed position - Limited range of motion - Tight, sore muscles	

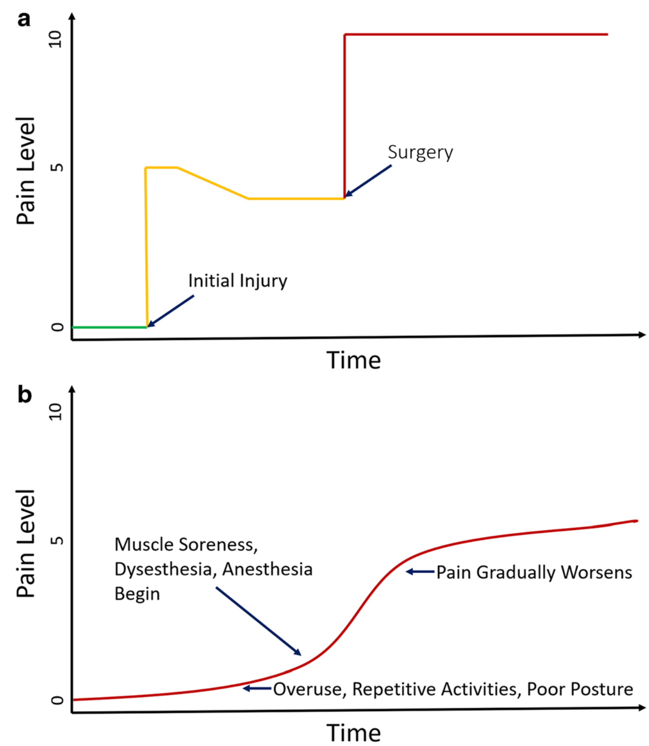


Fig. 3 Diagrams of patients' pain can help understand pain's source. **a** Patients with neuroma will often describe an initial injury accompanied by pain with certain descriptive adjectives. They will then have a surgery and immediately develop much worse pain with new, different, often neuropathic-associated adjectives. Their pain level is often near 10 out of 10. **b** Patients with pain relating to compression neuropathy, muscle imbalance, or myofascial pain will describe a gradual worsening of their symptoms without a major change in pain adjectives. Giving patients colored pencils and asking them to draw their pain in this way, with different colors representing different pain, can be very informative

numerous surgeries for a clavicle fracture, one of which dramatically increased his pain and resulted in radiating pain down his arm. Electromyography revealed a lateral cord injury. His neuropathic symptoms largely resolved; however, he continued to complain of a deep, dull ache in the shoulder and he was referred for "nerve pain." History revealed that pressing on his anterior shoulder improved his pain. Rotator cuff evaluation was performed, and an anterior labral tear was diagnosed. Treatment of the labrum and rotator cuff improved most of his pain symptoms. Another example is a patient with a pan-plexus injury who recovered wrist and finger flexion with some degree of spasticity but no extension, resulting in him holding his wrist in constant flexion. He presented complaining of burning pain in his radial digits and requesting amputation. The distribution was not characteristic of root avulsions, thoracic outlet, nor proximal nerve injury. Nerve conduction studies revealed carpal tunnel syndrome that was easily managed with release of the transverse carpal ligament resulting in improvement of the patient's pain.

Once we understand what we believe is the cause(s) of their pain, patient education about the anatomy of peripheral nerves, their dermatomes, and their function is imperative. This encourages patients to be active participants in their care

and allows the patient to identify and confirm for you the specific nerve that is injured. We run through a differential diagnosis and what would be expected with each and let the patient to tell us if one sounds more like what they experience than the others. This discussion between patient and physician helps build trust, a strong physician–patient relationship, and can itself be therapeutic [52].

Although exceedingly rare, there are some factitious pain syndromes in which surgery must be avoided (Table 6). Histories in these patients will not clearly fit any combination of the previously mentioned pain sources and treatments that should provide some relief will often make these patients worse. Warning signs of factitious disorders include severe swelling, especially with a circumferential band mark proximal to the swelling, multiple ulcerations, a clenched fist, multiple wounds or scars, worsening or changing symptoms without apparent cause, lack of a clear diagnosis despite multiple previous tests, operations, or expert consultations, and a desire for further testing and treatment despite previous unsuccessful treatments [53]. Listening to your gut and paying attention to your feelings when interacting with these patients can help you identify these difficult, and sometimes hostile, patients [54, 55]. Remember that the pre-operative period is finite while the postoperative period is infinite. Having a psychologist or psychiatrist involved in a pain team can facilitate triaging these patients to their much-needed care.

Beyond simple diagnosis of underlying sources of pain, it is incumbent on any physician treating pain to identify confounding factors that may intensify a patient's experience of pain. These include depression, anxiety, sadness, stress, post-traumatic stress disorder, pain catastrophizing, drug-abuse, and a history of physical, sexual, or emotional abuse, especially in childhood [8, 56–58]. Failure to concurrently address these factors before an operation increases the chance of treatment failure. We ask most of these questions on our intake form (Fig. 2). Screening for pain catastrophizing can be accomplished using the pain catastrophizing scale [59].

Physical Examination

Objective findings of nerve or musculoskeletal injury that corroborate a patient's history and symptoms are important before considering any operative intervention. Observation begins the moment the patient walks into your office and continues throughout the interaction. Note if the patient protects the injured extremity. If they complain of severe pain but use the extremity that should catch your attention and direct you away from surgery. Similarly, if they arrive with their extremity protected by a pillow or blanket that should indicate to you that they likely need other aspects of pain generation (sympathetic overactivity, pain catastrophizing, and other maladaptive behaviors) addressed before any consideration is given to surgery. Pay attention to their affect; lack of eye contact and hiding behind dark glasses and a hat are bad signs. Note what their spouse is doing. Ideally, they are interested and engaged but not speaking for, doting on, or otherwise enabling them. Conversely, if they are disengaged that is also a bad sign.

Physical examination of the patient with chronic pain requires empathy and buy-in from the patient. Before beginning, it is important to ask the patient if it is okay to touch them, their point of maximum pain, and if there are any areas that you should avoid. This information is very helpful in identifying trigger points of pain, the severity of pain, and narrowing the differential diagnosis. If a patient touches the dermatome of the suspected injured nerve, that suggests low-grade injury and need for decompression but not neuroma excision and repair or transposition. Apprehension or tears at the thought of being touched in this area, allodynia, and hypesthesia usually indicate higher grade nerve injury or central sensitization of pain that must be addressed. One should then begin with the most innocuous aspects of the exam like

Table 6 Factitious pain disorders to be avoided

Factitious disorder	Presentation	Distinguishing feature from CRPS
Factitious lymphedema	- History of painless swelling without knowledge of source - Often attributed to occupational activities - Swelling always stops distal to the shoulder or pelvis - Hospitalization or shoulder spica cast application rapidly resolve the edema	- Mild swelling with erythema common in CRPS, severe swelling is not - Swelling without erythema and other trophic changes uncommon in CRPS
Factitious ulceration	- History of trivial trauma with subsequent lesions that will not heal - Covering with a cast results in wound healing. Wounds often reappear after removal of cast	- Ulceration is not a typical feature of CRPS
Clenched fist and other dysfunctional postures	- Claimed immobility of the hand - Classically small, ring, and long fingers held in tight clenched fist while the index and thumb are fully mobile - Other variations of thumb adduction, index flexion, or finger extension possible - Lack of trophic changes seen with CRPS	- Patient with CRPS usually hold their metacarpophalangeal joints in extension

observation and sensory examination before progressing to potentially painful maneuvers like strength testing or provocative maneuvers. Areas of pain are saved for last.

Complete neuromuscular examination of the affected limb is attempted, and results are compared to the contralateral limb. First, observe for swelling, skin changes, warmth, sweating, and any scars. Sensation is tested with the ten test which compares patients' perceived amount of sensation from 0 to 10 in the affected limb to the corresponding regions of contralateral normal limb before attempting 2-point discrimination [60]. Using a piece of ice in a similar fashion to assess abnormalities in cold perception is also used by some in detecting neuropathies [61]. If the patient will tolerate it, 2-point discrimination is then performed. Nerve distributions of the various cutaneous nerves or nerve root dermatomes are specifically tested and documented. Active and passive ranges of motion of the joints in the extremity are documented. Strength testing is then performed, specifically isolating muscles specific to the various nerves in the extremity proximal and distal to known points of compression. Provocative tests for points of nerve compression are then attempted (Phalen's test for carpal tunnel, resisted pronation for pronator syndrome, etc.). The scratch-collapse can be very helpful in testing for proximal points of compression and determining which point among many is most significant in the case of multiple entrapment points along the same nerve [62–68]. Finally, the Tinel test is then performed [69, 70]. Start proximally to the area of suspected injury and progress distally along the nerve course. If you start at the point of maximum anticipated pain, you may provoke a significant pain response and end the exam. Inability to complete even innocuous portions of the exam indicates the need for aggressive medical and psychological management before any surgery is considered.

Once you have completed the physical examination, diagnostic blocks can be performed to test your suspected diagnosis and determine what effect decompression or neurectomy might have [67]. Blocks provide patients with an idea of the potential area of altered sensation with nerve resection but does not guarantee operative success [71]. Nerve blocks can usually be performed in a clinic, but occasionally require sedation or advanced imaging only available to pain specialists. Before any injection, objective measures such as VAS pain level, grip strength, pinch strength, and joint range of motion should be recorded. If a cutaneous neuroma is suspected, start with an injection of a small amount of local anesthetic very superficially within the scar. This should improve pain and function. Then, move to block the nerve(s) you suspect are injured in order of their suspected contribution to the patient's pain. A proximal point along the nerve that is isolated from other nerves is chosen to allow assessment of that one nerve's contribution. Wait an adequate time for the injection to have an effect and reassess the objective measures of pain and function before moving onto the next nerve, if more than one nerve is suspected to be involved. To prevent nerve injection injury, perform your injection proximal to the zone of previous injury and advise the patient to inform you of any symptom of nerve irritation. Ultrasound may also be used in experienced hands. Carefully note changes in the patients' reported pain level, function, and behavior after each block. Failure to improve pain with nerve block should dissuade you from operating.

If at this point you are unsure of any aspect of your examination, bring the patient back for repeat examination. Additional imaging can also be ordered but is not necessary if you have a convincing story and physical examination. Nerve conduction studies are the gold standard diagnostic modality for nerve entrapment, and should be obtained in most patients, provided they can tolerate the exam [72]. However, electrical studies only measure myelinated axons and therefore can miss compression only affecting small pain fibers, reducing their sensitivity in patients in whom the predominant complaint is pain [73, 74]. Ultrasound has become a widely available tool for assessing peripheral nerves but should not be substituted for careful physical examination [75, 76]. It has the added benefit of being non-invasive and allowing the examiner to correlate the patient saying where the point of maximum pain is with the area of imaging [67]. In our experience, ultrasound is highly operator dependent and not particularly sensitive for nerve compression or neuroma [77]. MR neurography has also become an accepted method for evaluating compression or injury of the peripheral nerves and has the added advantage of giving high-resolution imaging of the surrounding anatomy and associated inflammation [78–80]. Unfortunately, in many centers, it is not readily available.

Surgical Management

Pre-Optimization

In our opinion, the best way to treat chronic pain is to prevent it from happening in the first place. This can be accomplished by judicious patient selection, recognizing and treating risk factors for chronic pain before, during, and after surgery, and recognizing patients who are not improving as expected early, so that adjuvant interventions can be implemented. About 20% of patients develop chronic pain after any surgery and pre-operative pain intensity and pain catastrophizing are two of the strongest risk factors for developing chronic pain [8, 81–83]. Management of these risk factors is again facilitated in a team setting. Study of the effect of pre-operative psychological intervention is a promising area of research [56].

In patients with CRPS, it is our practice to defer treatment until the disorder is at least partially controlled with the use of pre-operative sympathetic blocks and pain medications. Like the treatment of migraines, there are numerous medications

that have been shown to help treat different facets of CRPS and selection of these agents is patient specific and directed by the patient's pain physician. At our institution, most patients with chronic pain are on a tricyclic antidepressant and gabapentin or pregabalin prior to any surgery. Vitamin C has been shown in four randomized trials to reduce the risk of CRPS following trauma or surgery and we suggest that they take 500 mg or more daily [84].

Peri-Operative Care

The patient pain diagram is reviewed with the patient on the day prior to surgery to reconfirm the diagnosis, assess pre-operative pain management, and solidify the surgical plan. If operating for neuroma, we have the patient mark their point of maximum tenderness and any trigger points with a permanent marker. After undergoing the induction of general anesthesia, patients receive a pre-operative IV regional block (Bier) with lidocaine and dexmedetomidine [85–88]. If this is not possible because we are not operating on a limb amenable to tourniquet application, a pre-operative proximal nerve block or epidural is performed. In this case, the block should be done with the patient awake and advised to declare any nerve symptom during block placement. A catheter is left in place for post-operative analgesia. We never perform a nerve block in a sedated patient.

When operating for compression, especially in the setting of pain, you get one best chance. Minimally invasive, limited access incisions should be avoided. It is important to get wide exposure to optimize your ability to visualize and protect the nerve. If performing revision surgery, it is important to identify the nerve within normal anatomy proximal and distal before entering the scarred and distorted anatomy of the previously dissected field. All possible points of compression within the field should be visualized and released. This includes any new points of kinking or tightness if you are transposing the ulnar nerve [89]. Neurolysis of the nerve from surrounding scar or synovitis is performed. The nerve should lay loosely within a healthy wound bed, ideally protected deep within the surrounding muscles. The senior author's preferred techniques for nerve decompression are available at https://surgicaleducation.wustl.edu, in her book "Nerve Surgery" [90], or in "Green's Operative Hand Surgery" [27].

When operating for neuroma, it is rarely necessary to first expose the neuroma within the scarred, previously operated field. Rather, exposure of the nerve proximal is much easier and safer. The "tug test," wherein you gently pull the nerve, will demonstrate if you have the correct nerve. In this case, you will see the trigger point or point of maximum pain marked by the patient retract. Prior to making any cut to the nerve, we crush the nerve as proximally as possible within the operative field, creating an axonotmetic injury (Sunderland II), to set the point front of regeneration far away from the cut nerve end [49]. Our clinical experience in patients with neuropathic pain suggests that neurotmetic injury (Sunderland IV, V, or Mackinnon VI) is much more painful than an axonotmetic injury. We believe that this proximal crush allows the brain to experience only one less severe insult (if any given the regional anesthesia) and minimizes or eliminates the brain's perception of the distal cut or neuroma excision that is performed.

In our experience, it is always best to reconstruct a painful nerve injury if possible. We prefer to reconstruct mixed and motor nerves with autograft whenever possible [91]. We will also reconstruct critical sensory nerves with autograft. Non-critical sensory nerves with a small diameter and gap less than 3 cm are reconstructed with acellular allograft [92, 93]. When selecting autograft, we prefer to borrow from the injured nerve to avoid creating new areas of anesthesia and potentially painful new neuromas [94]. If this is not possible, we will use the medial antebrachial cutaneous nerve if already operating in the upper extremity, or the sural nerve if operating in the lower extremity or depending on patient preference. Whenever harvesting a nerve autograft, we prefer to leave enough length at the distal end of the nerve perform an end-to-side coaptation to a nearby non-painful cutaneous nerve. This allows spontaneous sprouting of sensory axons to return some sensation to the donor nerve dermatome and we believe this prevents potentially painful sprouting from pain sensitized adjacent dermatomes [50, 95].

If the nerve affected by neuroma is not critical and reconstruction is impossible or impractical, then our preference is to perform a proximal crush, followed by transposition of the cut nerve end deep within muscle [71]. In patients with CRPS, keratinocytes at the skin have been shown to have altered gene expression and to secrete pain-inducing chemokines [37]. Therefore, our preference is to move the nerve into a deep muscle with minimal excursion so that stimulation of the cut nerve end is minimized. In recent years, we have also been "capping" the nerve end with a 5-cm nerve allograft in the hopes of arresting axonal regeneration [92, 93]. Our group recently performed a meta-analysis of surgical neuroma management that found no difference in outcomes among the various ways of managing neuroma so long as the neuroma was excised. However, transposition or coverage with a flap to move the neuroma away from the skin was significantly better in patients who had 2 or more prior neuroma operations, or who had pain lasting longer than 2 years [5]. Our own clinical experience with neuroma crush and deep transposition shows improvement in most patients [7, 49, 96].

Recently, targeted muscle reinnervation (TMR) and regenerative peripheral nerve interface (RPNI) procedures have been reported to have positive outcomes for the treatment of neuroma pain [97]. These two techniques were developed to allow volitional control of muscles, or pieces of muscles, in amputated limbs by cut nerves that normally power the

amputated body parts. The idea is that a nerve signal is converted into a muscle movement that can be recorded and used to direct a motor-powered prosthesis. Proponents of these techniques suggest that giving the nerve end an active target will improve neuroma outcomes. To date, published literature of the effectiveness of these techniques consists of only very small studies whose outcomes do not differ significantly from other published techniques [5, 98, 99]. However, we suspect that TMR, which involves an end-to-end coaptation of the cut nerve to a motor branch into muscle on the deep surface of that muscle, essentially transposing the cut nerve end under a muscle, will likely produce better results in amputees than traditional methods of nerve management in amputation stumps (traction neurectomy or suture ligation, both techniques used elsewhere to produce pain in rat pain models [100, 101]).

Post-Operative Care

At the time of incision closure, a catheter that infuses Marcaine is inserted in the operative bed to provide ongoing anesthesia for 2 days. A very lose, bulky splint is placed to protect and immobilize them. Patients are admitted for overnight observation, ensuring adequate pain control. They are placed on scheduled acetaminophen and ibuprofen and their home pain medications are also continued. On post-operative day 2, we see them back in the clinic, remove their pain catheter, and remove their dressing. They are sent immediately to physical therapy to commence gentle stretching, range of motion, and nerve gliding exercises [102]. Issues of pain exacerbation and narcotic seeking are uncommon in our carefully selected and pre-optimized surgical patients. In fact, over half of the patients chronically using opioid pain medications that we operate on for pain have stopped taking those medications 3 months after surgery [7]. We encourage patients to take time to relax, meditate, practice deep breathing, continue psychological therapy and psychiatric treatment, get adequate sleep, eat a healthy diet, exercise, perform their physical therapy exercises, be active, and socialize. We believe that giving them lots of self-care activities to perform provides, if nothing else, some illusion of control over their pain and allows them to become more active participants in their recovery.

Conclusions

In conclusion, chronic intractable pain should be a diagnosis of exclusion made only after treatable sources of neuropathic and musculoskeletal pain have been ruled out by surgeons and physicians experienced in treating those problems. This is best done in the setting of a pain management team that includes surgeons, pain management doctors, psychiatrists or psychologists, physical or occupational therapists, and case managers. With careful patient examination, selection, and pre-operative optimization, pain can be clinically significantly improved in most patients. Mastering the management of patients with pain improves your ability to treat, identify and treat your own patients who may be developing persistent pain. It can also be quite rewarding, as you will never have a patient as grateful as the one you rescue from devastating, life-altering pain.

Required Author Forms Disclosure forms provided by the authors are available with the online version of this article.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

References

1. Dzau VJ, Pizzo PA. Relieving pain in America: insights from an Institute of Medicine committee. JAMA 2014;312(15):1507–8.
2. Gatchel RJ, Reuben DB, Dagenais S, Turk DC, Chou R, Hershey AD, et al. Research Agenda for the Prevention of Pain and Its Impact: Report of the Work Group on the Prevention of Acute and Chronic Pain of the Federal Pain Research Strategy. J Pain 2018;19(8):837–51.
3. Noordenbos W, Wall PD. Implications of the failure of nerve resection and graft to cure chronic pain produced by nerve lesions. J Neurol Neurosurg Psychiatry 1981;44(12):1068–73.
4. Cetas JS, Saedi T, Burchiel KJ. Destructive procedures for the treatment of nonmalignant pain: a structured literature review. J Neurosurg 2008;109(3):389–404.
5. Poppler LH, Parikh RP, Bichanich MJ, Rebehn K, Bettlach CR, Mackinnon SE, et al. Surgical interventions for the treatment of painful neuroma: a comparative meta-analysis. Pain 2018;159(2):214–23.
6. Koman AL, Smith BP, Smith TL. A Practical Guide for Complex Regional Pain Syndrome in the Acute Stage and Late Stage. In: Wolfe SW, editor. Green's Operative Hand Surgery. 2. 7th Edition. Philadelphia, PA: Elsevier; 2017. p. 1797–827.
7. Santosa KB, Lapidus JB, Larson EL, et al. Pattterns of Opiod Use Among Peripheral Nerve Surgery Patients. Presentation at American Society of Peripheral Nerve, Palm Springs, CA; January 2019.
8. Kehlet H, Jensen TS, Woolf CJ. Persistent postsurgical pain: risk factors and prevention. Lancet 2006;367(9522):1618–25.
9. Shipton E. Post-surgical neuropathic pain. ANZ J Surg 2008;78(7):548–55.
10. Yancey P, Brand P. The Gift of Pain: Why We Hurt and What We Can Do About It. Grand Rapids, MI: Zondervan Publishing House; 1997.
11. Bourne S, Machado AG, Nagel SJ. Basic anatomy and physiology of pain pathways. Neurosurg Clin N Am. 2014;25(4):629–38.
12. Nijs J, Torres-Cueco R, van Wilgen CP, Girbes EL, Struyf F, Roussel N, et al. Applying modern pain neuroscience in clinical practice: criteria for the classification of central sensitization pain. Pain Physician. 2014;17(5):447–57.
13. Woolf CJ. Central sensitization: implications for the diagnosis and treatment of pain. Pain. 2011;152(3 Suppl):S2–15.
14. Simon L. Partial denervation for pain relief in arthritis of the knee. Orv Hetil 1951;92(43):1406–8.
15. Zaidenberg EE, Palumbo D, Martinez E, Pastrana M, Farias Cisneros E, Zaidenberg CR. Innervation of the interphalangeal joint of the thumb: anatomical study. J Hand Surg Eur Vol 2018;43(6):631–4.

16. Tuffaha SH, Quan A, Hashemi S, et al. Selective Thumb Carpometacarpal Joint Denervation for Painful Arthritis: Clinical Outcomes and Cadaveric Study. J Hand Surg 2018.
17. Zhong G, Liang Z, Kan J, Muheremu A. Selective peripheral nerve resection for treatment of persistent pain around the knee joint after total knee arthroplasty. J Int Med Res 2018;46(6):2301–6.
18. Hohenberger GM, Maier MJ, Dolcet C, Weiglein AH, Schwarz A, Matzi V. Sensory nerve supply of the distal radio-ulnar joint with regard to wrist denervation. J Hand Surg Eur Vol 2017;42(6):586–91.
19. Geldmacher J, Legal HR, Brug E. Results of denervation of the wrist and wrist joint by Wilhelm's method. Hand 1972;4(1):57–9.
20. Ducic I. Surgical Management of Chronic Headaches, Migraines, and Neuralgias. In: Mackinnon SE, editor. Nerve Surgery. New York, NY: Thieme; 2014. p. 572–90.
21. Davidge KM, Sammer DM. Median Nerve Entrapment and Injury. In: Mackinnon SE, editor. Nerve Surgery. New York, NY: Thieme; 2014. p. 207–50.
22. Davidge KM, Boyd KU. Ulnar Nerve Entrapment and Injury. In: Mackinnon SE, editor. Nerve Surgery. New York, NY: Thieme; 2014. p. 251–88.
23. Boyd KU, Brown JM. Injury and Compression Neuropathy in the Lower Extremity. In: Mackinnon SE, editor. Nerve Surgery. New York, NY: Thieme; 2014. p. 338–90.
24. Boyd KU, Dvali LT, Patterson MM, Patterson BM, Davidge KM. Radial Nerve Entrapment and Injury. In: Mackinnon SE, editor. Nerve Surgery. New York, NY: Thieme; 2014. p. 289–310.
25. Poppler LH, Groves AP, Sacks G, Bansal A, Davidge KM, Sledge JA, et al. Subclinical Peroneal Neuropathy: A Common, Unrecognized, and Preventable Finding Associated With a Recent History of Falling in Hospitalized Patients. Ann Fam Med 2016;14(6):526–33.
26. Mackinnon SE. Pathophysiology of nerve compression. Hand Clin 2002;18(2):231–41.
27. Mackinnon SE, Novak SB. Compression Neuropathies. In: Wolfe SW, editor. Green's Operative Hand Surgery. 1. 7th ed. Philadelphia, PA: Elsevier; 2017. p. 921–58.
28. Narakas AO. The role of thoracic outlet syndrome in the double crush syndrome. Ann Chir Main Memb Super 1990;9(5):331–40.
29. Osterman AL. The double crush syndrome. Orthop Clin North Am 1988;19(1):147–55.
30. Upton AR, McComas AJ. The double crush in nerve entrapment syndromes. Lancet 1973;2(7825):359–62.
31. Campbell JN. Neuroma Pain. In: Gebhart GF, Schmidt RF, editors. Encyclopedia of pain (2nd ed). Berlin: Springer-Verlag; 2013. p. 2056–8.
32. Aasvang E, Kehlet H. Chronic postoperative pain: the case of inguinal herniorrhaphy. Br J Anaesth 2005;95(1):69–76.
33. Fisher GT, Boswick JA, Jr. Neuroma formation following digital amputations. J Trauma 1983;23(2):136–42.
34. Gotoda Y, Kambara N, Sakai T, Kishi Y, Kodama K, Koyama T. The morbidity, time course and predictive factors for persistent post-thoracotomy pain. Eur J Pain 2001;5(1):89–96.
35. Carroll I. Pharmacologic Management of Upper Extremity Chronic Nerve Pain. Hand Clin 2016;32(1):51–61.
36. Schwartzman RJ, Erwin KL, Alexander GM. The natural history of complex regional pain syndrome. Clin J Pain 2009;25(4):273–80.
37. Tajerian M, Clark JD. New Concepts in Complex Regional Pain Syndrome. Hand Clin 2016;32(1):41–9.
38. Harden RN, Bruehl S, Stanton-Hicks M, Wilson PR. Proposed new diagnostic criteria for complex regional pain syndrome. Pain Med. 2007;8(4):326–31.
39. Available from: http://www.healthmeasures.net/.
40. Hudak PL, Amadio PC, Bombardier C. Development of an upper extremity outcome measure: the DASH (disabilities of the arm, shoulder and hand) [corrected]. The Upper Extremity Collaborative Group (UECG). Am J Ind Med 1996;29(6):602–8.
41. Joyce CR, Zutshi DW, Hrubes V, Mason RM. Comparison of fixed interval and visual analogue scales for rating chronic pain. Eur J Clin Pharmacol. 1975;8(6):415–20.
42. Bieri D, Reeve RA, Champion GD, Addicoat L, Ziegler JB. The Faces Pain Scale for the self-assessment of the severity of pain experienced by children: development, initial validation, and preliminary investigation for ratio scale properties. Pain 1990;41(2):139–50.
43. Jenkinson C, Coulter A, Wright L. Short form 36 (SF36) health survey questionnaire: normative data for adults of working age. BMJ. 1993;306(6890):1437–40.
44. Melzack R. The short-form McGill Pain Questionnaire. Pain 1987;30(2):191–7.
45. Bellamy N, Campbell J, Haraoui B, Buchbinder R, Hobby K, Roth JH, et al. Dimensionality and clinical importance of pain and disability in hand osteoarthritis: Development of the Australian/Canadian (AUSCAN) Osteoarthritis Hand Index. Osteoarthr Cartil. 2002;10(11):855–62.
46. Chung KC, Pillsbury MS, Walters MR, Hayward RA. Reliability and validity testing of the Michigan Hand Outcomes Questionnaire. J Hand Surg. 1998;23(4):575–87.
47. Beaton DE, Wright JG, Katz JN. Development of the QuickDASH: comparison of three item-reduction approaches. J Bone Joint Surg Am. 2005;87(5):1038–46.
48. MacDermid JC, Tottenham V. Responsiveness of the disability of the arm, shoulder, and hand (DASH) and patient-rated wrist/hand evaluation (PRWHE) in evaluating change after hand therapy. J Hand Ther. 2004;17(1):18–23.
49. Domeshek LF, Krauss EM, Snyder-Warwick AK, Laurido-Soto O, Hasak JM, Skolnick GB, et al. Surgical Treatment of Neuromas Improves Patient-Reported Pain, Depression, and Quality of Life. Plast Reconstr Surg. 2017;139(2):407–18.
50. Li Y, Dorsi MJ, Meyer RA, Belzberg AJ. Mechanical hyperalgesia after an L5 spinal nerve lesion in the rat is not dependent on input from injured nerve fibers. Pain. 2000;85(3):493–502.
51. Sheth RN, Dorsi MJ, Li Y, Murinson BB, Belzberg AJ, Griffin JW, et al. Mechanical hyperalgesia after an L5 ventral rhizotomy or an L5 ganglionectomy in the rat. Pain. 2002;96(1–2):63–72.
52. Fuentes J, Armijo-Olivo S, Funabashi M, Miciak M, Dick B, Warren S, et al. Enhanced therapeutic alliance modulates pain intensity and muscle pain sensitivity in patients with chronic low back pain: an experimental controlled study. Phys Ther. 2014;94(4):477–89.
53. Louis DS, Kasdan ML. Factitious Disorders. In: Wolfe SW, editor. Green's Operative Hand Surgery. 2. 7 ed. Philadelphia, PA: Elsevier; 2017. p. 1828–31.
54. Groves JE. Taking care of the hateful patient. N Engl J Med. 1978;298(16):883–7.
55. Strous RD, Ulman AM, Kotler M. The hateful patient revisited: Relevance for 21st century medicine. Eur J Intern Med. 2006;17(6):387–93.
56. Darnall BD. Pain Psychology and Pain Catastrophizing in the Perioperative Setting: A Review of Impacts, Interventions, and Unmet Needs. Hand Clin. 2016;32(1):33–9.
57. Granot M, Ferber SG. The roles of pain catastrophizing and anxiety in the prediction of postoperative pain intensity: a prospective study. Clin J Pain. 2005;21(5):439–45.
58. Helmerhorst GT, Vranceanu AM, Vrahas M, Smith M, Ring D. Risk factors for continued opioid use one to two months after surgery for musculoskeletal trauma. J Bone Joint Surg Am. 2014;96(6):495–9.
59. Sullivan MJ, Bishop SR, Pivik J. The Pain Catastrophizing Scale: development and validation psychological assessment. Psychol Assess. 1995;7(4):524–32.
60. Strauch B, Lang A. The ten test revisited. Plast Reconstr Surg. 2003;112(2):593–4.

61. Shy ME, Frohman EM, So YT, Arezzo JC, Cornblath DR, Giuliani MJ, et al. Quantitative sensory testing: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology. 2003;60(6):898–904.
62. Brown JM, Mokhtee D, Evangelista MS, Mackinnon SE. Scratch Collapse Test Localizes Osborne's Band as the Point of Maximal Nerve Compression in Cubital Tunnel Syndrome. Hand. 2010;5(2):141–7.
63. Cheng CJ, Mackinnon-Patterson B, Beck JL, Mackinnon SE. Scratch collapse test for evaluation of carpal and cubital tunnel syndrome. J Hand Surg. 2008;33(9):1518–24.
64. Davidge KM, Gontre G, Tang D, Boyd KU, Yee A, Damiano MS, et al. The "hierarchical" Scratch Collapse Test for identifying multilevel ulnar nerve compression. Hand. 2015;10(3):388–95.
65. Gillenwater J, Cheng J, Mackinnon SE. Evaluation of the scratch collapse test in peroneal nerve compression. Plast Reconstr Surg. 2011;128(4):933–9.
66. Makanji HS, Becker SJ, Mudgal CS, Jupiter JB, Ring D. Evaluation of the scratch collapse test for the diagnosis of carpal tunnel syndrome. J Hand Surg Eur Vol. 2013.
67. Curtin C. Pain Examination and Diagnosis. Hand Clin. 2016;32(1):21–6.
68. Kahn LC, Yee A, Mackinnon SE. Important Details in Performing and Interpreting the Scratch Collapse Test. Plast Reconstr Surg. 2018;141(2):399–407.
69. Dellon, AL. Tinel or not tinel. J Hand Surg [Am]. 1984;9(2):216.
70. Lifchez SD, Means KR, Jr., Dunn RE, Williams EH, Dellon AL. Intra- and inter-examiner variability in performing Tinel's test. J Hand Surg. 2010;35(2):212–6.
71. Colbert SH. Painful sequelae of Peripheral Nerve Injuries. In: Nerve Surgery. Susan E. Mackinnon, Editor. New York, NY: Thieme; 2014. p. 591–619.
72. Nathan PA, Keniston RC, Meadows KD, Lockwood RS. Predictive value of nerve conduction measurements at the carpal tunnel. Muscle Nerve. 1993;16(12):1377–82.
73. Rubin DI. Technical issues and potential complications of nerve conduction studies and needle electromyography. Neurol Clin. 2012;30(2):685–710.
74. Witt JC, Hentz JG, Stevens JC. Carpal tunnel syndrome with normal nerve conduction studies. Muscle Nerve. 2004;29(4):515–22.
75. Buchberger W, Schon G, Strasser K, Jungwirth W. High-resolution ultrasonography of the carpal tunnel. J Ultrasound Med. 1991;10(10):531–7.
76. Bignotti B, Signori A, Sormani MP, Molfetta L, Martinoli C, Tagliafico A. Ultrasound versus magnetic resonance imaging for Morton neuroma: systematic review and meta-analysis. Eur Radiol. 2015;25(8):2254–62.
77. Mehrpour M, Mirzaasgari Z, Rohani M, Safdarian M. Diagnostic value of median nerve ultrasonography for screening of carpal tunnel syndrome in hypothyroid patients: A cross-sectional study. Iran J Neurol. 2016;15(2):70–4.
78. Kollmer J, Bendszus M, Pham M. MR Neurography: Diagnostic Imaging in the PNS. Clin Neuroradiol. 2015;25 Suppl 2:283–9.
79. Bendszus M, Wessig C, Solymosi L, Reiners K, Koltzenburg M. MRI of peripheral nerve degeneration and regeneration: correlation with electrophysiology and histology. Exp Neurol. 2004;188(1):171–7.
80. Dailey AT, Tsuruda JS, Filler AG, Maravilla KR, Goodkin R, Kliot M. Magnetic resonance neurography of peripheral nerve degeneration and regeneration. Lancet. 1997;350(9086):1221–2.
81. Kalkman CJ, Visser K, Moen J, Bonsel GJ, Grobbee DE, Moons KG. Preoperative prediction of severe postoperative pain. Pain. 2003;105(3):415–23.
82. Dwyer CL, Soong M, Hunter A, Dashe J, Tolo E, Kasparyan NG. Prospective Evaluation of an Opioid Reduction Protocol in Hand Surgery. J Hand Surg. 2018;43(6):516–22.e1.
83. Pavlin DJ, Sullivan MJ, Freund PR, Roesen K. Catastrophizing: a risk factor for postsurgical pain. Clin J Pain. 2005;21(1):83–90.
84. Shibuya N, Humphers JM, Agarwal MR, Jupiter DC. Efficacy and safety of high-dose vitamin C on complex regional pain syndrome in extremity trauma and surgery–systematic review and meta-analysis. J Foot Ankle Surg. 2013;52(1):62–6.
85. Yang Y, Xia Z, Meng Q, Liu K, Xiao Y, Shi L. Dexmedetomidine relieves neuropathic pain by inhibiting hyperpolarization-activated cyclic nucleotide-gated currents in dorsal root ganglia neurons. Neuroreport. 2018;29(12):1001–6.
86. Kalappa S, Sridhara RB, Kumaraswamy S. Dexmedetomidine as an Adjuvant to Pre-Emptive Caudal Epidural Ropivacaine for Lumbosacral Spine Surgeries. J Clin Diagn Res. 2016;10(1):Uc22–4.
87. Dai S, Qi Y, Fu J, Li N, Zhang X, Zhang J, et al. Dexmedetomidine attenuates persistent postsurgical pain by upregulating K(+)-Cl(−) cotransporter-2 in the spinal dorsal horn in rats. J Pain Res. 2018;11:993–1004.
88. Peng K, Zhang J, Meng XW, Liu HY, Ji FH. Optimization of Postoperative Intravenous Patient-Controlled Analgesia with Opioid-Dexmedetomidine Combinations: An Updated Meta-Analysis with Trial Sequential Analysis of Randomized Controlled Trials. Pain Physician. 2017;20(7):569–96.
89. Felder JM 3rd, Mackinnon SE, Patterson MM. The 7 Structures Distal to the Elbow That Are Critical to Successful Anterior Transposition of the Ulnar Nerve. Hand. 2018:1558944718771390.
90. Mackinnon SE. Nerve Surgery. 1st. Ed. ed. New York, NY: Thieme; 2014 9/15/2014. 624 p.
91. Moore AM, MacEwan M, Santosa KB, Chenard KE, Ray WZ, Hunter DA, et al. Acellular nerve allografts in peripheral nerve regeneration: a comparative study. Muscle Nerve. 2011;44(2):221–34.
92. Saheb-Al-Zamani M, Yan Y, Farber SJ, Hunter DA, Newton P, Wood MD, et al. Limited regeneration in long acellular nerve allografts is associated with increased Schwann cell senescence. Exp Neurol. 2013;247C:165–77.
93. Poppler LH, Ee X, Schellhardt L, Hoben GM, Pan D, Hunter DA, et al. Axonal Growth Arrests After an Increased Accumulation of Schwann Cells Expressing Senescence Markers and Stromal Cells in Acellular Nerve Allografts. Tissue Eng Part A. 2016;22(13–14):949–61.
94. Poppler LH, Davidge K, Lu JC, Armstrong J, Fox IK, Mackinnon SE. Alternatives to sural nerve grafts in the upper extremity. Hand. 2015;10(1):68–75.
95. Goheen-Robillard B, Myckatyn TM, Mackinnon SE, Hunter DA. End-to-side neurorrhaphy and lateral axonal sprouting in a long graft rat model. Laryngoscope 2002;112(5):899–905.
96. Watson CPN, Mackinnon SE, Dostrovsky JO, Bennett GJ, Farran RP, Carlson T. Nerve resection, crush and re-location relieve complex regional pain syndrome type II: A case report. Pain. 2014;155(6):1168–73.
97. Ives GC, Kung TA, Nghiem BT, Ursu DC, Brown DL, Cederna PS, et al. Current State of the Surgical Treatment of Terminal Neuromas. Neurosurgery. 2018;83(3):354–64.
98. Souza JM, Cheesborough JE, Ko JH, Cho MS, Kuiken TA, Dumanian GA. Targeted muscle reinnervation: a novel approach to postamputation neuroma pain. Clin Orthop Relat Res. 2014;472(10):2984–90.
99. Woo SL, Kung TA, Brown DL, Leonard JA, Kelly BM, Cederna PS. Regenerative Peripheral Nerve Interfaces for the Treatment of Postamputation Neuroma Pain: A Pilot Study. Plast Reconstr Surg Glob Open. 2016;4(12):e1038.

100. Ho Kim S, Mo Chung J. An experimental model for peripheral neuropathy produced by segmental spinal nerve ligation in the rat. Pain 1992;50(3):355–63.
101. Rodrigues-Filho R, Santos ARS, Bertelli JA, Calixto JB. Avulsion injury of the rat brachial plexus triggers hyperalgesia and allodynia in the hindpaws: a new model for the study of neuropathic pain. Brain Res 2003;982(2):186–94.
102. Ellis RF, Hing WA. Neural mobilization: a systematic review of randomized controlled trials with an analysis of therapeutic efficacy. J Man Manip Ther 2008;16(1):8–22.