# Neuropathic pain in orthopedic conditions: a comprehensive review

## Dor neuropática nas condições ortopédicas: uma revisão abrangente

**Talitha Koo Yen**[1], **Raphael Salomão de Carvalho**[1], **Victor Hugo Daibert Bretones**[1], **Bruno Couto Gonçalves**[1]

*1. Faculdade de Medicina da Universidade de Santo Amaro, São Paulo, SP, Brazil.*

## Abstract

Neuropathic pain (NP) is a complex and disabling condition frequently associated with orthopedic disorders such as radiculopathies, entrapment syndromes, postoperative pain, and complex regional pain syndrome. This narrative review aims to summarize current scientific evidence regarding the pathophysiology, diagnosis, and treatment of NP within the orthopedic context. Databases such as PubMed, Cochrane, and Embase were searched for clinical trials, meta-analyses, and guidelines published up to 2024. The review presents updated pharmacological recommendations, including first-line agents such as antidepressants and gabapentinoids, as well as topical therapies, opioids, cannabinoids, and interventional procedures. Special attention is given to the role of ultrasound-guided blocks and neuromodulation techniques like spinal cord stimulation. Evidence supports a multidisciplinary and individualized approach, particularly in cases refractory to conventional therapy. This review reinforces the need for early recognition of NP components in musculoskeletal pain syndromes to improve functional outcomes and quality of life.

**Keywords:** Neuralgia; Orthopedics; Chronic pain; Antidepressive agents; Spinal cord stimulation; Pain management.

## Resumo

A dor neuropática (DN) é uma condição complexa e incapacitante, frequentemente presente em patologias ortopédicas como radiculopatias, síndromes compressivas, dor pós-operatória e síndrome dolorosa regional complexa. Esta revisão narrativa tem como objetivo compilar as evidências científicas atuais sobre fisiopatologia, diagnóstico e tratamento da DN no contexto ortopédico. Foram analisados ensaios clínicos, metanálises e diretrizes disponíveis nas bases de dados PubMed, Cochrane e Embase até o ano de 2024. O artigo aborda as recomendações terapêuticas atualizadas, incluindo fármacos de primeira linha como antidepressivos e gabapentinoides, além de tratamentos tópicos, opioides, canabinoides e procedimentos intervencionistas. Destaca-se o papel de bloqueios guiados por ultrassom e técnicas de neuromodulação como a estimulação medular. As evidências reforçam a abordagem multidisciplinar e individualizada, especialmente nos casos refratários ao tratamento convencional. A revisão enfatiza a importância do reconhecimento precoce dos componentes neuropáticos da dor musculoesquelética, visando melhor funcionalidade e qualidade de vida.

**Palavras-chave:** Neuralgia; Ortopedia; Dor crônica; Antidepressivos; Estimulação da medula espinal; Manejo da dor.

Study performed at the Faculdade de Medicina da Universidade de Santo Amaro, São Paulo, SP, Brazil.
**Correspondence:** Talitha Koo Yen. R. Prof. Enéas de Siqueira Neto, 340 - Jardim das Imbuias, 04829-300, São Paulo, SP, Brazil. **Email:** tkooyen@gmail.com.
**Conflict of Interest:** None.
**Source of funding:** None.
**Received:** April 15, 2025.
**Accepted:** April 28, 2025.

**Citation: Yen TK, Carvalho RS, Bretones VHD, Gonçalves BC. Neuropathic pain in orthopedic conditions: a comprehensive review. Braz Musculoskelet Pain Soc. 2025;1(1):e10**

## Introduction

Neuropathic pain imposes a substantial economic and social burden, often leading to loss of productivity, increased healthcare costs, and long-term disability. Despite its prevalence, accurately diagnosing this condition remains a major clinical hurdle due to its complex and varied presentation[1-4]. While general prevalence rates of neuropathic pain hover between 7% and 10%, this figure rises markedly in specific conditions such as diabetes, herpes zoster, and post-surgical complications—where neuropathic mechanisms are frequently involved[5]. Moreover, neuropathic pain was more prevalent among women (60.5% of patients), reached a peak at 50–64 years of age, and was more frequently reported by manual workers, as well as among people from rural areas[6].

Pain, according to the IASP, is an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage[3]. Neuropathic pain is defined as a lesion or disease of the somatosensory system, which is responsible for the proprioception, sensorial, motor and thermic perception[7,8]. It is now considered as a distinct clinical entity despite a large variety of etiologies. Epidemiological surveys have shown that many patients with neuropathic pain do not receive appropriate treatment for their pain. This may be due to lack of diagnostic accuracy and the use of relatively ineffective drugs, but also insufficient knowledge about drugs action mechanism and effectiviness and their appropriate use in clinical practice[4].

Typical neuropathic pain conditions such as postherpetic neuralgia, painful diabetic neuropathy, and central poststroke pain[9], can pose diagnostic problems, but the underlying cause is obvious. For certain mixed conditions like complex regional syndrome, radiculopathy, it may be even more difficult to delineate the boundaries for neuropathic and non-neuropathic pain[10].

Pure neuropathic pain has no literature in the orthopedic field, and its diagnosis within the specialty is associated with mixed pain characteristics, both nociceptive and neuropathic[10]. However, the prevalence of neuropathic pain is high in orthopedic diseases, therefore the objective of this review is to review neuropathic pain in orthopedic diseases[11].

### DN4 – QUESTIONNAIRE

**To estimate the probability of neuropathic pain, please answer yes or no for each item of the following four questions.**

**INTERVIEW OF THE PATIENT**

**QUESTION 1:**

| Does the pain have one or more of the following characteristics? | YES | NO |
|---|---|---|
| Burning | ❑ | ❑ |
| Painful cold | ❑ | ❑ |
| Electric shocks | ❑ | ❑ |

**QUESTION 2:**

| Is the pain associated with one or more of the following symptoms in the same area? | YES | NO |
|---|---|---|
| Tingling | ❑ | ❑ |
| Pins and needles | ❑ | ❑ |
| Numbness | ❑ | ❑ |
| Itching | ❑ | ❑ |

**EXAMINATION OF THE PATIENT**

**QUESTION 3:**

| Is the pain located in an area where the physical examination may reveal one or more of the following characteristics? | YES | NO |
|---|---|---|
| Hypoesthesia to touch | ❑ | ❑ |
| Hypoesthesia to pinprick | ❑ | ❑ |

**QUESTION 4:**

| In the painful area, can the pain be caused or increased by: | YES | NO |
|---|---|---|
| Brushing? | ❑ | ❑ |

**YES = 1 point**
**NO = 0 points**

**Patient's Score: /10**

**Figure 1.** DN4 Questionnaire for Neuropathic Pain Screening.
**Source:** Bouhassira et al. (2005)[68].

## Definition and physiopathology

The definition of neuropathic pain has changed since its first documentation, the newest and most accepted definition of the pathology is described as pain caused by a lesion or disease of the somatosensory system[7,8] whether peripheral or central. Unlike nociceptive pain, which results from tissue damage, This type of pain emerges from dysfunctions within the somatosensory pathways, often presenting with spontaneous pain like burning or shooting, and evoked pain such as hyperalgesia or allodynia. Following nerve damage, neuroinflammation is initiated, marked by activation of glial cells and cytokine release, which together foster a hypersensitive pain environment[12]. The underlying mechanisms include ectopic impulse generation in damaged or regenerating neurons (such as in neuromas, dorsal root ganglia, or thalamus), peripheral sensitization from ion channel changes (e.g., upregulation of Nav1.7 Nav1.8), and expression, increasing the excitability of sensory neurons. And central sensitization— an abnormal amplification of pain signals due to reduced inhibitory mechanisms and increased synaptic excitability in areas such as the dorsal horn of the spinal cord. Additional processes like glial activation, loss of inhibition, and maladaptive plasticity in the spinal cord and brain also contribute to

chronicity and symptom diversity. Persistent neuronal hyperexcitability in neuropathic pain is sustained by genetic alterations, inflammatory signals, and disrupted descending pain control mechanisms[13]. Psychological and social dimensions, including stress and belief systems, may further influence how neuropathic pain evolves and persists[14]. Understanding that neuropathic pain pathophysiology has multiple mechanisms depending on the disease associated with it leads the paths for an efficient treatment[8,15,16].

## Clinical findings

Since no specific biomarker or definitive test exists, the diagnosis of neuropathic pain relies predominantly on clinical evaluation. Key elements for diagnostic confirmation include a detailed clinical history, pain localization consistent with somatosensory pathways, and detectable sensory alterations upon physical examination. Patients often report both spontaneous sensations and pain triggered by stimuli, reflecting the complex sensory processing alterations involved. Descriptive terms used by patients include burning, stabbing, shock-like, or cold-induced discomfort, which often arise without external provocation. These may occur intermittently or continuously, and are often accompanied by abnormal sensations such as paresthesia (unpleasant but not painful) or dysesthesia (unpleasant and painful). In some cases, spontaneous pain occurs in the absence of any stimulus, while in others, daily activities like clothing contact or cold air trigger significant discomfort. Among evoked responses, allodynia—pain triggered by harmless stimuli—and hyperalgesia—an exaggerated response to painful input—are frequently observed. Additional sensory disturbances include lingering pain after stimulus cessation (aftersensations), exaggerated reactions to repetitive input (hyperpathia), and pain felt away from the original site of injury (referred sensations)[17]. Given the diagnostic complexity, a comprehensive neurological exam plays a central role in confirming neuropathic pain, particularly through identification of sensory deficits. Table 1 outlines the sensory findings typically explored during clinical assessment, based on established neurodiagnostic criteria[3,18].

## Questionnaires

Even with established diagnostic frameworks, distinguishing neuropathic pain from other chronic pain conditions often remains difficult due to overlapping clinical presentations and subjective and intermittent symptoms. Screening tools such as DN4 and painDETECT, when used alongside bedside sensory tests, serve as practical aids in recognizing neuropathic characteristics.

The Douleur Neuropathique 4 questionnaire (DN4), presented in figure 1, comprises 10 items—seven focused on reported symptoms and three derived from clinical examination. A total score of 4 or more is indicative of neuropathic pain, supported by its high sensitivity and specificity[19].

The painDETECT questionnaire, presented in figure 2, was initially developed to detect neuropathic components in patients with lumbar pain, the but with time gained broader application across various chronic pain conditions. The painDETECT is a self-applicable questionnaire. Its structure includes four domains, assessing pain intensity, spatial distribution (pattern of

**Table 1.** Signs and symptoms of neuropathic pain

| SYMPTOM | DEFINITION | PHYSICAL EXAM |
|---|---|---|
| **Mechanical hypoesthesia** | Reduced perception, numbness for non painful mechanical stimulus | Touch the skin with mechanical stimulus |
| **Thermal hypoesthesia** | Reduced sensation thermal stimulus | Touch the skin with thermal stimulus |
| **Mechanical hypoalgesia** | Reduced sensation to painful mechanical stimulus or blunt pressure | Light manual pressure |
| **Thermal hypoalgesia** | Reduced sensation to painful thermal stimulus | Touch the skin with noxious thermal stimulus |
| **Pall hypesthesia** | Reduced perception of vibration | Application of 64 Hz tuning fork over a bony prominence of the extremities, head or trunk |
| **Paresthesia** | Non painful ongoing sensation (pins or needles) - numbness | — |
| **Paroxysmal pain** | Electric shock like pain | — |
| **Ongoing pain** | Painful ongoing sensation (often described as burning) | — |
| **Allodynia** | Non painful mechanical stimulus evoke a painful sensation | Stroking skin with a cotton |
| **Mechanical hyperalgesia** | Slight painful mechanical stimulus evoke an increased painful sensation | Light manual pressure with sharpened object |

pain course, body map and radiating pain), and sensory qualities and descriptions. Scores range from 1 to 38, with values under 13 suggesting low probability and scores over 18 indicating likely neuropathic involvement[20,21]. Despite their utility, questionnaire outcomes do not always align with subjective patient experiences, highlighting the continued importance of clinical judgment in diagnosis.

## Confirmatory exams

Complementary tests such as imaging or electrodiagnostic studies assist in detecting structural or functional abnormalities within the somatosensory system. Within this classification model, neuropathic pain is categorized as "possible" (neurological lesion or disease; pain distribution neuroanatomically plausible), "probable" (pain requires supporting evidence obtained by a clinical examination of sensory signs) and "confirmed" (objective diagnostic test confirms the lesion or disease of the somatosensory nervous system)[8,16,17].

The diagnosis of neuropathic pain (NP) often requires complementary exams beyond clinical evaluation, especially when a clear anatomical cause is suspected[22]. Electrodiagnostic methods—including NCS (nerve conduction studies) and EMG (electromyography)—are valuable for characterizing the anatomical location and nature (axonal vs. demyelinating) of peripheral nerve involvement (mono, multi, or polyneuropathy), although their sensitivity is limited for small-fiber neuropathies[23,24]. Imaging is crucial when structural lesions are suspected, with each modality offering specific advantages based on the anatomical region and suspected pathology. X-rays are useful for bone pathologies, ultrasound (US) for superficial nerve entrapments and tumors, CT for bony and oncologic lesions, and MRI for evaluating both central and peripheral nervous system conditions. Each method offers specific advantages depending on cost, availability, and the suspected condition[25]. Infrared thermography, a non-invasive tool, detects subtle skin temperature variations linked to neuropathic pain. Although it presents high sensitivity—particularly for conditions like CRPS and diabetic neuropathy—its specificity is lower, making it more useful as an adjunct rather than a standalone diagnostic tool[26]. The table below summarizes the main imaging techniques applied in the diagnostic investigation of neuropathic pain, outlining their respective strengths, limitations, and clinical indications (Table 2).

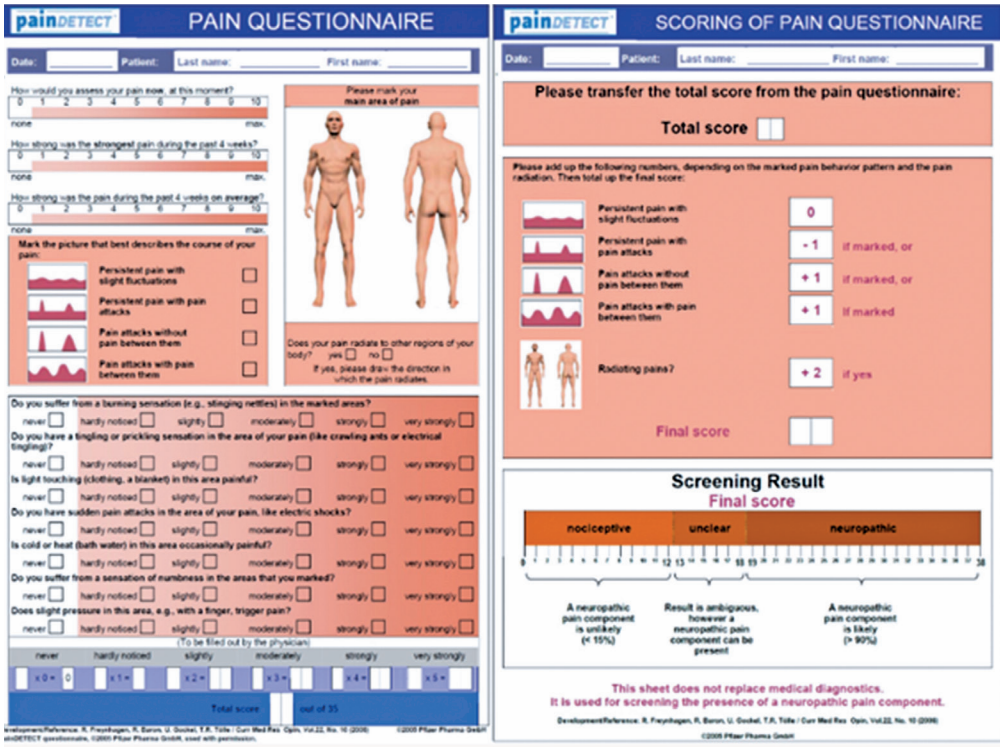


**Figure 2.** painDETECT Questionnaire for Identifying Neuropathic Pain.
**Source:** Adapted from Freynhagen et al. (2006)

## Neuropathic pain in orthopedic diseases

Although orthopedic conditions rarely manifest as purely neuropathic syndromes, neuropathic pain components are frequently observed across a wide range of musculoskeletal disorders. A common orthopedic condition of neuropathic pain is radiculopathy[27]. Radicular pain often arises from inflammation or mechanical compression of spinal nerve roots, typically in the context of disc herniation or degenerative spinal pathology. The clinical presentation typically includes pain along the affected dermatome, frequently associated with sensory disturbances or motor impairment. Most common painful radiculopathy are cervical radiculopathy, lumbar radiculopathy and lumbar spinal stenosis. In contrast to other neuropathic syndromes, evoked pain such as tactile or thermal allodynia tends to be less pronounced in radiculopathy. Experimental evidence supports that inflammation and mechanical stress on the dorsal root ganglion (DRG) may trigger ectopic discharges, contributing to the genesis of radicular pain. Recent human studies using DRG recordings have demonstrated spontaneous activity correlated with pain severity, reinforcing the DRG's role as a critical generator of radicular neuropathic pain[17]. Cervical radiculopathy typically manifests as sharp, electric-like pain radiating from the neck to the upper limb, driven by nerve root compression or irritation[28]. It is generally considered a mixed condition of nociceptive and neuropathic pain (NP).

Globally, low back pain remains a primary driver of disability. A substantial proportion of affected individuals also report leg pain, which exacerbates functional limitations and reduces quality of life. LBLP is clinically diagnosed as either sciatica or referred leg pain. Sciatica refers to radiating leg pain often extending below the knee, potentially accompanied by paresthesia, motor deficits, or altered reflexes in a dermatomal distribution. The pathophysiological mechanisms underlying sciatica are thought to be neuropathic whereas those with underlying referred leg pain are thought to be nociceptive[29].

Lumbar spinal stenosis, characterized by narrowing of the spinal canal with encroachment on neural structures surrounding bone and soft tissue, frequently involves a neuropathic component—present in approximately one-third of patients—due to simultaneous mechanical or ischemic compromise of neural structures[30,31].

These orthopedic scenarios underscore the multifactorial nature of pain in musculoskeletal conditions, where neuropathic mechanisms may overlap with nociceptive drivers.

Another frequent orthopedic condition is neuropathic pain after peripheral nerve injury. It is heterogeneous condition that can arise after trauma, surgery, or compression of nerves. Despite similar degrees of injury, not all patients develop pain, suggesting that individual genetic, psychological, and neurophysiological factors modulate susceptibility. The primary mechanism involves ectopic discharges from damaged nerves, neuromas, or the dorsal root ganglia (DRG), generating ongoing and evoked pain. Upregulation of voltage-gated sodium channels (e.g., Nav1.3, Nav1.7, Nav1.8) and pro-inflammatory signaling pathways (e.g., p38 MAPK) contribute to neuronal hyperexcitability. Central sensitization and cortical reorganization are also implicated, especially in cases with referred pain, widespread allodynia, or phantom limb pain after amputation[17]. Amputees patients have a high prevalence of postoperative neuropathic pain, approximately 70% experience some type of pain, which can be intense in up to 15% of cases, and acute or chronic, depending on the duration. Post-amputation pain can present itself in two forms, which often coexist in the same patient: pain in the residual limb or stump (PL) and phantom limb pain (PLP), a painful sensation referring to the limb or part of it that was surgically removed. Studies have reported that lower limb amputees patients suffering from PLP enrolled in imagery therapy programs present with significant pain reduction. However additional studies are suggested to strengthen the evidence[32].

Trauma to the brachial plexus, frequently resulting from motorcycle accidents, is a severe cause of upper limb disability. Its impact extends beyond motor

**Table 2.** Imaging Modalities in Neuropathic Pain

| Method | Advantages | Limitations | Main Indications |
|---|---|---|---|
| **X-ray** | Accessible, low cost | Poor soft tissue contrast | Trauma, osteoarthritis |
| **US (Ultrasound)** | Dynamic, no radiation | Operator-dependent | Entrapments, tumors |
| **CT** | 3D imaging, good for bones | Radiation, soft tissue limits | Tumors, trauma |
| **MRI** | High resolution, CNS & PNS | Expensive, slow | Neuropathies, tumors |
| **TI (Thermography)** | Non-invasive, detects temp change | Not specific | CRPS, diabetic & small fiber NP |

function, often contributing to persistent neuropathic pain. The current treatments target on restoring the upper extremity function to the pre-injury status as much as possible. Current treatment strategies include microsurgical techniques such as nerve grafting, neurotization, and muscle transfers, aiming to restore both motor control and protective sensation. Satisfactory outcomes of shoulder abduction, elbow flexion and hand function have been reported. However, this severe disabling injury does not affect only on the physical functions but also psychological aspects from chronic pain[33].

Carpal Tunnel Syndrome (CTS) is an entrapment neuropathy. The estimated prevalence is 5%- 16% in the general population. It occurs due to the compression of the median nerve beneath the transverse carpal ligament, and the increased pressure within the tunnel results in mechanical compression and/or local ischemia in the nerve.In carpal tunnel syndrome (CTS), patients typically experience hand pain, paresthesias, and reduced grip strength, often leading to functional impairment in daily tasks. While CTS is often linked to musculoskeletal overload, neuropathic components may emerge due to median nerve compression and associated ischemia[34,35].

Post-traumatic neuropathic pain is a major factor affecting the quality of life after finger trauma and is reported with considerable variance in the literature. Post-traumatic neuropathic pain patients suffer from spontaneous pain in the absence of noxious stimuli.

Several other orthopedic conditions may not present with straight forward neural lesions however may develop neuropathic pain as frequently described in literature. Rotator cuff tear is one of the major causes of pain and dysfunction of the shoulder in the middle-aged population. According to a recent epidemiological study, the prevalence of rotator cuff tears was found to be 20.7% in the general population, with a mean age of 58 years (range, 22–87 years), and increased with age. Although rotator cuff injuries are typically nociceptive in nature, some patients report persistent pain unresponsive to standard anti-inflammatory therapy, suggesting a possible neuropathic component[36,37].

Shoulder arthroplasty's objective is to improve pain and disability of patients with advanced glenohumeral osteoarthritis. However postoperative pain following shoulder arthroplasty may persist in a subset of patients and can include both nociceptive and neuropathic elements, complicating recovery.

The management of pain in patients with foot and ankle pathology can be challenging. Cumulative data suggest that, in addition to nociceptive mechanisms, other neuropathic mechanisms can contribute to pain in a subset of people with orthopedic conditions. Preoperative diagnosis of neuropathic pain (NP) can potentially change decision making and management of foot and ankle pathologies[38,39] (Table 3).

Pain is a major symptom of patients with osteoarthritis (OA) and has a variety of characteristics suggesting differing underlying mechanisms. Although OA is traditionally considered to be nociceptive, some patients describe aspects of their pain as burning or shooting. Such characteristics suggest mechanisms that are shared with neuropathic pain Despite the success of arthroplasty, a significant portion of patients experience chronic postsurgical pain (CPSP). CPSP seems to be the main cause of postoperative dissatisfaction.In fact, neuropathic pain has repeatedly been proposed as a major cause of persistent pain after TKA[40,41].

These findings reinforce the need for orthopedic surgeons to recognize neuropathic features even in traditionally nociceptive conditions, particularly in postoperative and degenerative joint scenarios.

## Treatment

These orthopedic scenarios underscore the multifactorial nature of pain in musculoskeletal conditions, where neuropathic mechanisms may overlap with nociceptive drivers.

**Table 3.** Prevalence of neuropathic pain in orthopedic conditions

| Orthopedic Condition | Neuropathic Pain Prevalence |
|---|---|
| Rotator Cuff Tear | 15,8% |
| Shoulder osteoarthritis | 13% |
| Shoulder Post Arthroplasty | 22% |
| Brachial Plexus Injury | 82,7% |
| Carpal Tunnel Syndrome | 36-76,7% |
| Peritrochanteric Syndrome | 31% |
| Hip Osteoarthritis | 18,5%-24,5% |
| Hip Post Arthroplasty | 5,5%-24% |
| Knee Osteoarthritis | 36,5%-45,9% |
| Knee Post Arthroplasty | 11% |
| Ankle Osteoarthritis | 44,9% |
| Achilles Tendinopathy | 29% |
| Morton Neuroma | 63% |
| Neck Pain | 50% |
| Low Back Pain | 16-55% |
| Lumbar Spinal Stenosis | 36% |
| Finger Amputation | 18% |

Although orthopedic pathologies often involve mixed pain components, addressing the underlying musculoskeletal disorder remains a fundamental step in treatment. However, neuropathic pain may persist even after structural correction or functional recovery, requiring targeted interventions beyond orthopedic management alone[42,43]. Evidence increasingly supports a multidisciplinary strategy—integrating pharmacologic agents, rehabilitation protocols, and interventional techniques—for managing refractory neuropathic pain. Below we review literature recommended treatment for neuropathic pain.

## Non pharmacological treatment

Non-pharmacological intervention, led by rehabilitation, plays a relevant role and should be implemented from the early phase of neuropathic pain management, acting in synergy with other interventions in order to achieve the best outcome. Although systematic reviews show the lack of evidence on various rehabilitative practices to treat this challenging condition[42].

Exercise can be considered as a feasible, and effective alternative treatment or complementary therapy for most patients with NP caused by different diseases. A few examples are neuromuscular rehabilitation, therapeutic exercise instruction, aquatic therapy. More high-quality randomized controlled trials are required to provide more superior evidence in the future[44].

Chronic pain patients can benefit from patient education measures, either when used alone or as part of an integrated cognitive-behavioral program, and for NP patients is no different, education around these issues can further help minimize the negative effects of stress, disabling beliefs, and upsetting emotions, Patient education and behavioral counseling can empower individuals to adopt strategies that mitigate the impact of chronic neuropathic pain, facilitating recovery of function and well-being[10]. However, psychotherapies (CBT and mindfulness) received weak recommendations as adjunctive treatments, with moderate-quality evidence supporting improvements in pain and quality of life[45].

Acupuncture and other alternative techniques, including mirror therapy and hypnosis, lack robust evidence in neuropathic pain management, though isolated studies suggest potential benefit in select cases[46]. Auricular acupuncture, aromatherapy, laser, and massage showed inconclusive evidence, while vitamin E had a weak recommendation against its use.

TENS, often integrated into physiotherapy protocols, demonstrated modest analgesic effects and remains a viable option for localized peripheral neuropathic pain, albeit with limited strength of recommendation. While repetitive transcranial magnetic stimulation (rTMS) over the motor cortex was also weakly recommended. Other forms of rTMS (prefrontal cortex or insula), transcranial direct current stimulation (tDCS), and cranial electrotherapy stimulation (CES) had inconclusive or weak-against recommendations[45]. The table below summarizes the evidence and strength of recommendation for various non-pharmacological modalities used in neuropathic pain (Table 4).

## Pharmacological treatment

Although neuropathic pain may result from a wide range of conditions, current guidelines recommend a standardized pharmacological strategy based on shared mechanisms of pathophysiology. Its management remains challenging due to diagnostic limitations, variability in clinical presentation, and the modest efficacy of available drugs. Therapeutic choices must consider the underlying etiology and be tailored

**Table 4.** Non pharmaceutical and non invasive treatments for neuropathic pain

| Therapy | Effectiveness | Evidence | Recommendation |
|---|---|---|---|
| **Cognitive Behavioral Therapy (CBT)** | Improved pain and QoL as adjunctive therapy | Moderate | Weak in favor (as adjunct) |
| **Mindfulness-based therapy** | Effective in diabetic NP; improves QoL and catastrophizing | Moderate | Weak in favor (as adjunct) |
| **Vitamin E** | No significant benefit in high-quality trials | Moderate | Weak against |
| **Aromatherapy, laser, auricular acupuncture** | Positive results in isolated trials only | Low to Moderate | Inconclusive |
| **Mirror therapy, hypnosis, physiotherapy, acupuncture** | No eligible trials found | | No conclusion (lack of robust data) |
| **TENS** | Modest analgesic effect, well tolerated | Moderate | Weak in favor (for peripheral NP) |
| **rTMS (motor cortex)** | Prolonged analgesia in most studies | Moderate | Weak in favor |
| **rTMS (PFC, insula), tDCS, CES** | No consistent benefit | Low | Inconclusive or Weak against |

accordingly, even though many commonly used medications are off-label for this indication. Moreover, the effectiveness of these drugs is often partial, and their use may be limited by side effects or risk of misuse[43].

Treatment algorithms typically begin with first-line agents such as tricyclic antidepressants (e.g., amitriptyline), gabapentinoids (gabapentin, pregabalin), and serotonin-norepinephrine reuptake inhibitors (duloxetine, venlafaxine). For localized neuropathic pain, topical formulations like lidocaine patches or capsaicin cream are recommended. Second- and third-line therapies include cannabinoids, botulinum toxin injections, and, in selected cases, weak or strong opioids[47]. Recent guidelines emphasize the importance of distinguishing between focal and generalized neuropathic pain syndromes, as therapeutic decisions may differ accordingly. This distinction is a cornerstone in the French algorithm for neuropathic pain management[45], which proposes tailored approaches depending on the distribution and nature of symptoms, as presented in figure 3.

## Antidepressants

Tricyclic antidepressants (TCAs), particularly amitriptyline, and serotonin-norepinephrine reuptake inhibitors (SNRIs), such as duloxetine and venlafaxine, are consistently cited in clinical guidelines as first-line options for the treatment of neuropathic pain. Their analgesic effect is thought to involve modulation of descending inhibitory pathways, primarily through increased availability of serotonin and noradrenaline at the spinal level. Beyond monoaminergic modulation, TCAs also exhibit interactions with sodium channels, NMDA receptors[48], and opioid receptors, which may enhance their efficacy in certain clinical scenarios. These agents can provide meaningful pain relief even in patients without comorbid depression, supporting their role as analgesics rather than purely psychotropics. Notably, the therapeutic response often requires two to four weeks to emerge, a timeframe longer than that observed with traditional analgesics, which suggests involvement of neuroadaptive processes rather than immediate receptor activation[49]. The evidence base supporting their use includes multiple randomized controlled trials and meta-analyses, particularly in diabetic neuropathy, postherpetic neuralgia, and radiculopathy. Their benefit must be balanced with tolerability, especially regarding anticholinergic side effects, which may limit their use in older or frail populations[48].

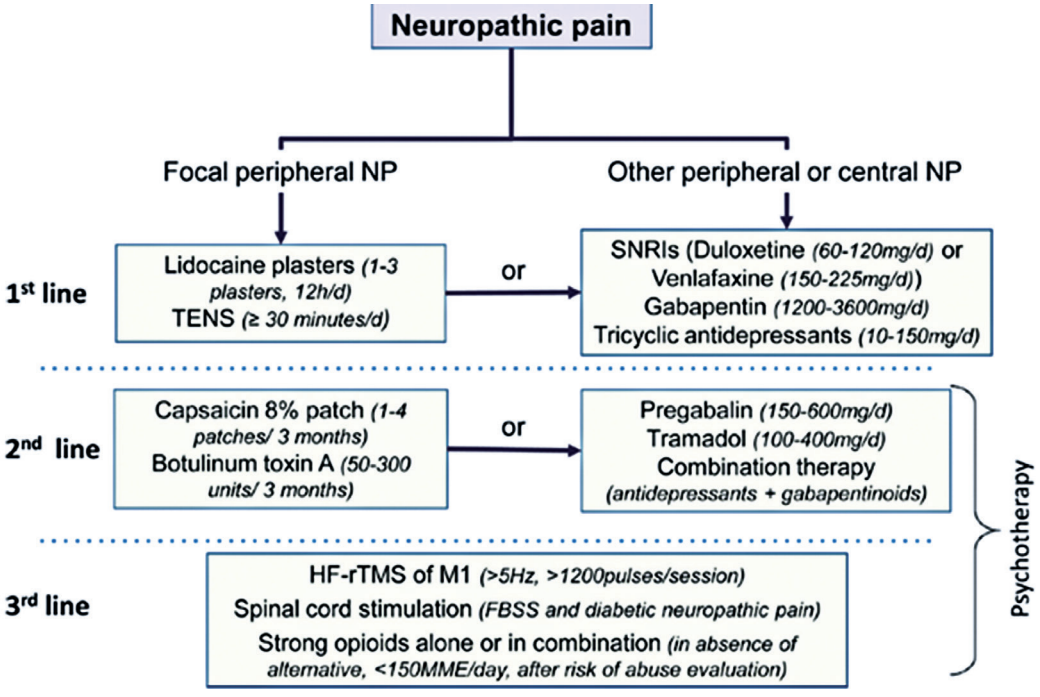


**Figure 3.** French algorithm for neuropathic pain management.
**Source:** Adapted Moisset et al. (2020).

## Gabapentinoids

Gabapentinoids, initially developed as anticonvulsants, have demonstrated consistent efficacy in managing neuropathic pain, particularly in cases characterized by burning sensations and sensory hypersensitivity. Their mechanism involves modulation of voltage-gated calcium channels, resulting in decreased excitatory neurotransmitter release and attenuation of central sensitization. Gabapentin was the first agent of this class, originally approved for partial seizures and subsequently for diabetic neuropathy and postherpetic neuralgia. Its pharmacokinetics are nonlinear, with variable absorption that necessitates gradual dose escalation and divided dosing, sometimes reaching up to 3600 mg/day. Despite a slower onset of action, gabapentin is generally well tolerated, particularly in older adults. Pregabalin, a second-generation molecule, offers improved pharmacokinetic predictability, higher bioavailability, and faster onset. It typically requires lower doses with twice-daily administration. While it is often better tolerated overall, side effects such as dizziness, somnolence, peripheral edema, and blurred vision are dose-dependent and more frequently observed. Confusion and ataxia are also reported, especially in elderly individuals. Rare cases of misuse and dependence have been noted for both drugs, but these are typically reversible upon dose reduction or discontinuation[48,50].

## Topical use medications

For localized neuropathic pain (LNP), topical agents provide a targeted and safer alternative, particularly in patients who are unable to tolerate systemic therapies. Among these, 5% lidocaine patches are recommended as a first-line treatment, while 8% capsaicin patches are often used as a second-line option.

Lidocaine exerts its effect primarily through sodium channel blockade on damaged or sensitized peripheral nerve fibers, without significantly affecting normal sensation. It may also modulate TRPV1-positive fibers and exerts additional local anti-inflammatory and anesthetic effects[51].

Capsaicin, derived from chili peppers, activates TRPV1 receptors located on nociceptors, leading to an initial depolarization followed by reversible defunctionalization of the nerve terminals. Although the initial application may provoke burning pain, erythema, and discomfort, these symptoms usually resolve within a few hours. The 8% capsaicin patch has shown effectiveness in chronic peripheral neuropathic pain and may outperform systemic agents in selected patients. Its prolonged analgesic effect—lasting weeks to months—makes it a useful option, though application must be performed in a clinical setting due to its intense local irritant effect. Premedication with topical anesthetics and close monitoring are often required[48,52].

## Botulinum toxin (BTX)

Botulinum toxin (BTX), traditionally used for the treatment of spasticity and dystonia, has gained attention in recent years as a potential agent for neuropathic pain management. Its mechanism involves the inhibition of neurotransmitter release, including substance P and glutamate, from peripheral sensory neurons. Clinical studies have demonstrated its efficacy in conditions such as postherpetic neuralgia, trigeminal neuralgia, and peripheral nerve injury[53]. Although its analgesic effect may persist for several months, its use remains off-label in most countries and is generally considered when first-line treatments have failed[40].

## Opioids

Opioids used in neuropathic pain (NP) differ from traditional agents by exerting multimodal actions beyond mu-opioid receptor activation. Drugs like tramadol and tapentadol, for instance, combine weak opioid effects with inhibition of monoamine reuptake, which may contribute to enhanced analgesia in NP. Methadone adds NMDA antagonism to its opioid profile, which is particularly useful in refractory cases. Despite these properties, opioids are generally reserved for second- or third-line use due to concerns about dependence, tolerance, and side effects[45].

Current evidence suggests that opioids can provide modest relief in neuropathic pain, but with considerable risk. A Cochrane review by Häuser et al.[54] (2022) showed that while opioids may reduce pain intensity in some patients, the effect size is small and often not sustained long term. Therefore, their role should be limited to selected patients with severe, refractory NP and under close clinical monitoring[48,54].

## Cannabinoids

Cannabinoid-based therapies have gained growing interest in chronic pain management, particularly for neuropathic pain of central origin. Their mechanism involves activation of CB1 and CB2 receptors, modulating nociceptive pathways and neuroinflammation[55]. Evidence supporting their use in NP remains limited and inconsistent.

A systematic review by Mücke et al.[56] (Cannabinoids for chronic neuropathic pain, Cochrane 2018) concluded that cannabinoids may offer slight pain relief compared to placebo, but the number needed to treat is high, and side effects such as dizziness and sedation are common. As such, cannabinoids are considered a third-line option in NP management, recommended only after standard treatments fail[48,56].

## Other medications

Several adjuvant agents have been investigated in neuropathic pain with varying degrees of success. These include B-complex vitamins, alpha-lipoic acid (thioctic acid), palmitoylethanolamide (PEA), and nucleotide-based compounds, which may exert neuroprotective or anti-inflammatory effects. Other anticonvulsants such as oxcarbazepine, lamotrigine, and lacosamide have demonstrated limited efficacy in randomized controlled trials[45]. Intravenous lidocaine and ketamine demonstrated short-term benefit (1 to 3 weeks) but no sustained relief. These are suggested only for acute exacerbations of neuropathic pain, with weak recommendations based on low to moderate-quality evidence[45]. Clonidine, a central alpha-2 agonist, has been used in selected cases, particularly for sympathetically maintained pain. These agents are generally considered adjuncts and are rarely effective as monotherapies[48]. Table 5 presents recommendations for neuropathic pain medication.

## Invasive treatment

In cases where neuropathic pain (NP) remains refractory to pharmacological strategies, interventional approaches may be considered, particularly in orthopedic contexts such as lumbar disc herniation, complex regional pain syndrome (CRPS), nerve entrapment syndromes (e.g., carpal and cubital tunnel), and post-traumatic neuropathies. The primary aim of these techniques is not only symptom control, but also the restoration of function and quality of life through targeted neural modulation[57]. Interventional pain management is growing rapidaly, offering several techniques to relieve neuropathic pain as summarized in Table 6.

## Nerve blocks

Peripheral nerve blocks, often performed under ultrasound guidance, offer both diagnostic and therapeutic benefits. These procedures involve the administration of local anesthetics—sometimes combined with corticosteroids—near specific nerves or fascial planes. Their use is well-established in conditions like postherpetic neuralgia, radiculopathy, and failed back surgery syndrome. Ultrasound guidance enhances safety and precision by providing real-time anatomical visualization, enabling techniques such as hydrodissection, selective nerve blockades, and perineural drug delivery[58].

A particularly promising technique is the erector spinae plane (ESP) block, which involves the deposition of anesthetic deep to the erector spinae muscle, targeting the dorsal and ventral rami of thoracic spinal nerves. It produces a multi-dermatomal analgesic effect and has been successful in managing refractory thoracic neuropathic pain. Unlike more anterior plane blocks (e.g., pectoral or serratus blocks), the ESP block provides both posterior and anterior coverage, and its consistent sonoanatomy supports catheter-based applications for continuous analgesia[59].

Other ultrasound-guided procedures, such as sympathetic blocks (e.g., stellate ganglion block) and targeted interventions for occipital neuralgia, genicular neuropathic pain, and postsurgical syndromes, continue to expand the interventional toolbox in NP management. The evidence base for these modalities is growing, and they are increasingly integrated into multimodal treatment plans for patients unresponsive to conventional therapies[58].

## Intrathecal therapies

Intrathecal therapies have been explored in the management of refractory neuropathic pain, particularly in cancer-related and spinal conditions. However, clinical evidence remains limited. The use of intrathecal methylprednisolone, for example, has yielded inconclusive results due to methodological concerns and lack of reproducibility in clinical trials. Similarly, other agents such as morphine, clonidine, and ziconotide have not been rigorously studied in high-quality trials specifically targeting neuropathic pain, precluding strong recommendations for their routine use. As such, these interventions are typically reserved for highly selected cases within multidisciplinary pain programs[61].

## Radiofrequency

Pulsed radiofrequency (PRF) delivers low-temperature electrical fields to targeted nerves, modulating their function without causing thermal neurolysis. This technique has shown some benefit,

**Table 5.** Medication used for neuropathic pain, dosage, side effects and recommendations.[45]

| Medication | Dosage (Typical Range) | Side Effects | Recommendations | Line of Treatment |
|---|---|---|---|---|
| **Duloxetine** | 60-120 mg/day | Nausea, dry mouth, somnolence, loss of appetite | Strong | First-line |
| **Venlafaxine** | 150-225 mg/day | Hypertension, nausea, insomnia | Strong | First-line |
| **Gabapentin** | 1200-3600 mg/day | Dizziness, drowsiness, peripheral edema | Strong | First-line |
| **TCA** | 25-150 mg/day | Anticholinergic effects, hypotension, cardiac toxicity | Strong | First-line |
| **Lidocaine Plasters** | 1-3 plasters/ 12hs/day | Local skin irritation | Weak | First-line (peripheral NP) |
| **Pregabalin** | 150-600 mg/day | Dizziness, drowsiness, weight gain | Weak (due to misuse risk and low efficacy) | Second-line |
| **Capsaicine patches** | 1-4 patches every 3 months | Burning sensation at application site | Weak | Second-line (peripheral NP) |
| **Botulinum Toxin** | 50-300UI every 3 months | Injection site pain, muscle weakness | Weak | Second-line |
| **Combination Therapy** | Varies drugs | Additive side effects depending on combination | Weak | Second-line/ Third Line |
| **Tramadol** | 100-400 mg/day | Nausea, dizziness, potential for abuse | Weak (short term use only) | Second-line |
| **Strong Opioids (morfine)** | <120 mg/day | Constipation, sedation, risk of dependence | Weak (last resort, high risk) | Third-line |
| **Strong Opioids (oxycodone)** | <120 mg/day | Constipation, sedation, risk of dependence | Weak (last resort, high risk) | Third-line |
| **Strong Opioids (Tapentadol)** | 500-600 mg/day | Nausea/vomiting, constipation, lethargy, seizures, ataxia | Weak (last resort, high risk) | Second-line |
| **Capsaicin cream** | 0.025-0.075 cream | Skin irritation | Inconclusive | Not Recommended |
| **Clonidine (topical)** | varies | Hypotension (topical) | Inconclusive | Not Recommended |
| **Oxcarbazepine** | varies | Dizziness, nausea, hyponatremia | Inconclusive | Unclear |
| **Lacosamide** | Varies | Dizziness, fatigue, nausea | Inconclusive | Unclear |
| **IV Ketamine** | 0.25-1 mg/kg/day | Hallucinations, liver/ kidney toxicity | Inconclusive | Not Routine |
| **IV Lidocaine** | 3-7.5 mg/kg/day | Cardiac arrhythmias, hypotension | Inconclusive | Not Routine |
| **Cannabinoids** | Varies (e.g sativa) | Drowsiness, dizziness, cognitive effects | Inconclusive | Not Routine |

**Table 6.** Invasive treatments for neuropathic pain

| Therapy | Effectiveness | Quality of Evidence | Recommendation |
|---|---|---|---|
| **Nerve blocks** | Conflicting results (positive and negative trials) | Moderate | Inconclusive |
| **Intrathecal methylprednisolone** | Non-reproducible and criticized results | Low to Moderate | Inconclusive |
| **Intrathecal morphine, clonidine, etc.** | No neuropathic pain-specific high-quality trials | — | Inconclusive |
| **Pulsed radiofrequency** | Effective only for thoracic PHN | Moderate | Weak in favor (for thoracic PHN only) |
| **Spinal cord stimulation (SCS)** | Large effect sizes, open-label studies | Moderate | Weak in favor (for FBSS and diabetic NP) |
| **DRG stimulation / EMCS** | Sparse or inconsistent data | Low | Inconclusive |

particularly in thoracic postherpetic neuralgia (PHN), where moderate-quality studies support a weak recommendation. While the mechanism is not fully understood, PRF may influence pain pathways by altering gene expression and inflammatory signaling in sensory neurons. Evidence remains limited to specific indications, and its use should be individualized[45].

Conventional radiofrequency ablation (RFA) employs thermal lesions to interrupt pain transmission pathways and has become an established option for localized, refractory neuropathic pain. It is commonly applied to genicular nerves for chronic knee pain, dorsal root ganglia in radiculopathy, and medial branches for facet-related spinal pain. Compared to nerve blocks, RFA offers longer-lasting relief, often reducing the need for opioids and improving physical function. Repeated treatments may be necessary, but overall, the technique is well tolerated and increasingly used in outpatient settings[61].

## Invasive neurostimulation (Neuromodulation)

Invasive neuromodulation techniques such as spinal cord stimulation (SCS) and dorsal root ganglion (DRG) stimulation have become important options in the treatment of refractory neuropathic pain. These modalities are particularly indicated in conditions like failed back surgery syndrome (FBSS), complex regional pain syndrome (CRPS), and painful diabetic neuropathy. In these cases, conventional pharmacological approaches often fail to provide adequate relief, and patients may experience improved outcomes through targeted neuromodulation[45,61-63].

SCS works by delivering electrical impulses to the dorsal columns of the spinal cord via epidural electrodes, which modulate the transmission of pain signals through both segmental and supraspinal mechanisms. This includes activation of inhibitory interneurons, suppression of wide dynamic range neurons, and facilitation of descending inhibitory pathways. DRG stimulation offers a more focal approach by targeting specific sensory ganglia, allowing for precise modulation of dermatomal pain, especially in focal syndromes such as groin or foot pain.

Evidence for SCS has strengthened significantly in recent years. A 2021 systematic review and meta-analysis by Duarte et al.[64] (JAMA Neurology) concluded that SCS provides moderate-quality evidence for pain reduction in FBSS and diabetic neuropathy. Therefore Neuromodulation Appropriateness Consensus Committee (NACC) and other international guidelines assign a moderate to strong recommendation for SCS in carefully selected patients with FBSS and CRPS (Level of Evidence: B)[64-67].

## Conclusion

Neuropathic pain represents a severe clinical entity with profound negative effects on patients' quality of life, frequently resulting in suffering, disability, and significant social and economic burden. Within orthopedic conditions, neuropathic pain is highly prevalent and often coexists with mechanical and inflammatory nociceptive components. When unrecognized, its presence leads to inadequate treatment strategies and poor therapeutic outcomes. Therefore, it is essential that orthopedic specialists—and other professionals involved in musculoskeletal care—develop the ability to identify neuropathic pain and remain up to date with evidence-based guidelines to ensure optimal, individualized management, whether through pharmacological, interventional, or multidisciplinary approaches.

**Authors' Contribution:** TKY: conceived and planned the activities that led to the study, wrote the paper, participated in the reviewing process, approved the final version;RSC, and VHDB, and BCG: participated in the reviewing process, , approved the final version.

## References

1. van Hecke O, Austin SK, Khan RA, Smith BH, Torrance N, Rice ASC, et al. Neuropathic pain in the general population: a systematic review of epidemiological studies. Pain. 2014;155(4):654-62.
2. Bril V, England J, Franklin GM, Backonja M, Cohen J, Del Toro D, et al. Evidence-based guideline: treatment of painful diabetic neuropathy. Neurology. 2011;76(20):1758-65.
3. Kerstman E, Ahn S, Battu S, Tariq S, Grabois M. Neuropathic pain. Handb Clin Neurol. 2013;110:175-87.
4. Finnerup NB, Attal N, Haroutounian S, McNicol E, Baron R, Dworkin RH, et al. Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis. Lancet Neurol. 2015;14(2):162-73.
5. Bates D, Schultheis BC, Hanes MC, Jolly SM, Chakravarthy KV,

Deer TR, et al. A comprehensive algorithm for management of neuropathic pain. Pain Med. 2019;20(Suppl 1):S2-12. doi:10.1093/pm/pnz075. Erratum in: Pain Med. 2023; 24(2):219. doi:10.1093/pm/pnac194.

6. Cavalli E, Mammana S, Nicoletti F, Bramanti P, Mazzon E. The neuropathic pain: an overview of the current treatment and future therapeutic approaches. Int J Immunopathol Pharmacol. 2019;33:2058738419838383.
7. International Association for the Study of Pain (IASP). IASP taxonomy. 2019 [cited 2025 Apr 23]. Available from: https://www.iasp-pain.org/terminology?navItemNumber=576.
8. Colloca L, Ludman T, Bouhassira D, Baron R, Dickenson AH, Yarnitsky D, et al. Neuropathic pain. Lancet Neurol. 2017;16(4):232-44.
9. Scholz J, Finnerup NB, Attal N, Aziz Q, Baron R, Bennett MI, et al. Classification Committee of the Neuropathic Pain Special Interest Group (NeuPSIG). The IASP classification of chronic pain for ICD-11: chronic neuropathic pain. Pain. 2019;160(1):53-9.
10. González-Rodríguez P, García-Sancho J, González-Rodríguez P. Physiology of the human skin. Physiol Rev. 2019;99(4):1455-96.
11. Baron R. Mechanics of disease: neuropathic pain - a clinical perspective. Nat Clin Pract Neurol. 2006;2(2):95-106.
12. Costigan M, Scholz J, Woolf CJ. Neuropathic pain: a maladaptive response of the nervous system to damage. Annu Rev Neurosci. 2009;32:1-32.
13. Woolf CJ. Central sensitization: implications for the diagnosis and treatment of pain. Pain. 2011;152(3 Suppl):S2-15.
14. Jensen TS, Finnerup NB. Allodynia and hyperalgesia in neuropathic pain: clinical manifestations and mechanisms. Lancet Neurol. 2011;10(10):924-35.
15. Zilliox LA. Neuropathic pain. Curr Opin Neurol. 2017; 30(2):149-55.
16. Baron R, Binder A, Wasner G. Neuropathic pain: diagnosis, pathophysiological mechanisms, and treatment. Lancet Neurol. 2010;9(8):807-19.
17. Finnerup NB, Kuner R, Jensen TS. Neuropathic pain: from mechanisms to treatment. Physiol Rev. 2021;101(1):259-301.
18. Gierthmühlen J, Baron R. Neuropathic pain. Semin Neurol. 2016;36(5):462-8.
19. Mathieson S, Maher CG, Terwee CB, De Campos TF, Lin CW. Neuropathic pain screening questionnaires have limited measurement properties. A systematic review. Journal of clinical epidemiology. 2015;68(8):957-66.
20. Rio JPMD, Bittencourt JV, Corrêa LA, Freynhagen R, Reis FJJD, Melo TB, et al. Cross-cultural adaptation of the painDETECT questionnaire into Brazilian Portuguese. Braz J Anesthesiol. 2022;72(1):44-8.
21. Freynhagen R, Baron R, Gockel U, Tölle TR. painDETECT: a new screening questionnaire to identify neuropathic components in patients with back pain. Curr Med Res Opin. 2006;22(10):1911-20
22. Porto FH de G, Porto GCLM, Brotto MWL. Additional tests to investigate neuropathic pain. The value of electroneuromyography for neuropathic pain. Rev dor [Internet]. 2016;17:23-6.
23. Rodrigues CL. O papel da eletroneuromiografia no diagnóstico da dor neuropática. In: Palladini MC, Castro APCR,
24. Pelloso LRCA, Fonseca PRB, organizadores. Tratado de dor neuropática - Sociedade Brasileira para Estudo da Dor (SBED). Rio de Janeiro: Atheneu; 2021. p.49-60
25. SBOT. Guia de dor neuropática. São Paulo: Editora Alef. 2023. pp. 1-53.
26. Liggieri AC, Kobayashi R, Rodrigues TM. Dor neuropática no paciente ortopédico. In: Palladini MC, Castro APCR, Pelloso LRCA, Fonseca PRB, organizadores. Tratado de dor neuropática - Sociedade Brasileira para Estudo da Dor (SBED). Rio de Janeiro: Atheneu; 2021. p. 204.
27. Scholz J, Finnerup NB, Attal N, Aziz Q, Baron R, Bennett MI, et al. Classification Committee of the Neuropathic Pain Special Interest Group (NeuPSIG). The IASP classification of chronic pain for ICD-11: chronic neuropathic pain. Pain. 2019;160(1):53-9.
28. Kwon J, Oh D, Lee B, Lee H, Ko M, Moon S, et al. Neuropathic pain component in patients with cervical radicular pain: a single-center retrospective study. Medicina (Kaunas). 2022;58(9):1191.
29. Harrisson SA, Burch J, Moore RA, Smith BH, Williams AC, Torrance N, et al. Prognosis of patients with neuropathic low back-related leg pain: an exploratory study using prospective data from UK primary care. J Pain. 2024;25(2):533-44.
30. Park SY, An HS, Moon SH, Lee HM, Suh SW, Chen D, et al. Neuropathic pain components in patients with lumbar spinal stenosis. Yonsei Med J. 2015;56(4):1044-50.
31. Attal N, Perrot S, Fermanian J, Bouhassira D. The neuropathic components of chronic low back pain: a prospective multicenter study using the DN4 Questionnaire. J Pain. 2011;12(10):1080-7.
32. Xavier NFR, Almeida JCF, Rocha PRS, Funez MI. Prevention and control of chronic post-amputation pain of extremities: systematic review. Brjp 2020; 3(4):359-65.
33. Sonohata M, Tsuruta T, Mine H, Morimoto T, Mawatari M. The relationship between neuropathic pain, and the function of the upper limbs based on clinical severity according to electrophysiological studies in patients with carpal tunnel syndrome. Open Orthop J. 2013;7:99-102.
34. Ceceli E, Gumruk S, Okumus M, Kocaoglu S, Goksu H, Karagoz A. Comparison of 2 methods of neuropathic pain assessment in carpal tunnel syndrome and hand functions. Neurosciences (Riyadh). 2018;23(1):23-8.
35. Tantigate D, Wongtrakul S, Vathana T, Limthongthang R, Songcharoen P. Neuropathic pain in brachial plexus injury. Hand Surg. 2015;20(1):39-45.
36. Karasugi T, Ide J, Kitamura T, Okamoto N, Tokunaga T, Mizuta H. Neuropathic pain in patients with rotator cuff tears. BMC Musculoskelet Disord. 2016;17(1):451.
37. Souza VS, Ribeiro HDW, Machado JC, Medeiros LF, Castro MS, Souza A. Perfil nociceptivo e uso de analgésicos em pacientes submetidos à cirurgia de reparo do manguito rotador: coorte prospectiva. Rev Bras Ortop. 2022;57(5):856-62.
38. Razmjou H, Woodhouse LJ, Holtby R. Neuropathic pain after shoulder arthroplasty: prevalence, impact on physical

and mental function, and demographic determinants. Physiother Can. 2018;70(3):212-20.

39. Hasegawa M, Tone S, Naito Y, Sudo A. Possible neuropathic pain in patients with osteoarthritis of the knee before and after total knee arthroplasty. J Pain Res. 2021;14:3011-5.
40. Sidon E, Rogero R, McDonald E, Daecher A, Shakked R, Pedowitz DI, et al. Prevalence of neuropathic pain symptoms in foot and ankle patients. Foot Ankle Int. 2019;40(6):629-33.
41. Crbia N, van der Vlies CH, Cleffken BI, Selles RW, Hovius SER, Nijhuis THJ. High prevalence of chronic pain with neuropathic characteristics after open reduction and internal fixation of ankle fractures. Foot Ankle Int. 2017;38(9):987-96.
42. Bernetti A, Agostini F, de Sire A, Mangone M, Tognolo L, Di Cesare A, et al. Neuropathic pain and rehabilitation: a systematic review of international guidelines. Diagnostics (Basel). 2021;11(1):74.
43. Fitzmaurice BC, Rayen ATA. Treatments for neuropathic pain: up-to-date evidence and recommendations. BJA Educ. 2018;18(9):277-83.
44. Zhang YH, Hu HY, Xiong YC, Peng C, Hu L, Kong YZ, et al. Exercise for neuropathic pain: a systematic review and expert consensus. Front Med (Lausanne). 2021;8:756940.
45. Moisset X, Bouhassira D, Avez Couturier J, Alchaar H, Conradi S, Delmotte MH, et al. Pharmacological and non-pharmacological treatments for neuropathic pain: systematic review and French recommendations. Rev Neurol (Paris). 2020;176(5):325-52.
46. Ju ZY, Wang K, Cui HS, Yao Y, Liu SM, Zhou J, et al. Acupuncture for neuropathic pain in adults. Cochrane Database Syst Rev. 2017;12(12):CD012057.
47. Moisset X. Neuropathic pain: evidence-based recommendations. Presse Med. 2024;53(2):104232.
48. Attal N. Pharmacological treatments of neuropathic pain: The latest recommendations. Rev Neurol (Paris). 2019;175(1-2):46-50.
49. Obata H. Analgesic Mechanisms of Antidepressants for Neuropathic Pain. Int J Mol Sci. 2017;18(11):2483.
50. Bockbrader HN, Wesche D, Miler R, Chapel S, Janiczek N, Burger P. A comparison of the pharmacokinetics and pharmacodynamics of pregabalina and gabapentin. Clin Pharmacokinet. 2010;49(10):661-9.
51. Liggieri A, Palladini M. Lidocaine 5% patch in the treatment of localized neuropathic pain due to nerve compression. Case reports. Br J P [Internet]. 2023;6(2):215-9.
52. Leffler A, Lattrell A, Kronewald S, Niedermirtl F, Nau C. Activation of TRPA1 by membrane permeable local anesthetics. Mol Pain. 2011;7:62.
53. Park J, Park HJ. Botulinum Toxin for the Treatment of Neuropathic Pain. Toxins (Basel). 2017;9(9):260.
54. Häuser W, Morlion B, Vowles KE, Bannister K, Buchser E, Casale R, et al. European clinical practice recommendations on opioids for chronic non-cancer pain: Part 1. Eur J Pain. 2022;26(1):31-49.
55. Guindon J, Hohmann AG. The endocannabinoid system and pain. CNS Neurol Disord Drug Targets. 2009;8(6):403-21.
56. Mücke M, Phillips T, Radbruch L, Petzke F, Häuser W. Cannabis-based medicines for chronic neuropathic pain in adults. Cochrane Database Syst Rev. 2018;3(3):CD012182.
57. Manchikanti L, Abdi S, Atturi S, Benyamin RM, Boswell MV, Buenaventura RM, et al. An update of comprehensive evidence-based guidelines for interventional techniques in chronic spinal pain. Part II: guidance and recommendations. Pain Physician. 2013;16(2 Suppl):S49-S283.
58. Manchikanti L. The growth of interventional pain management in the new millennium: a critical analysis of utilization in the medicare population. Pain Physician. 2004;7(4):465-82.
59. Kirkpatrick K, Khan MH, Dengue Y, Shah KB. A review of stellate ganglion block as an adjunctive treatment modality. Cureus. 2023;15(2):e35174.
60. Eksert S, Akay S, Kaya M, Kantemir A, Keklikci K. Ultrasoundguided femoral nerve blockage in a patellar dislocation: an effective technique for emergency physicians. Ultrasound Emerg Med. 2015;1(1):12-5.
61. Bottros MM, Christo PJ. Current perspectives on intrathecal drug delivery. Journal of Pain Research. 2014;7:615-26.
62. Cohen SP, Bicket MC, Jamison D, Wilkinson I, Rathmell JP. Consensus guidelines on interventional therapies for low back pain. Reg Anesth Pain Med. 2020;45(6):424-67.
63. Palladini MC, Castro APC, Pelloso LRC, Fonseca PRB, Raffaini AT, Gonçalves AC. et al. Tratado de dor neuropática. São Paulo: Atheneu; 2021.
64. Duarte RV, Nevitt S, McNicol E, Bettany-Saltikov J, Deane J, Normand C, et al. Systematic review and meta-analysis of spinal cord stimulation in the treatment of neuropathic pain. JAMA Neurol. 2020;77(8):922-30.
65. da Cunha PHM, de Andrade DC. The deep and the deeper: Spinal cord and deep brain stimulation for neuropathic pain. Presse Med. 2024;53(2):104231
66. Deer TR, Krames ES, Mekhail N, Pope JE, Leong MS, Levy RM, et al. The appropriate use of neurostimulation of the spinal cord and peripheral nervous system for the treatment of chronic pain and ischemic diseases: The Neuromodulation Appropriateness Consensus Committee. Neuromodulation. 2020;23(7):623-46.
67. Kapural L, Yu C, Doust MW, Gliner BE, Vallejo R, Sitzman BT, et al. Comparison of 10-kHz high-frequency and traditional low-frequency spinal cord stimulation for the treatment of chronic back and leg pain: 12-month results from a multicenter randomized controlled pivotal trial. Anesthesiology. 2015;123(4):851-60.
68. Bouhassira D, Attal N, Alchaar H, Boureau F, Brochet B, Bruxelle J, et al. Comparison of pain syndromes associated with nervous or somatic lesions and development of a new neuropathic pain diagnostic questionnaire (DN4). Pain. 2005;114(1-2):29-36.