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Review Article

Consensus of Chinese Painologist Experts on Diagnosis and Treatment of Phantom Limb Pain

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Abstract

Phantom limb pain (PLP), defined as neuropathic pain perceived in the missing portion of an amputated limb, represents a common and refractory condition significantly impairing patient rehabilitation and quality of life. Its pathogenesis is multifactorial, involving complex interactions between peripheral mechanisms (e.g., neuroma formation, ectopic discharges), central nervous system reorganization (including cortical remapping and spinal cord sensitization), and psychological components. Patients frequently present with heterogeneous pain descriptors, such as burning, shooting, or cramping sensations, which often coexist with residual limb pain, complicating clinical assessment. Despite the availability of diverse therapeutic interventions-ranging from pharmacotherapy (e.g., gabapentinoids, antidepressants, NMDA receptor antagonists) and physical modalities (e.g., transcranial magnetic stimulation, mirror therapy) to interventional procedures (e.g., nerve blocks, neuromodulation) and psychological approaches-treatment outcomes remain variable, and standardized clinical guidelines are lacking. This consensus, formulated by a panel of Chinese pain specialists, systematically reviews contemporary evidence on the

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epidemiology, pathophysiology, diagnosis, and management of PLP. It aims to establish practical, evidence-based recommendations to guide the standardized diagnosis and stratified treatment of PLP, thereby optimizing therapeutic efficacy and improving functional outcomes for affected individuals.

Keywords

Phantom Limb Pain, Diagnosis, Treatment, Expert Consensus

1. Introduction

Phantom limb pain (PLP) refers to persistent nociceptive sensations perceived in the amputated portion of a limb [1]. After amputation, patients report phantom limb sensation (PLS), characterized by non-painful perceptions of the missing limb's position, shape, movement, temperature (cold or heat), or itching [2]. Additionally, many individuals report painful sensations such as burning, stabbing, throbbing, or electric shock-like pain, which is referred to as PLP [3]. Over 80% of amputees experience PLP, which significantly impairs residual limb function and rehabilitation [4]. It is estimated that by 2050, the amputee population in the United States will increase from 1.6 million in 2005 to 3.6 million [5]. The exact mechanisms underlying PLP remain unclear but likely involve peripheral, central, and psychological factors [2]. Due to its high incidence and therapeutic resistance, PLP represents a significant public health challenge. Over 25 treatment modalities exist, yet standardized protocols are lacking [6]. To address this gap, the Chinese Journal of Pain Medicine Editorial Board convened a multidisciplinary expert panel to establish the Chinese Expert Consensus on the Diagnosis and Treatment of PLP, aiming to standardize evidence-based clinical practices.

2. Epidemiology

The reported incidence of PLP ranges widely from 2% to 98% [7-9], with variations attributed to differences in study populations, amputation sites (upper or lower limb), study designs (prospective, retrospective, or cross-sectional), and assessment methods (interviews or questionnaires). Additional contributing factors include the lack of a standardized definition for PLP, and challenges in differentiating PLP from residual limb pain (RLP) and PLS [10].

Early studies reported PLP incidence rates of 72.4% at 8 days and 66.7% at 6 months post-amputation [11]. Nikolajsen et al. [12] reported PLP in 67% of amputees within the first week and 75% at 6 months. In a small mixed-etiology cohort (n=22), PLP incidence was 2.2% at 1 month post-amputation, whereas in non-traumatic amputees (n=52), it reached 82.7% at 12 months [13]. However, a 2010 study found a significantly lower PLP incidence (32%) at 6 months post-amputation [14]. This decline may be attributed to improved understanding of PLP mechanisms, widespread adoption of preventive analgesia concepts, and enhanced perioperative pain management strategies [15].

3. Pathogenesis

The pathogenesis of PLP is complex, involving multiple mechanisms such as abnormal changes in the peripheral and central nervous systems, as well as psychological factors.

3.1. Peripheral Mechanisms

PLP is considered a type of neuropathic pain. Peripheral nerve injury caused by amputation can trigger an inflammatory response, releasing algogenic substances such as substance P, prostaglandins, bradykinin, and cytokines, which sensitize peripheral nociceptors and induce peripheral sensitization [16, 17]. Subsequent axonal regeneration and neuroma formation further sustain aberrant ectopic discharges, exacerbating peripheral sensitization [18]. Since cortical somatotopic maps retain pre-amputation sensory memories, residual peripheral nerve activity may be misinterpreted as originating from the missing limb, contributing to PLP [19, 20]. Research by Feng Aimin et al. [21] demonstrated that maintaining afferent input from the peripheral nerves at the residual limb through substitute stimulation can alleviate post-amputation RLP and mirror pain in the contralateral limb in rats. Furthermore, PLP has also been associated with sympathetic nervous system dysfunction [2].

3.2. Central Mechanisms

At the spinal cord level, PLP involves dorsal horn neurons sensitization, synaptic remodeling, and diminished spinal disinhibition [22]. At supraspinal levels, several hypotheses have been proposed to explain the mechanisms underlying PLP [23]:

3.2.1. Thalamic Modulation

Nociceptive signals project via the thalamus to cortical regions. After amputation, the thalamic nuclei representing the amputated region remain functionally active, and stimulation

of these nuclei can evoke PLS and PLP [24].

3.2.2. Cortical Reorganization

Adjacent cortical areas invade the amputated limb's sensorimotor representation, with fMRI studies confirming reorganization correlates with PLP severity and chronicity [25-27].

3.2.3. Pain Neuromatrix Dysfuction

The primary sensory cortex, anterior cingulate cortex, insula, amygdala, cerebellum, and limbic system together constitute the neural network matrix for pain perception [28], and its functional abnormalities can lead to PLP [29].

3.2.4. Proprioceptive Memory

Based on proprioceptive input theory, amputees may retain and recall the final pre-amputation proprioceptive input from the missing limb [30].

3.2.5. Neuroplasticity

Plastic changes in neurons and glial cells, affecting ion channels, protein receptors, neurotransmitters, and metabolic signaling pathways, constitute the molecular basis of PLP [31-34].

3.3. Psychological Mechanism

The profound psychological trauma and stress response induced by amputation lead to emotions such as fear, anxiety, and depression in patients, making psychological mechanisms a significant factor in PLP [35].

4. Clinical Manifestations

PLP manifests across four primary dimensions: pain intensity, frequency of episodes, duration, and description of pain qualities [36].

4.1. Pain Intensity

One study using the McGill Pain Questionnaire found that PLP intensity was comparable to chronic low back pain, non-terminal cancer pain, and labor pain [37]. Another study reported an average PLP intensity of 5.3/10 on a numerical rating scale [1].

4.2. Frequency of Episodes

PLP is typically intermittent, with only a minority of patients experiencing constant pain. Episodes often occur daily, every few days, or weekly, and less commonly monthly or yearly [3].

4.3. Duration

The duration is typically a few seconds, several minutes, or a few hours, and rarely extends to several days or longer [3].

4.4. Description of Pain Qualities

PLP is often described as "crushing," "cutting," or "drilling" pain [35]. PLP is not a singular symptom but a cluster of overlapping and coexisting symptoms, each of which presents with varying intensity and frequency, making it difficult for patients to articulate verbally. A multicenter cross-sectional study found that trauma-induced lower-limb amputees required a median of 13 descriptors (range: 6-20) to express their sensations, with 30% of patients needing to use more than 10 descriptors [38]. In addition to pain, the most frequent descriptors described by subjects for 7 consecutive days in a week included: burning, stinging, coldness, throbbing, and electric shocks. The complaints were listed in descending order of frequency as follows: movement sensation, itching, electric shock sensation, stinging sensation, and pulsating sensation. The intensity of each pain characteristic, as per the visual analog scale, was ranked in descending order as follows: electric shock, burning, stinging, and pricking [38].

4.5. Somatotopic Distribution

PLP primarily localizes to the distal phantom limb (e.g., fingers/palms for upper-limb amputees; toes/dorsum/ball/ankle for lower-limb amputees).

4.6. Temporal Course

Up to 90.0% of amputees develop neuropathic pain within days to weeks post-amputation, with severity escalating significantly within 1 year [39]. It is estimated that 65% of amputees experience PLP within 1 month, and 82% within 1 year [40].

5. Diagnosis and Differential Diagnosis

5.1. Assessment

The Visual Analog Scale (VAS), Numeric Rating Scale (NRS), and McGill Pain Questionnaire (MPQ) are the most commonly used tools for measuring PLP. The Chinese Scale for Neuropathic Pain Diagnosis and Efficacy Assessment is a multidimensional pain assessment tool suitable for evaluating PLP in Chinese populations [41]. The Prosthesis Evaluation Questionnaire (PEQ) assesses non-painful PLS. Pain severity should be measured through both the average and worst pain intensity experienced over at least one week [42]. Psychological assessment is an essential part of PLP evaluation [43].

5.2. Diagnosis

Currently, no physiological or molecular biomarkers can definitively predict the development of PLP post-amputation [44]. Therefore, the clinical diagnosis of PLP relies on patient history and physical examination [45]. The nonspecific and highly variable symptoms of PLP make diagnosis challenging, requiring a comprehensive medical history, examinations, testing, and exclusion of other potential neuropathies.

First, the distinction between PLS and PLP must be clarified. PLS refers to the non-painful perception of the absent limb after amputation [1]. PLP is a type of PLS characterized primarily by pain, with the following manifestations:

(1) Persistent perception of the amputated limb accompanied by severe pain;

(2) Clinical manifestations consistent with characteristic PLP features;

(3) Physical examination reveals significant tenderness at the residual limb, hardened scar tissue, tenderness along the proximal nerve trunk, sensitive skin at the residual limb, and slight touch or pressure on trigger points can cause radiating PLP;

It should be differentiated from RLP after amputation. When it is difficult to distinguish from RLP, diagnostic block can be performed. Local injection often alleviates RLP but does not relieve PLP.

Imaging characteristics: Although the cause of PLP may not be the swollen neuroma itself, locating the injured nerve and scanning distally often reveals a hypoechoic mass (swollen neuroma) [46].

5.3. Differential Diagnosis

5.3.1. Residual Limb Pain

The International Association for the Study of Pain (IASP) defines RLP as pain in the remaining portion of the amputated limb [1]. While common in the early post-amputation period, most cases resolve with wound healing. Clinical examination frequently identifies pain-generating pathologies such as infection, osteophyte formation, neuromas, or restrictive scar tissue formation. Further assessment may demonstrate hyperalgesia and allodynia [47]. Although PLP and RLP frequently coexist, RLP typically occurs immediately post-amputation and often resolves with treatment of the underlying cause, whereas PLP may dominate 1-12 months post-amputation, is typically refractory to standard therapies, and shows no correlation with surgical wound healing progresses [4].

5.3.2. Chronic Low Back Pain

Studies indicate higher prevalence of back pain in amputees versus the general population [48]. Careful differentiation is required when pain originates from facet joints or sacroiliac joints, which patients may misinterpret as PLP in lower-limb amputees.

5.3.3. Vascular Pain

As most amputations result from vascular insufficiency, ischemic injury must be excluded in PLP patients. Distal perfusion testing (e.g., transcutaneous oxygen tension <20 mmHg at stump level indicates ischemia) can rule out vascular etiologies.

5.3.4. Neuroma-related Pain

A positive Tinel's sign is a classic feature of a neuroma. Percussion of the injured nerve or neuroma can trigger pain in the residual limb stump.

5.3.5. Prosthesis-related Pain

Shrinkage of the residual limb may cause the stump shape to no longer match the original mold, potentially leading to skin erosion at pressure points. A careful soft tissue examination of the stump can effectively rule this out.

5.3.6. Infection

Conditions such as osteomyelitis or stump infection should be excluded as potential causes of pain.

6. Treatment Methods

The primary databases searched for this consensus include PubMed, China National Knowledge Infrastructure (CNKI), and Wanfang Data. The evidence quality rating and recommendation grading were both referenced from internationally established standards [49]. The evidence levels are classified as A, B, and C. For details, see Tables 1 and 2.

Table 1. Levels of evidence.

Levels of evidence	Definition
A	Data derived from multiple randomized clinical trials or meta-analyses
B	Data derived from a single randomized clinical trial or large non-randomized studies
C	Consensus of opinion of the experts and/or small studies, retrospective studies, registries

Table 2. Classes of recommendations.

	Definition	Wording to use
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Is recommended or is indicated
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of given treatment or procedure	
Class IIa	Weight of evidence/opinion is in favour of usefulness/efficacy	Should be considered
Class IIb	Usefulness/efficacy is less well established by evidence/opinion	May be considered
Class III	Evidence or general agreement that the given treatment or procedure is not usefulness/effective, and in some cases may be harmful	Is not recommended

6.1. Pharmacological Management

The selection of medications for PLP should consider multiple factors, such as analgesic efficacy, adverse effects, management of accompanying sleep and emotional disorders, drug interactions, risk of substance abuse, and cost-effectiveness of treatment [50, 51]. Drug therapy should be individualized. If monotherapy fails to provide satisfactory pain relief, combination therapy should be considered.

6.1.1. Calcium Channel Modulators

Gabapentin is commonly used for neuropathic pain management. Its primary mechanism involves binding to the α2δ subunit of voltage-gated calcium channels, thereby reducing calcium influx [52, 53]. This action decreases excitatory neurotransmitter release and suppresses both hyperalgesia and central sensitization. Clinical studies demonstrate that gabapentin monotherapy is superior to placebo in alleviating PLP [54, 55].

Evidence level: A; Recommendation grade: I.

Currently, only limited case reports exist regarding pregabalin application for PLP [56, 57]. Evidence level: C; Recommendation grade: IIb.

6.1.2. Tricyclic Antidepressants

Amitriptyline, a traditional antidepressant, exerts analgesic effects primarily through selective inhibition of serotonin and norepinephrine reuptake, thereby enhancing endogenous pain inhibition in the central nervous system. It demonstrates efficacy in various neuropathic pain conditions, including PLP. Common adverse effects are primarily anticholinergic and cardiovascular reactions, such as dry mouth, constipation, dysuria, nausea, vomiting, tachycardia, and orthostatic hypotension [58]. Two randomized controlled trials comparing amitriptyline with placebo yielded conflicting results [59].

Evidence level: B; Recommendation grade: “II”

6.1.3. Calcitonin

Calcitonin is secreted by the parafollicular C cells of the thyroid gland and reduces blood calcium levels by inhibiting osteoclast activity. Recombinant human calcitonin has been used to treat osteoporosis and osteolytic pain. A double-blind crossover trial demonstrated that intravenous administration of 200 U calcitonin is effective in treating PLP [60].

Evidence level: B; Recommendation grade: IIa.

6.1.4. NMDA Receptor Antagonists

Hyperactivity of NMDA receptors may be one of the factors contributing to the maintenance of PLP [61]. Studies have shown that ketamine administration can significantly increase pain thresholds in patients with PLP. NMDA receptor antagonists may be effective for PLP, but may cause adverse effects including cystitis, hallucinations, and cardiovascular effects [61, 62]. Dextromethorphan has shown effectiveness in alleviating PLP with a more favorable side effect profile compared to ketamine [63].

Evidence level: A; Recommendation grade: I.

Memantine is an NMDA glutamate receptor antagonist that can alleviate symptoms of neuropathic pain, including PLP [64]. Research by Hackworth et al. [65] demonstrated that memantine reduces acute and subacute PLP. However, this medication has not been proven effective for chronic PLP [66, 67].

Evidence level: A; Recommendation grade: “II”

6.1.5. Opioid Analgesics

Common opioid medications include morphine, oxycodone, and fentanyl. These medications exert their therapeutic effects by binding to opioid receptors in pain perception and modulation regions such as the spinal cord, medulla oblongata, midbrain, and thalamus, thereby elevating pain thresholds and reducing pain perception. Clinical studies have demonstrated that morphine can significantly alleviate pain symptoms in PLP patients compared to control groups [68, 69]. However,

opioid therapy may be associated with notable adverse effects including fatigue, dizziness, sweating, constipation, dysuria, nausea, vertigo, pruritus, and shortness of breath [68].

Evidence level: A; Recommendation grade: I.

6.2. Physical Therapy

Current physical therapy approaches for PLP primarily include transcutaneous electrical nerve stimulation (TENS) [70] and repetitive transcranial magnetic stimulation (rTMS) [71]. (See Figures 1, 2).

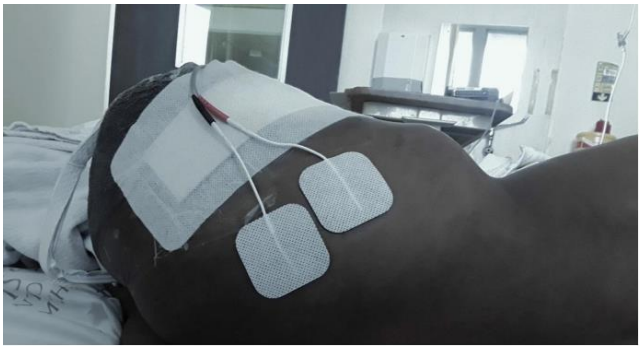

Figure 1. *Patient with PLP after left lower limb amputation receiving TENS therapy. The mechanism of TENS involves activating low-threshold Aβ fibers to close the spinal 'gates' for pain.*

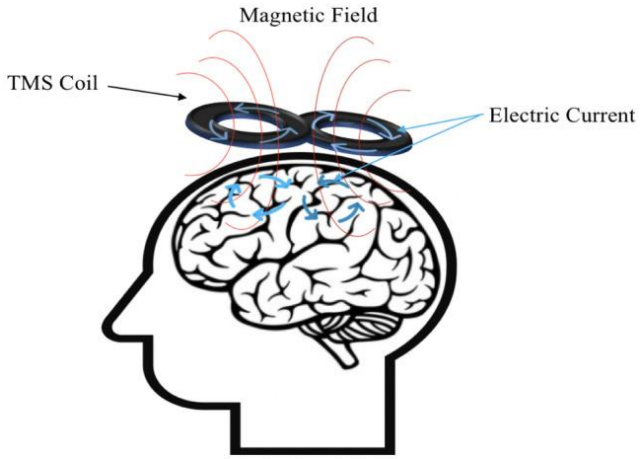

Figure 2. *Schematic diagram of rTMS. During rTMS, an electric current is used to create a repetitively pulsed magnetic field. When applied over the scalp, this induces an electric current within a discrete area of the brain with resultant changes in neuronal polarization. The end result is altered neuronal activity in the area where the rTMS is applied.*

TENS is a non-invasive therapy based on the "gate control theory". Its mechanism involves activation of low-threshold Aβ fibers to close pain gates, while simultaneously initiating the endogenous analgesic system to release endorphins and enkephalins. This upregulates or activates opioid receptors, thereby alleviating PLP [72]. Multiple studies have reported TENS's positive effects in treating PLP [73, 74]. Lundeberg's study involving 24 PLP patients, TENS achieved a 75% pain relief rate compared to 44% with placebo [75]. Two domestic studies randomized patients into control (mirror therapy alone) and treatment (TENS + mirror therapy) groups, demonstrating superior efficacy with combined therapy [76, 77]. A recent Cochrane review noted that while multiple studies show TENS reduces visual analog scale, McGill Pain Questionnaire, and general pain scores in PLP, methodological heterogeneity precludes definitive recommendations [78].

Evidence level: A; Recommendation grade: "II".

rTMS is a non-invasive neuromodulation technique that uses magnetic fields to induce cortical currents, thereby modulating neuronal activity. By stimulating specific brain regions to alter neural network patterns, rTMS can alleviate pain and improve neurological function [71, 79-81]. Studies have shown a significantly increase in serum β-endorphin levels post-rTMS, suggesting an analgesic effect mediated by β-endorphin [79]. A systematic review found 18 of 24 studies demonstrated rTMS's significant efficacy for neuropathic pain including PLP [82]. Currently regarded as a safe, non-invasive approach with therapeutic potential, rTMS requires further investigation.

Evidence level: A; Recommendation grade: I.

6.3. Psychological Therapy

PLP, due to its unique pain mechanisms - particularly involving central sensitization and cortical plasticity - is recognized as a chronic pain disorder with distinct biological, psychological, and social multifactorial influences [83-85]. Mechanisms such as cortical reorganization, memory alterations, and catastrophic thinking have been increasingly validated, making psychotherapeutic interventions targeting central cortical modulation one of the key treatment approaches for PLP [84, 85]. Psychological interventions addressing trauma or pain-related memories have been shown to achieve long-term, significant relief from PLP [86]. Therapies addressing unresolved trauma and pain-related memories can reduce the intensity of PLP by diminishing the emotional dimension of these memories or integrating somatic memories.

Commonly used psychotherapeutic approaches include cognitive-behavioral therapy, psychodynamic therapy, motivational interviewing, and supportive psychotherapy. Among these, mirror therapy, graded motor imagery (GMI), and virtual reality (VR) therapy are commonly applied in the treatment of PLP.

Mirror therapy utilizes visual feedback from a mirror to create the illusion of the "reappearance" of the missing limb, thereby treating PLP. Amputees who underwent 4 weeks of mirror training showed significant pain reduction [87-89]. These findings suggest that visual feedback can modulate PLP. The method is simple, requires no specialized equipment or complex setup, and demonstrates clear clinical efficacy [90].

However, further refinement is needed in methodology, treatment duration, and other aspects. The evidence level is A, with a recommendation grade I. (See Figure 3).

Figure 3. *Schematic diagram of mirror therapy. Mirror therapy utilizes visual feedback from a mirror to create the illusion of the missing limb's reappearance with the aim of treating PLP.*

GMI typically involves a 4-6 week treatment cycle. It generally progresses through three phases: preparation for the motor imagery program, imagined movement training, and graded mirror movement adaptation. Throughout the treatment, physiotherapists conduct weekly consultations, monitoring, and discussions based on the patient's pain improvement. GMI treatment usually leads to improvements in both pain and functional outcomes for phantom limb pain patients, with these benefits maintained during 6-month follow-ups [91, 92]. The evidence level is B, with a recommendation grade of IIa.

VR refers to computer technology that simulates human sensory experiences to create an immersive three-dimensional environment, making users feel physically present within it [93]. This technology exerts broad regulatory effects on cognitive functions, including: enhancing attention and reaction speed, improving spatial perception and memory, and facilitating emotional experience and cognitive processing. In therapeutic applications, VR can generate a virtual, intact avatar, where movements of the amputee's residual limb are translated into motions of the virtual limb. This approach enables relaxation and exercise training, thereby alleviating pain [94, 95]. Such immersive therapy shows promising potential for more effective PLP management in the future. The evidence level is C, with a recommendation grade of IIb.

Mental imagery, phantom exercise training, and sensory discrimination training can also improve pain intensity and functional outcomes in PLP [96, 97].

6.4. Traditional Chinese Medicine (TCM) Treatment

Several studies have explored acupuncture as an adjunctive therapy for PLP. Trevelyan et al. [98] conducted a multicenter randomized controlled trial and concluded that acupuncture may be effective in treating PLP. Freed et al. [99] investigated the therapeutic effects of acupuncture on post-traumatic mental disorders and PLP, demonstrating that acupuncture influences cortical brain function. Other reports primarily consist of case studies, such as auricular acupuncture for PLP [100], scalp acupuncture [101], and electroacupuncture [102], all of which yielded satisfactory outcomes. Additionally, acupuncture applied to the contralateral (healthy) limb has been used to treat PLP with positive results [103].

For TCM acupuncture in PLP management, the evidence level is B, with a recommendation grade of IIa.″

6.5. Herbal Medicine Treatment′

The Jianghuang Gegen (The herbal formula includes Curcumae Longae Rhizoma and Puerariae Lobatae Radix)Decoction, administered orally for 6 weeks in combination with comprehensive therapies (e.g., exercise therapy, mirror therapy, electrical stimulation), has been shown to improve the treatment efficacy rate from 80% to 95% in managing PLP after diabetic foot amputation, though it does not enhance the cure rate [104]. External herbal washes containing Schizonepeta tenuifolia (Jingjie) and Saposhnikovia divaricata (Fangfeng), when used in combination with multimodal therapy, have been shown to significantly reduce pain assessment scores in patients with post-traumatic PLP. Additionally, oral herbal medicine and topical herbal washes for traumatic upper- or lower-limb amputations have demonstrated improved overall efficacy rates and reduced visual analog scale (VAS) scores, with no significant differences between upper- and lower-limb subgroups [105]. Haitongpi (a herbal name) Decoction steam therapy as a primary treatment for unilateral traumatic PLP has been found to significantly decrease pain assessment indices, present pain intensity scores, VAS scores, and depression scores [106].

Evidence level: B; Recommendation grade: IIb.

6.6. Nerve Block Therapy

Nerve block therapy serves as a critical intervention for PLP.

For lower extremity pain management, common nerve block techniques include sciatic nerve block, femoral nerve block, lumbar plexus block, tibial nerve block, common peroneal nerve block, and lumbar sympathetic ganglion block. For upper extremity pain, standard approaches include involve brachial plexus block, median nerve block, radial nerve

block, and ulnar nerve block.

The selection of nerve block technique depends on the amputation level of the affected limb:

Lumbar sympathetic ganglion block is indicated for above-knee amputations or below-knee amputations secondary to peripheral vascular disease or trauma [107];

Brachial plexus block is indicated for Selective above-elbow amputations (tumor-related) [108], Below-elbow amputations (infraclavicular approach), Shoulder disarticulations (interscalene approach) [109, 110].

Radial, ulnar, and median nerve blocks are indicated for Single-digit amputations (selection of individual or combined blocks based on digital nerve distribution) [111] or Wrist-level amputations [112].

Sciatic and femoral nerve blocks are indicated for unilateral below-knee amputations or Unilateral above-knee amputations due to peripheral vascular disease [113-118].

Lumbar plexus block is indicated for Unilateral below-hip amputations caused by malignancy or trauma [113, 119].

Tibial and common peroneal nerve blocks are indicated for Below-knee amputations, Ankle-level or digital foot amputations (single/combined blocks based on neural distribution) [120].

Commonly used local anesthetics and their concentrations include 0.5% ropivacaine/0.75% ropivacaine/0.25% bupivacaine/2% lidocaine [107-119]. The nerve block technique may be administered as either single-shot injection or continuous catheter infusion.

Overall, nerve block therapy demonstrates significant efficacy in alleviating PLP and improving patients' quality of life, though the degree and duration of pain relief vary individually. While peripheral nerve blocks typically provide acute pain relief, some patients can achieve long-term therapeutic benefits [113, 120]. Borghi et al. [114] demonstrated that sciatic nerve blocks may reduce the incidence of PLP in amputees. Studies indicate that 6-day peripheral nerve blockade can provide pain relief persisting at both 4 weeks and 6-month follow-up [112, 113, 121]. According to the Practice Guidelines for Chronic Pain Management by the American Society of Anesthesiologists (ASA), lumbar sympathetic nerve blockade is indicated as a therapeutic option for PLP. Case report studies have demonstrated that lumbar sympathetic block is both safe and effective for alleviating PLP symptoms [107]. However, its therapeutic effectiveness remains debated. A randomized, double-blind study evaluating the impact of sciatic nerve block on chronic pain development at 6 months post traumatic below-knee amputation demonstrated that preemptive sciatic nerve blockade failed to reduce either the incidence or severity of chronic post-amputation pain [115]. Although nerve blocks can provide effective pain relief, there are some potential risks and adverse effects, including hematoma, sensory loss, local infection, etc. The approach to nerve blocks should be individualized, requiring close collaboration between the physician and the patient to develop the most appropriate treatment plan based on the characteristics of the pain and the patient's overall health condition. In summary, nerve block therapy plays a significant role in the management of phantom limb pain. Despite some potential risks and controversial conclusions, nerve blocks remain an important component of phantom limb pain treatment. Patients and physicians should work closely together and continuously monitor symptoms during the treatment process to ensure the effectiveness and safety of the treatment.

The evidence level is A, and the recommendation level is I.

6.7. Radiofrequency Therapy

Radiofrequency therapy is a commonly used nerve-targeting treatment for PLP encompassing two main types: radiofrequency ablation and pulsed radiofrequency. The principle of this technique involves placing an electrode directly or via targeted puncture near a peripheral nerve or the dorsal root ganglion (DRG), then applying electrical current to modulate or disrupt the transmission of pain signals to the central nervous system, ultimately achieving pain relief or elimination.

6.7.1. Radiofrequency Ablation

Current evidence suggests that radiofrequency ablation has a certain therapeutic effect on pain caused by stump neuromas after amputation [122, 123]. Additionally, for PLP, targeting peripheral nerves with radiofrequency ablation can also play a positive therapeutic role [124]. Although radiofrequency ablation has shown some efficacy in the treatment of PLP, there are also some limitations and risks. Radiofrequency ablation is a destructive and invasive treatment method, and there is currently no evidence-based medical evidence to clearly support its application in PLP.

6.7.2. Pulsed Radiofrequency

Pulsed radiofrequency (PRF) delivers intermittent high-frequency electrical currents to neural tissue while avoiding thermal damage. Small-scale studies have demonstrated that PRF targeting the L4 and L5 dorsal root ganglia (DRG), as well as peripheral PRF modulation of the femoral and sciatic nerves, can effectively alleviate refractory PLP [125, 126]. DRG radiofrequency modulation may represent a promising therapeutic approach for PLP, with benefits including pain reduction, alleviation of anxiety and depression, and improved quality of life [127]. However, further research is needed to establish clinical recommendations. Current evidence level: C; Recommendation grade: IIa.

6.8. Neuromodulation

Neuromodulation includes methods such as spinal cord stimulation (SCS) and deep brain stimulation (DBS). These treatment approaches aim to alleviate PLP by altering neuronal excitability and modulating neural signal transmission.

6.8.1. Spinal Cord Stimulation

SCS is based on the gate control theory, which alleviates pain by continuously stimulating the Aβ nerve fibers in the dorsal column of the spinal cord, thereby interfering with or blocking the transmission of pain signals through C and Aδ nerve fibers to the central nervous system [128]. SCS has been used for the treatment of PLP for over 50 years [129]. Recent studies have shown that SCS can alter the excitability of "wide-dynamic-range" neurons, promote physiological inhibitory mechanisms, and modify the activity of various neurotransmitters [130]. Multiple studies have demonstrated positive therapeutic effects of SCS in treating PLP [131]. A systematic review revealed that 7 out of 12 included studies indicated significant improvement in PLP with SCS, while the remaining 5 showed no efficacy [132]. Based on current evidence, spinal cord stimulation is considered a viable alternative to traditional treatments for PLP.

Evidence level C, recommendation grade IIa.

6.8.2. Deep Brain Stimulation

DBS involves implanting tiny electrodes into specific brain regions and connecting them to a pulse generator, which can be programmed via an external device to apply electrical stimulation to alter neural activity, thereby alleviating or improving neurological disorders. Studies have reported that the overall pain relief rate of DBS in the treatment of PLP is approximately 50% to 91% [133]. However, the application of DBS in the treatment of PLP is still in the research stage and is not a conventional treatment strategy. With advancements in science and technology and a deeper understanding of the mechanisms of PLP, DBS may become an effective treatment in the future. Nevertheless, strict evaluation and selection of patients are still required before using DBS to treat PLP to ensure the safety and effectiveness of the treatment.

Evidence Level C, Recommendation Level IIb.

6.9. Surgical Intervention

For patients who have not responded well to conservative and minimally invasive interventional treatments, surgical intervention may be considered. Given the complex peripheral and central mechanisms, as well as the biopsychosocial factors involved in PLP, the efficacy of various surgical procedures remains unclear. It is recommended to maximize patient benefits by considering the patient's condition and etiology, comprehensively evaluating the risk-benefit ratio, and formulating a personalized surgical plan.

Traditional surgical approaches for peripheral involvement mechanisms such as neuroma commonly employ neurotomy and nerve implantation to treat PLP. Current research indicates that modified techniques such as targeted nerve implantation and combined collagen nerve wrapping offer better treatment options [134]. Compared to traditional surgery, targeted muscle reinnervation surgery and peripheral nerve interface regeneration can further alleviate PLP through bionic reconstruction and improved prosthetic function. Multiple studies currently support their positive role in the treatment and rehabilitation of PLP [135, 136], with functional prosthetics proving more effective than cosmetic prosthetics, as their myoelectric function addresses the issue of sensorimotor feedback post-amputation [137, 138].

Evidence level B, recommendation grade IIa.

Dorsal root entry zone lesioning is a classic surgical procedure for treating brachial plexus root avulsion. A retrospective analysis showed that among 37 patients who underwent this surgery, 45.9% experienced disappearance or alteration of PLS, and 67.6% experienced relief from PLP. The differences may be influenced by changes at the supraspinal level and central plasticity [139].

Evidence level C, recommendation grade IIa.

Cryoneurolysis blocks pain signal transmission by freezing nerves at low temperatures (commonly using nitrous oxide at about -70°C). Multiple cohort studies have shown it to be safe and effective in treating PLP. However, a multicenter randomized controlled trial by Ilfeld et al. [140] indicated that ultrasound-guided percutaneous cryoneurolysis provided no significant benefit for PLP after 4 months. Patients with transtibial amputations showed better outcomes compared to those with transankle-foot and transfemoral amputations [141]. Evidence level A, recommendation grade "II"

6.10. Other Treatment Modalities

A Delphi expert consensus study suggested that addressing neural mechanisms in the brain, such as cortical functional reorganization, may alleviate phantom limb pain [85]. Sensory discrimination training is a technique that provides sensory input to the residual limb's adjacent areas using fabrics with varying softness/texture (e.g., cotton vs. hook-and-loop fasteners). By resolving the mismatch between the brain's sensory output and amputated limb's feedback, this approach promotes cortical reorganization and pain reduction [142-144].

7. Prevention and Prognosis

Some clinical trials have shown that epidural preemptive analgesia and postoperative regional blocks are effective in preventing PLP, but there are limitations in study design and small sample sizes. Therefore, larger-scale, well-designed, randomized controlled clinical trials are needed to better determine whether regional block can prevent and reduce the occurrence of PLP [43]. In addition to regional block, it has been shown that the NMDA receptor antagonist memantine significantly reduces the incidence of phantom limb pain compared to placebo [2]. There is no evidence that reducing the severity of phantom limb pain improves function. phantom limb pain is associated with depressive symptoms, which may reduce treatment efficacy, function, and quality of life. Severe phantom limb pain has a negative impact on

daily activities, prosthetic use, mobility, and social activities [145].

The diagnosis and treatment of PLP are highly challenging. The Chinese Journal of Painology has organized domestic experts to propose diagnostic and therapeutic recommendations and formulate this consensus based on summarizing the current evidence both domestically and internationally, aiming to provide a basis for clinical diagnosis and treatment. However, research on phantom limb pain remains insufficient to date. There is an urgent need to conduct large-sample, multicenter randomized controlled studies combined with real-world studies to obtain more robust evidence-based evidence to assist in precise diagnosis and individualized treatment, thereby helping more patients alleviate pain. Furthermore, due to the complexity of clinical practical issues, it is hoped that experts and physicians in related fields will actively provide feedback and suggestions. It is also anticipated that new clinical practice issues can be further collected in the future to supplement and revise the consensus.

Abbreviations

PLP	Phantom Limb Pain
PLS	Phantom Limb Sensation
RLP	Residual Limb Pain

Conflicts of Interest

The authors declare no conflicts of interest.

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