Evidence-Based Interventional Pain Medicine According to Clinical Diagnoses

21. Phantom Pain

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■ **Abstract:** Phantom pain is pain caused by elimination or interruption of sensory nerve impulses by destroying or injuring the sensory nerve fibers after amputation or deafferentation. The reported incidence of phantom limb pain after trauma, injury or peripheral vascular diseases is 60% to 80%. Over half the patients with phantom pain have stump pain as well. Phantom pain can also occur in other parts of the body; it has been described after mastectomies and enucleation of the eye.

Most patients with phantom pain have intermittent pain, with intervals that range from 1 day to several weeks. Even intervals of over a year have been reported. The pain often presents itself in the form of attacks that vary in duration from a few seconds to minutes or hours. In most cases, the pain is experienced distally in the missing limb, in places with the most extensive innervation density and cortical representation. Although there are still many questions as to the underlying mechanisms, peripheral as well as central neuronal mechanisms seem to be involved.

Conservative therapy consists of drug treatment with amitriptyline, tramadol, carbamazepine, ketamine, or morphine.

Based on the available evidence some effect may be expected from drug treatment.

When conservative treatment fails, pulsed radiofrequency treatment of the stump neuroma or of the spinal ganglion (DRG) or spinal cord stimulation could be considered (evidence score 0). These treatments should only be applied in a study design. ■

Key Words: evidence-based medicine, phantom pain, amputation, phantom limb pain

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INTRODUCTION

This review on phantom pain is part of the series "Evidence-based Interventional Pain Medicine according to clinical diagnoses". Recommendations formulated in this chapter are based on "Grading strength of recommendations and quality of evidence in clinical guidelines" described by Guyatt et al.,[1] and adapted by van Kleef et al. in the editorial accompanying the first article of this series[2] (Table 1). The latest literature update was performed in September 2010.

Complete or partial amputation of a limb does not always result in pain. It is termed phantom pain when the patient feels pain or dysesthesia in limbs that are no longer present (deafferentation). It is important to distinguish phantom pain from other amputation sequelae, including phantom sensation, telescoping, and stump pain. Phantom sensations are nonpainful and typically manifest as kinetic, kinesthetic, or exteroceptive perceptions. Telescoping is a progressive sensation resulting in the distal limb being perceived more proximally. Stump pain is residual limb pain, commonly localized to distal existing body part. If patients suffer from phantom pain, the onset is usually amputation secondary to trauma or surgical intervention. Ambrosius Paré described this type of pain in the sixteenth century.

It is estimated that over 1.5 million amputees live in the United States, where the majority have had amputations of the lower limbs below the knee.[3] The reported incidence of phantom limb pain varies widely from as low as 2% to 80%. More recent epidemiological studies report a much higher percentage of amputees having phantom limb pain. A retrospective study in patients with combat related traumatic amputations found that 78% of participants experienced phantom limb pain at some time since amputation, and 68% of them received treatment from their health care provider.[4] Patients prospectively followed after limb amputation due to peripheral vascular disease show a comparable incidence of phantom limb pain (78.8%), and stump pain (51.2%) 6 months after amputation.[5] In one study, probably the largest field survey performed in Europe, a questionnaire containing 62 questions was filled in by 537 out of 1,088 amputees. Of the amputees who responded, 14.8% were pain free, 74.5% had phantom limb pain, 45.2% had stump pain and 35.5% had a combination of both.[6]

Seventeen years after the war between Iraq and Iran, 64% of 200 soldiers who had lost limbs during this war suffered from phantom pain, 32% from phantom movement pain, while 24% suffered from stump pain.[7] Telephone interviews held between 1998 and 2000, in which 914 people participated, showed that the incidences during the past 4 weeks prior to the interview amounted to 79.9% for phantom pain and 67.7% for stump pain, respectively. A quarter of the people who were interviewed had a visual analogue scale (VAS) pain score ranging from 7 to 10.

MECHANISM

It is assumed that every individual develops a proprioceptive, tactile and visual image of the body. For a long time, the cortical representation of these images was thought to remain unchanged after amputation.

Table 1. Summary of Evidence Scores and Implications for Recommendation

Score	Description	Implication
1 A+	Effectiveness demonstrated in various RCTs of good quality. The benefits clearly outweigh risk and burdens	Positive recommendation
1 B+	One RCT or more RCTs with methodologic weaknesses, demonstrate effectiveness. The benefits clearly outweigh risk and burdens	Positive recommendation
2 B+	One or more RCTs with methodologic weaknesses, demonstrate effectiveness. Benefits closely balanced with risk and burdens	Positive recommendation
2 B±	Multiple RCTs, with methodologic weaknesses, yield contradictory results better or worse than the control treatment. Benefits closely balanced with risk and burdens, or uncertainty in the estimates of benefits, risk and burdens.	Considered, preferably study-related
2 C+	Effectiveness only demonstrated in observational studies. Given that there is no conclusive evidence of the effect, benefits closely balanced need with risk and burdens	Considered, preferably study-related
0	There is no literature or there are case reports available, but these are insufficient to suggest effectiveness and/or safety. These treatments should only be applied in relation to studies.	Only study-related
2 C−	Observational studies indicate no or too short-lived effectiveness. Given that there is no positive clinical effect, risk and burdens outweigh the benefit	Negative recommendation
2 B−	One or more RCTs with methodologic weaknesses, or large observational studies that do not indicate any superiority to the control treatment. Given that there is no positive clinical effect, risk and burdens outweigh the benefit	Negative recommendation
2 A−	RCT of a good quality which does not exhibit any clinical effect. Given that there is no positive clinical effect, risk and burdens outweigh the benefit	Negative recommendation

RCT, randomized controlled trial.

Although there are still many questions as to the underlying mechanisms, peripheral as well as central neuronal mechanisms seem to be involved.[8] There are also indications that neuroplastic changes take place including changes of the cortical representation.

Peripheral input can play a part in the perception of phantom pain. When peripheral nerves are cut or injured, regenerative sprouting of the injured axon occurs. The enlarged and disorganized endings of C fibers and demyelinated A-fibers show an increased rate of spontaneous activity. Spontaneous and abnormal activity has been perceived in neuromas at the nerve endings and in the spinal ganglia after peripheral mechanic or chemical stimulation as a consequence of up-regulation of the sodium channels. Ectopic discharge in the dorsal root ganglion has also been implicated as a potential mechanism. Ectopic discharge may be induced by emotional distress leading to increased circulating levels of epinephrine. Factors such as temperature, oxygenation, and local inflammation may play a role. Therefore, the sensitivity of these neuromas or ganglia may increase due to epinephrine or stress, in combination with increasing norepinephrine from sympathetic efferents, which are located in close proximity to afferent sensory nerve cells, for example in the case of sprouting. This results in exacerbation of phantom pain. Peripheral factors may be of varying importance in the origin and modulation of phantom limb pain, but also central factors play must play a role.[9]

The spinal cord may be involved as well. Changes in activity levels in neuromas and ganglia may result in long-term adaptations in the central projecting neurons in the posterior horn. This may lead to spontaneous neuronal activity, changes in RNA transcription, increased metabolic activity in the spinal cord and may cause the receptive fields to enlarge; all these factors result in central (spinal) sensitization.

Apart from functional changes, anatomical changes have been observed as well. Afferent C fibers of lamina II in the spinal cord may degenerate, so that the number of synapses with second-order neurons diminishes. Therefore, Aβ mechano-sensitive afferents, normally present in deeper layers, may connect with the exposed nociceptive second-order neurons within lamina II which may induce sprouting of A-fiber terminals in these areas, where they are normally not represented. The incoming A-fiber input might then be interpreted as noxious and could be the anatomical substrate of allodynia. In this way, normal stimuli through Aβ neurons may lead to other sensations, such as pain. Eventually, neuroplastic changes will occur in the thalamus in subcortical and in cortical structures. It becomes clear that there is a relationship between the spinal cord and higher centres in cases where pain-free amputees had transient phantom pain after spinal anesthesia, while conversely patients with phantom pain became pain free after a focal cerebral infarction or a spinal cord lesion.

An especially relevant mechanism may be the invasion of regions of the spinal cord where the amputated limb was previously represented. Neuropeptides such as Substance P, normally expressed by nociceptor primary afferent Aδ- and C fibers may also become expressed by Aβ-fibers after peripheral nerve injury. Supraspinal changes related to phantom limb pain involve the brainstem, the thalamus and the cortex.[9]

Changes in the functional and structural architecture of primary somatosensory cortex after amputation and deafferentation in adult monkeys are demonstrated. Reorganizational changes in the sensory and motor maps were shown. Also in people with arm or hand amputations a shift of the mouth into the hand representation in primary somatosensory cortex was illustrated. The larger the shift of the mouth representation into the zone that formerly represented the amputated hand and arm, the greater the phantom limb pain.

Reorganization of the motor system was limited to the cortex; spinal changes were not observed. Thalamic stimulation and recordings in amputees have shown that reorganizational changes also occur at the thalamic level and are closely related to the perception of phantom limbs and phantom limb pain.[9] The loss of a limb may have a substantial psychological impact. Fear, depression and anger may follow sorrow and may affect the pain. Depression is a significant predicting factor for severe pain and distress.[10] Just as in other chronic pain syndromes, psychosocial factors play a potential part in prolonging the pain, but specific psychological factors related to amputation appear to have a minor role in this respect. However, studies have shown that patients with phantom pain are more likely to be rigid and show more controlling behavior.

I. DIAGNOSIS

I.A HISTORY

Most patients with phantom pain have intermittent pain, with intervals that range from 1 day to several weeks. Even intervals of over a year have been reported. Pain often presents itself in the form of attacks that vary in duration from a few seconds to minutes or hours. Patients usually describe the pain as shooting, stabbing, piercing, cramping, pinching, or burning. In most cases, the pain is experienced distally in the missing limb, in places with the most extensive innervation density and cortical representation. Examples are fingers or toes.[11]

Phantom pain often begins within 14 days after the amputation. Half of the patients, however, suffer from pain within the first 24 hours after amputation. Some patients will not have pain until several years after amputation; however, phantom pain only becomes manifest a year after the amputation in fewer than 10% of the cases. Two years after the onset of the phantom pain, the prevalence of phantom pain has hardly decreased.

Some studies suggest a relationship between phantom limb pain and the etiology of amputation, while other studies could not indicate a relationship between the patient's general health status and the incidence.[11] Two recently published studies tried to identify if gender has an influence on the occurrence of phantom pain.[12,13] The longitudinal study over 3½ years reveals that men are less prone to experience phantom pain than women. Phantom pain occurs more after arm amputation than after leg amputation.[12] Phantom pain occurs almost immediately after surgery.[14] A postal survey in persons with limb loss, on the contrary, showed that a greater proportion of males reported phantom limb pain. This difference disappeared when corrected for the cause of amputation. Several sex differences in the overall biopsychosocial experience of pain did emerge.[13] Phantom limb pain does not seem to depend on the nature of the cause: surgical or traumatic.[15] In children and in people who have been missing a limb from birth, the incidence of phantom pain is lower. Phantom pain is more common in cases of bilateral amputation, amputation of the legs and in cases where the limb was amputated in a more proximal site.[16]

There are indications that severe pre-amputation and postoperative pain are risk factors for chronic phantom pain.[17] However, the literature reports contradictory results in this respect. It is also unclear whether pre-amputation pain is experienced as the same pain that is felt after amputation as phantom pain: on the one hand retrospective results have been reported, where the number of cases in which pre-amputation pain is experienced as phantom pain, ranges from 12.5% to 80%, whereas a prospective study by Nikolajsen et al.[18] does not show a relationship.

Phantom pain has also been described in parts of the body other than the limbs. Phantom pain after mastectomy occurred in 9 of 39 patients with a bilateral mastectomy, phantom sensations in 20 of 39 patients.[19] Phantom pain has also been described in a quarter of patients who underwent enucleation of the eye after which orbital implants had been inserted. The risk in these patients may have been increased by perioperative headaches and pain in the eye.[20] Tinnitus is presumably related to phantom pain as well, due to changes in the afferent input in the auditory, central neural system caused by axonal sprouting and hyperexcitation.[21] Recent rat studies performed by Tritsch et al.[22] point to the role of supporting cells in the middle ear: when exposed to loud noises, adenosine tri phosphate may be released by supporting cells and thus stimulate hair cells, even though the sound stimulus has disappeared. Process changes in tonotopic receptive fields within auditory structures such as the dorsal cochlear nucleus, inferior colliculus nucleus, and auditory somatosensory areas may also be involved in central neuroplastic changes.

Phantom sensations are painless sensations such as sensations of heat, tingling, telescoping (notably in fingers or toes) and the sensation that the limb becomes shorter over time. Approximately 50% of the amputees have stump pain as well, while 50% to 88% of the patients with phantom pain also suffer from stump pain. In many cases myofascial trigger points are present in the stump that can evoke phantom sensations and phantom pain.[23]

I.B PHYSICAL EXAMINATION

As yet physical examination is not very useful in cases of phantom pain, because the pain is localized in the missing body part and the pain mechanisms predominantly involve the peripheral and the central nervous system.

In stump pain, however, there is clearly a local pain source. For example, in 20% of phantom pain patients skin pathology and circulatory disorders, infections and neuromas may prolong the disorder. Local trigger points may be localized in the stump, especially in patients who have a prosthesis. These trigger points may provoke phantom pain.

I.D DIFFERENTIAL DIAGNOSIS

Phantom pain is a painful sensation in a part of the body that is no longer present. Stump pain is pain in the remaining stump where the source of the pain is in the stump itself. Phantom sensations: any form of painless sensation that the patient experiences in the part of the body that is no longer present.

In over half of patients, the phantom pain decreases or disappears over time. In cases where the pain is exacerbated special causes should be sought. Apart from changes in autonomous regulation or sympathicotonia due to temperature or weather changes, radicular pain (because of a nucleus pulposus hernia or radiculitis), angina (in cases of pain in the upper phantom limb), and malignant growths (metastasis) may provoke symptoms that may be taken for phantom pain. Infections with herpes zoster (shingles) should also be considered, especially in patients with reduced immunity.

II. TREATMENT OPTIONS

Phantom pain is generally quite therapy resistant. Treatments of phantom pain are rarely successful. In their review article Nikolajsen and Jensen point out that a literature search performed in 1980 identified 68 different treatment methods of which 50 are still in use.[11] Although many caregivers present more favorable reports of their results, fewer than 10% of patients indicate permanent pain relief. The various systematic reviews that have been published indicate that most treatments have no or only limited succes.[24–26] In addition, there are only a few sound studies that deal with phantom pain specifically. Since the systematic review of Sherman[26] was published in 1980, no groundbreaking therapeutic developments have been reported, and the systematic review by Halbert et al.[25] shows that epidural analgesia, regional nerve blocks, treatment with calcitonin, or ketamine do not provide any consistent results. There are, however, three positive studies that show that nerve blocks could have some effect. The analgesic effectiveness of transcutaneous electrical nerve stimulation for the treatment of phantom and/or stump pain was assessed in a Cochrane review. No randomized controlled studies (RCTs) were found thus preventing any conclusions.[27]

However, even if there are still many questions that remain open, there is greater insight into the underlying mechanism of phantom pain. It has been suggested that the focus of treatment should be specifically aimed at preventing chronicity by intervening sooner with respect to the structural and functional changes in the central and peripheral nervous system; these changes are a consequence of the deficient or detrimental somatosensory input and deafferentation after amputation. Unfortunately, in this respect the results of pre- and postoperative epidural blocks are ambiguous. There is much to be learnt about effective interventions with respect to neuroplasticity. It seems that a multimodal approach is essential, in which nociception, inflammation, hormonal, physiological, and mental changes all play an important part. Adequate information, proper surgical indications and techniques for amputation, if possible effective mental preparation and aftercare, long-term rehabilitation and optimum pain treatment are integral elements.

Another problem is that not all phantom pain patients receive treatment. A study by Hanley et al.[28] shows that 53% of patients with phantom pain (n = 183), 38% of whom with a severe form of phantom pain, never received treatment for the disorder. Those who did receive treatment suffered from severe pain and experienced considerable distress from the disorder. These patients were mostly treated with analgesics: paracetamol, morphine-like substances and non-steroidal anti-inflammatory drugs. In the perception of the patients, only opioids and chiropractic therapy were effective to some extent.

II.A CONSERVATIVE MANAGEMENT

Drug Therapy

Because phantom limb pain is classified as neuropathic pain, an approach to the pharmacological treatment according to published guidelines could be envisioned. Little is known, however, about the specific effectiveness of these medications in phantom pain. In a study by Wilder-Smith et al.,[29] tramadol as well as amitriptyline appear to be more effective than placebo treatment in phantom pain patients. Although the benefit of amitriptyline was not supported in a recent randomized placebo controlled trial of 39 patients,[30] carbamazepine, one of the older drugs used to treat neuropathic pain, proved to have favorable effects.[31,32] Studies that compared gabapentin with placebo did not show a difference for amputation patients with respect to the incidence and intensity of the phantom pain.[33] Another study, however, did demonstrate diminished pain intensity with gabapentin in comparison to placebo patients.[34]

A prospective study in 42 cancer patients assessed the value of treatment according to the World Health Organization analgesic ladder and found that the addition of opioids to antidepressants and anticonvulsants reduces the incidence of phantom pain from 60% 1 month post surgery to 32% 2 years after amputation.[35]

Oral morphine was compared to placebo in a double-blind crossover study in 12 patients with unilateral arm or leg amputation with phantom pain. The results suggested that pain was improved with oral morphine, with a concurrent potential reduction in cortical reorganization as determined by magnetoencephalographic recordings.[36]

A comparison between intravenous lidocaine and morphine in 31 patients with postamputation pain (either phantom pain combined with stump pain or phantom pain or stump pain exclusively) showed that stump pain responds well to both treatments, whereas phantom pain could only be relieved by morphine.[37] A recent randomized controlled crossover trial in patients with postamputation pain of 6 months or longer, having a pain intensity of at least 3 on a 10 point numeric rating scale, compared the efficacy of morphine, mexiletine and placebo. Therapy with morphine but not mexiletine resulted in a decrease in intensity of postamputation pain but was associated with higher rates of side effects and no improvement in self-reported levels of overall functional activity and pain-related interference in daily activity.[38]

In one RCT where intravenously administered ketamine was compared with placebo, pain and hyperalgesia decreased in patients with stump pain and phantom pain with ketamine in comparison with the control patients.[39] Conversely, in a placebo controlled RCT memantine, another *N*-methyl-D-aspartate receptor antagonist, proved not to be effective,[40–42] while more recent case reports continue to anecdotally support its use.[43] Benzodiazepines do not seem to be effective in cases of phantom pain. The effects of other drugs such as beta-blockers, calcitonin and capsaicin and mexiletine are anecdotal as yet.

Calcitonin, ketamine and their combination were tested in a randomized, double-blind crossover study for the management of chronic phantom limb pain. Ketamine, but not calcitonin, reduced phantom limb pain. The combination was not superior to ketamine alone.[44] Perioperatively ketamine maintained for 72 hours compared to placebo administration did not result in significant differences in subsequent postamputation pain severity over a 6-month period.[45]

The inflammatory cytokine tumor necrosis factor-alpha (TNF-α) plays an important role in neuropathic pain conditions; systemic drugs that block TNF-α alleviate pain and pain-related behavior. A report of six patients with phantom limb pain who were treated with a series of perineural injections of etanercept, a TNF-α antagonist, describes a significant improvement in 5 of 6 patients' residual limb pain at rest and with activity, phantom limb pain, functional capacity, and psychological well-being 3 months after injections.[46]

II.B INTERVENTIONAL MANAGEMENT

Epidural anesthesia, applied before, during or after amputation, seems to decrease the severity of phantom pain while the actual incidence does not decrease at all.[47] Various studies have examined the effectiveness of epidural anesthesia. Unfortunately, these studies have different designs and the results are variable and inconsistent.

Many studies have been performed examining pre- and postoperative nerve blocks, with and without catheter techniques. Lambert performed a randomized prospective study comparing preoperative epidural and intraoperative perineural analgesia for the prevention of postoperative stump pain and phantom limb pain and found preoperative epidural block 24 hours before amputation was not superior to intraoperative perineural infusion of local anesthetic in reducing phantom limb pain up to 1 year later, but was more effective in reducing immediate postoperative stump pain.[48] In spite of early pain reduction, the results for patients treated were no better than control patients and the same applied to the patients treated with epidural anesthesia. Favorable results that have been reported are mainly based on case reports.

The use of echographic controlled phenol instillation into neuroma was prospectively assessed in 82 patients. All patients had marked improvement and 12% were pain free after 1 to 3 instillations. The low complication rate (5% minor and 1.3% major complications) is attributed to the use of high resolution sonography.[49] Pre- peri- and postoperative continuous nervus ischiadicus (sciatic) block was assessed in 18 patients who were prospectively followed for 24 months. In this population, an incidence of phantom pain of 25% to 30% was observed.[50]

A case report on a patient with phantom pain treated with pulsed radiofrequency (PRF) of the n. ischiadicus showed pain relief and reduction of the need of analgesic medication for 4 months.[51] Another patient underwent pulsed radiofrequency of the proximal and distal ends of a sciatic neuroma with treatment at 42°C for 120 seconds under ultrasound guidance with VAS reduction of 90%, 90%, and 70% at 1, 3, and 6 months, respectively.[52] Two patients with primarily stump pain after lower limb amputation and difficulty tolerating the limb prosthesis were treated with PRF adjacent to the L4-L5 dorsal root ganglion. Both patients experienced at least 50% pain reduction for 6 months and tolerated better the prosthesis.[53]

The long-term effect of spinal cord stimulation in a patient with complex regional pain syndrome (CRPS) after two amputations of the right leg has been reported.[54] Katayama et al. investigated spinal cord stimulation, deep brain stimulation of the thalamic nucelas ventralis caudalis, and the motor cortex for treatment of phantom limb pain. Of the 19 patients, six had long-term pain control with spinal cord stimulation, defined as at least 80% pain reduction for at least 2 years.[55] More recently, a case series of four patients with postcancer resection lower extremity phantom limb pain experienced > 80% pain reduction immediately postoperatively, while only 75% had statistically significant reduction in VAS and total symptom score at a minimum of 8 months follow-up.[56]

Other invasive treatments have often been applied as well, including stump injections, trigger point injections, blocks of the sympathetic nervous system and intrathecal injections. In the case of myofascial trigger points, injections with botulinum A have been described. In several of these case studies, a reduction of the pain by 60% to 80% was claimed. In the 1980s, lesions in the dorsal root entry zone were applied. However, no long-term favorable results based on good quality studies have been mentioned in the literature since.

Other Forms of Therapy

Neuroimaging studies could indicate a cortical reorganization that may influence phantom limb pain. Animal work on stimulation-induced plasticity suggests that extensive behaviorally relevant stimulation of a body part leads to an expansion of its representation zone.[57] These observations have led to the development of treatment strategies based on active stimulation of the phantom limb. The use of myoelectric prosthetics was positively associated with both less phantom limb pain and less cortical reorganization.[58] A recent sham controlled crossover trial showed that mirror therapy is better than mental visualization or covered mirror therapy.[59]

Cases have been described in which mirror therapy was applied with success. The principle of this treatment is based on the idea that the central representation of the missing hand of the phantom could be recovered. This could relieve or eliminate the phantom pain.[60] The added value of the "virtual limb" was studied in a randomized controlled trial where patients who had undergone lower limb amputation were studied before, during and after repeated attempts to simultaneously move both intact and phantom legs. Subjects were randomly assigned to a condition in which they only viewed the movements of their intact limb (control) or a mirror condition in which they additionally viewed the movements of a "virtual limb". The mirror condition elicited a significantly greater number of phantom limb movements than the control condition. Both conditions resulted in a significant attenuation of phantom sensations and pain. Both, the control and the mirror condition reduced phantom limb pain. The use of mirror condition as a prolonged treatment of phantom limb pain may be favorable because a significantly greater number of phantom limb movements may reverse the chronic cortical reorganization.[61]

Some case reports with favorable results from the application of deep brain stimulation have been described. Patients with phantom pain appear to respond favorably. Here, the periventricular gray matter is treated by electrostimulation, in some cases in combination with the somatosensory thalamus. This technique is reported to have been especially effective in reducing the burning pain, the use of opioids, and improving the quality of life.[62] In another study 38 of 47 patients responded favorably to the experimental stimulation. Fifty-three percent of them had a lasting favorable effect from stimulation of the gray matter around the aqueduct, 13% from stimulation of the thalamus and 34% from stimulation of both these structures.

Some studies examining the application of transcranial magnetic stimulation show that this treatment has an inadequate effect on phantom pain.

Preventive Strategies

Theoretically the preventive strategy should be built upon two main pillars: surgical technique and pre-emptive analgesia. Despite the obligatory transection of major nerves in leg amputation, no attention has been paid in phantom limb studies to intra-operative handling of the nerves. This lack of attention is particularly surprising given that various nerve ligature models have been used to study chronic neuropathic pain in experimental studies. A survey among Danish orthopedic surgeons showed a surprisingly high use (about 30%) of ligation of the large diameter nerves during leg amputation[63] which, according to experimental preclinical data, may precipitate the development of chronic neuropathic pain.[64] Major orthopedic textbooks recommend ligation of the nerves during amputation. Since a clean nerve cut may lead to less persistent pain compared to a ligature or crush nerve injury, there is an urgent need for clinical studies investigating the role of nerve handling as a risk factor for phantom limb pain after limb amputation.[64]

Several pre-emptive analgesic strategies have been tested with variable results. Detailed discussion of these findings is beyond the scope of this review. It must, however, be stressed that a multimodal approach seems to generate better outcome. Such a multimodal approach can consist of: psychological counseling and treatment; cognitive behavioral therapy and pharmacological treatment using molecules with different mode of action in order to target the different mechanisms of phantom pain.[3,65]

A recently published series of case reports suggests that preventive mirror therapy reduces phantom limb pain.[66]

II.C COMPLICATIONS OF INTERVENTIONAL MANAGEMENT

In a review on the available literature regarding PRF over more than 1,200 patients no side effects have been reported.[67]

The potential complications of spinal cord are described in the article on CRPS.[68]

Table 2. Evidence for Interventional Management of Phantom Pain

Technique	Evaluation
Pulsed radiofrequency treatment of the stump neuroma	0
Pulsed radiofrequency treatment adjacent to the spinal ganglion (DRG)	0
Spinal cord stimulation	0

II.D EVIDENCE FOR INTERVENTIONAL MANAGEMENT

The summary of the evidence for interventional management of lumbosacral radicular pain is given in Table 2.

III. RECOMMENDATIONS

Based on the available evidence with respect to phantom pain the following recommendations can be made:

Initially phantom pain should be treated with drugs. PRF treatment and spinal cord stimulation can be considered, but should only take place within an experimental framework.

III.A CLINICAL PRACTICE ALGORITHM

Figure 1 represents the treatment algorithm for phantom pain.

III.B TECHNIQUES

For PRF treatment the neuroma can be identified by means of ultrasound, thus allowing precise needle placement.

The technique of spinal cord stimulation is described in the article on CRPS.[68]

Summary

The number of cases of phantom pain after amputation ranges from 60% to 80%. Over half the patients with phantom pain have stump pain as well. Myofascial trigger points often occur in stump pain. There are indications that neuroplastic changes also occur,

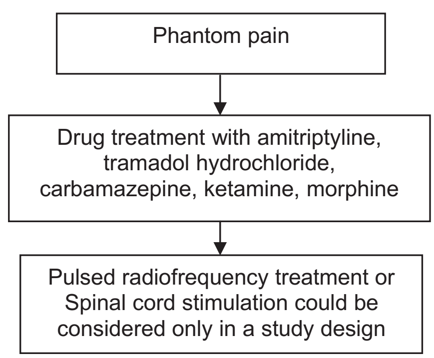

Figure 1. Treatment algorithm for the management of phantom pain.

including changes in cortical representation. Generally, phantom pain is fairly therapy resistant. Results reported in literature relating to the effectiveness of the interventional treatment are inconsistent. In the long term, these treatments are not very effective. Based on the available evidence some effect may be expected from drug treatment. PRF and spinal cord stimulation can only be considered in a study design.

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