Original article

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A stage-based approach to pain syndrome management in patients with warfare injuries to the peripheral nerves of the extremities

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Objective: To develop a stage-based treatment algorithm for pain syndrome in patients with warfare injuries to the peripheral nerves of the extremities and to determine the optimal timing for surgical intervention on peripheral nerves through analysis of the literature and our own clinical data.

Materials and methods: Pain management outcomes were analyzed in 1,053 patients with peripheral nerve injuries sustained during warfare. All patients underwent clinical and ultrasonographic examination, and pain intensity was assessed using the Visual Analogue Scale (VAS). Patients were divided into two treatment groups: primary conservative treatment and primary surgical treatment. The primary conservative treatment group included 265 patients who were managed using conservative methods (pharmacotherapy, nerve hydrodissection, administration of steroid anti-inflammatory agents, platelet-rich plasma injections, or botulinum toxin). The primary surgical treatment group comprised 788 patients with warfare injuries to the peripheral nerves of the extremities who required surgical nerve repair, including patients with painful neuromas after limb amputations. Pain intensity (VAS) was reassessed at 1, 3, 6, and 12 months after treatment.

Results: Conservative treatment demonstrated satisfactory outcomes in cases of mild pain syndrome with maintained positive dynamics during the first month from treatment initiation. Surgical treatment of warfare injuries to peripheral nerves resulted in a stable and predictable effect in the majority of cases. However, in the long-term follow-up period, some patients experienced worsening of regenerative pain during skeletal muscle reinnervation. Patients with painful neuromas represented the most challenging subgroup, as pain in these cases was typically chronic and difficult to manage.

Conclusions: Patients with warfare injuries to the peripheral nerves of the extremities should undergo ultrasound examination. In the absence of nerve compression or irritation and with preserved anatomical continuity, treatment should begin with pharmacotherapy; if necessary, nerve hydrodissection or injection therapy with steroids or botulinum toxin may be performed. In cases of significant compression, nerve disruption, or lack of effect after conservative treatment within 6 weeks, surgical intervention is recommended.

Key words: *pain, nerve, warfare injury, neurolysis, nerve grafting, targeted muscle reinnervation (TMR), regenerative peripheral nerve interface (RPNI).*

The distinctive features of modern warfare, characterized by the deployment of advanced military technologies, the predominance of artillery, and the extensive use of FPV drones, determine the severity and polystructural nature of combat injuries. The rapid increase in high-energy shrapnel and blast injury significantly complicates the provision of medical care, particularly the restoration of anatomical structures and functional capacity of the limbs.

According to the Department of Statistics of the National Military Medical Clinical Center "Main Military Clinical Hospital," between February 2022 and June 2023, combat-related limb injuries accounted for approximately 69% of all injuries, of which 85% were polystructural lesions. Regarding distribution between upper and lower extremities, combat injuries of the lower limbs slightly predominated (55%). Gunshot wounds involving only soft tissues were registered in 65–68% of patients; in two-thirds of these cases, they were accompanied by tissue defects (36–38% small and medium defects; 29–31% large and extensive defects). According to our data, between April 2014 and October 2025, approximately 32% of patients were diagnosed with gunshot injuries to the peripheral nerves of the extremities.

It is known that in cases of gunshot injury to a peripheral nerve, approximately 26% of patients become

disabled due to persistent neuropathic pain and loss of limb function. Reports from the National Health Service of Ukraine indicate that more than 90,000 limb amputations were performed between 2022 and 2024, many of which may have been complicated by the development of phantom limb pain or painful neuromas. According to various authors, among traumatic limb amputations caused by combat injuries, lower limb lesions predominate, with blast injury being the most common etiological factor.

Currently, clinicians have at their disposal a wide range of modalities for pain management, including contemporary multimodal anesthesia approaches, placement of perineural catheters and anesthetic infusion pumps, as well as surgical interventions aimed at reconstructing painful neuromas or implanting neurostimulators. Despite the clinical relevance of the problem and the availability of numerous therapeutic options, there is no universally accepted comprehensive approach to the management of pain syndrome in patients with gunshot injuries to the peripheral nerves of the extremities.

Objective: To develop a stage-based treatment algorithm for pain syndrome in patients with warfare injuries to the peripheral nerves of the extremities and to determine the optimal timing for surgical intervention on peripheral nerves through analysis of the literature and our own clinical data.

Materials and methods

Study participants

The treatment outcomes of pain syndrome in 1,053 patients (1,006 men and 47 women; mean age 34.1 ± 8.2 years) with gunshot injuries to the peripheral nerves between April 2014 and October 2025 were analyzed.

The study was approved by the Bioethics Committee of the Institute of Traumatology and Orthopedics of the National Academy of Medical Sciences of Ukraine (Minutes No. 1 dated January 19, 2026). The research was conducted in accordance with the bioethical principles of the Helsinki Convention of the Council of Europe on Human Rights and Biomedicine, as well as relevant legislation of Ukraine. The patient information sheet clearly outlined all study provisions and measures aimed at ensuring patient health protection, respect for human rights, dignity, and ethical standards. Written informed consent was obtained from all participants.

Inclusion criteria

The inclusion criteria were as follows: gunshot injury to the extremities sustained between April 2014 and October 2025; gunshot injury to the peripheral nerves of the extremities; presence of pain syndrome.

Exclusion criteria

The exclusion criteria included: non-gunshot peripheral nerve injury associated with combat-related limb trauma (e.g., injuries caused by external fixation device pins or tourniquet syndromes); absence of pain syndrome; follow-up period of less than 12 months.

Study design

All patients underwent clinical and ultrasonographic examination (***Fig. 1***). When indicated, radiography or computed tomography of the affected segment was performed. Baseline pain intensity was assessed using the Visual Analogue Scale (VAS): 0 cm — no pain; 1–3 cm — mild pain, occasionally requiring additional correction and generally not interfering with daily activities; 4–6 cm — moderate pain syndrome, potentially requiring additional pharmacological management and causing some discomfort, but tolerable during daytime; 6 cm — severe persistent pain requiring continuous medical treatment, significantly reducing quality of life and, in many cases, serving as an indication for surgical intervention. Depending on diagnostic findings, patients were divided into two groups: those receiving primary conservative treatment and those undergoing primary surgical treatment. Pain intensity according to the VAS was reassessed at 1, 3, 6, and 12 months after treatment. Through telephone follow-up, treatment outcomes were obtained for 683 patients (approximately 64.9%).

The advantages and disadvantages of each treatment modality, as well as their role in the management of pain syndrome in gunshot-related peripheral nerve injuries of the extremities, were analyzed.

Group characteristics

The primary conservative treatment group comprised 265 patients (246 men and 19 women; mean age 35.2 ± 6.5 years). In this cohort, conservative pain management strategies were employed, including medications containing the active substances lornoxicam, pregabalin, and antidepressants from the class of serotonin–norepinephrine reuptake inhibitors. Ultrasound-guided nerve hydrodissection was performed in cases where fibrotic tissue surrounded the nerve but did not preclude its visualization. Additional interventions included the administration of steroidal anti-inflammatory agents, platelet-rich plasma (prepared with a predominance of anti-inflammatory factors), and botulinum toxin. In the absence of a satisfactory response to conservative therapy (40 cases; 15.1%), patients were recommended for appropriate surgical intervention.

The primary surgical treatment group included 788 patients (760 men and 28 women; mean age 33.6 ± 9.0 years):

- 732 patients (704 men and 28 women; mean age 36.2 ± 10.2 years) with gunshot injuries to the peripheral nerves of the extremities requiring surgical repair (***Fig. 2***);

- 56 patients (all men; mean age 30.9 ± 7.8 years) with post-amputation sequelae following gunshot trauma, who developed pain syndrome due to the formation of painful neuromas (***Fig. 3***).

Approximately 53.1% of gunshot-related peripheral nerve injuries were associated with a primary nerve defect and required autoneuroplasty.

Statistical analysis

Statistical analysis was performed using standard descriptive statistical methods. Continuous variables are presented as the arithmetic mean (*M*) and standard deviation (*SD*). Comparisons between baseline (pre-treatment) values and those obtained at one year were conducted using the paired t-test. A p-value < 0.05 was considered statistically significant.

This article contains some figures that are displayed in color online but in black and white in the print edition

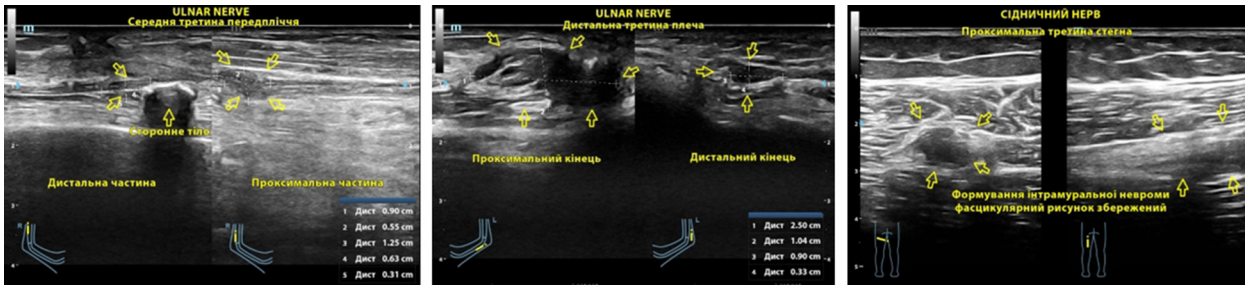

Fig. 1. Ultrasonographic patterns of various types of gunshot injuries to peripheral nerves

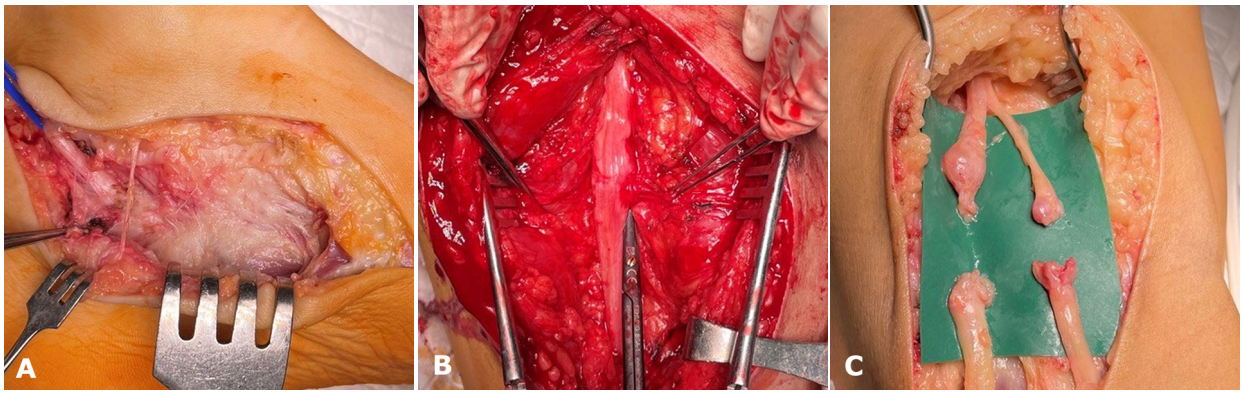

Fig.2. Principal types of gunshot injury to peripheral nerves: (a) nerve compression resulting from fibrotic degeneration of the mesoneurium;(b) formation of a fibrotic band (a zone of peripheral nerve fixation) preventing normal nerve gliding and leading to ischemia;(c) anatomical injury—complete nerve transection with a defect of the nerve tissue

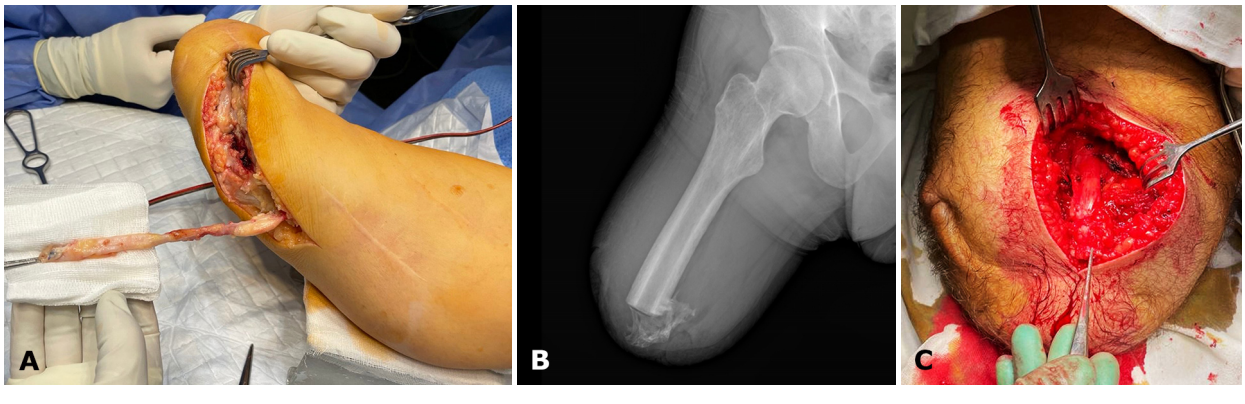

Fig. 3. Key factors contributing to the transformation of a neuroma into a painful neuroma: (a) nerve stump compression (by a ligature or fixation device); (b) nerve irritation (e.g., by a bony exostosis); (c) absence of visible irritation or compression (a possible autoimmune response cannot be excluded)

Results

In patients presenting with pain syndrome following gunshot injuries to peripheral nerves, conservative treatment was proposed as the first-line approach under the following conditions: preserved nerve continuity (according to ultrasonographic findings), absence of significant nerve compression or intraneural structural disruption, and involvement limited to superficial cutaneous branches of peripheral nerves. Management was initiated with pharmacological pain control. In the absence of clinical improvement, ultrasound-guided hydrodissection of the nerve trunk was performed (in cases of compression by fibrotically altered tissues), or injections of platelet-rich plasma (for mild pain syndrome) or a steroidal anti-inflammatory agent (for more pronounced pain syndrome) were administered. If a positive response to platelet-rich plasma or steroidal anti-inflammatory injection was observed but without substantial pain reduction, botulinum toxin injection was performed under conduction anesthesia or general sedation. In our study, platelet-rich plasma injections demonstrated only a modest positive effect.

If peripheral nerve injury was confirmed or if conservative treatment proved ineffective within 6 weeks, surgical intervention was undertaken. The procedures included peripheral nerve neurolysis (33.7% of cases), nerve suturing (10.5%, provided that tension-free approximation was feasible and adjacent joints demonstrated full passive mobility), and peripheral nerve autoneuroplasty (55.8%).

In all patients undergoing peripheral nerve surgery, lipofilling was performed using a mixture of aspirated subcutaneous adipose tissue and red bone marrow to restore the paraneural adipose cuff.

In patients with pain syndrome resulting from the formation of painful neuromas, the following surgical procedures were performed: neuroma resection with transposition of the nerve into deeper tissues (21.4% of cases); regenerative peripheral nerve interface (RPNI) creation (60.7%)—wrapping groups of fascicles of a mixed nerve with small fragments of denervated free skeletal muscle (***Fig. 4***); and targeted muscle reinnervation (TMR) (17.9%)—coaptation of the mixed nerve forming the painful neuroma to a motor nerve innervating the skeletal muscle of the residual limb (***Fig. 5***).

Neuroma resection with transposition reduced pain only during the acute postoperative period; however, recurrence of pain was observed later (up to 6 months), in some cases with increased intensity. Consequently, the majority of these patients required repeat surgical intervention.

In the postoperative period, all patients received multimodal analgesia (placement of a perineural catheter or anesthetic pump), pharmacological therapy with nonsteroidal anti-inflammatory drugs (lornoxicam), and anti-edema therapy (dexamethasone). This approach made it possible to avoid the use of opioid analgesics in the postoperative period.

Discussion

According to the data presented in ***Table 1***, pain reduction following treatment in patients with gunshot injuries to peripheral nerves was statistically significant across all treatment modalities ($p < 0.05$).

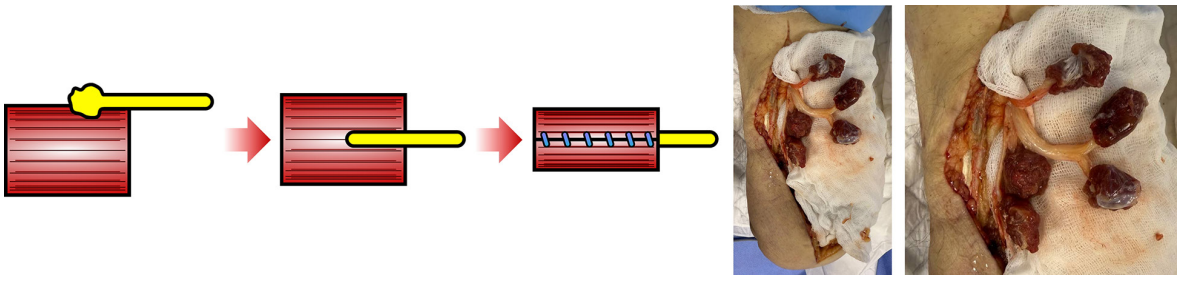

Fig. 4. Formation of a regenerative peripheral nerve interface (RPNI)

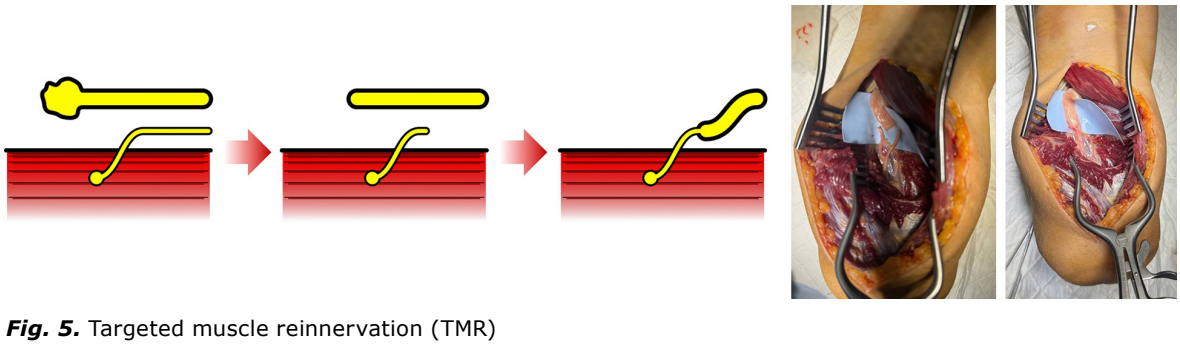

Fig. 5. Targeted muscle reinnervation (TMR)

Table 1. Assessment of pain intensity according to the VAS, depending on the treatment modality, cm

Treatment modality	Before treatment	In 1 month	In 3 months	In 6 months	In 12 months	p-value
Pharmacological therapy, n=99	2,2 ± 0,9	1,6 ± 0,8	1,2 ± 0,7	1,1 ± 0,5	1,1 ± 0,4	< 0,0001
Hydrodissection, n=29	3,9 ± 1,1	1,9 ± 0,2	1,6 ± 1,2	1,8 ± 1,3	1,9 ± 1,1	< 0,0001
Injection therapy, n=44	4,3 ± 1,3	1,1 ± 0,4	1,4 ± 1,1	1,7 ± 1,5	1,6 ± 1,9	< 0,0001
Neurolysis, n=161	5,6 ± 2,1	4,7 ± 1,5	4,2 ± 1,7	2,1 ± 1,1	1,8 ± 1,2	< 0,0001
Nerve reconstruction, n=315	4,2 ± 1,1	1,2 ± 0,6	2,1 ± 0,8	1,6 ± 1,0	2,1 ± 0,9	< 0,0001
Neuroma transposition, n=8	6,3 ± 2,1	1,1 ± 0,4	3,4 ± 2,1	4,6 ± 1,8	2,2 ± 1,5	0,0004
RPNI, n=22	6,7 ± 1,7	1,2 ± 1,4	1,4 ± 1,1	2,1 ± 1,6	2,2 ± 0,9	< 0,0001
TMR, n=7	6,2 ± 1,6	1,1 ± 0,8	1,1 ± 1,2	1,5 ± 0,6	2,1 ± 1,2	0,0003

Conservative management provided satisfactory results in cases of mild pain syndrome, particularly when a positive clinical trend was observed during the first month of treatment (***Fig. 6***). Pharmacological therapy as a standalone modality should be considered the first-line treatment in patients with mild pain intensity (up to 3 cm on the VAS) and as baseline therapy in combination with hydrodissection, injection-based interventions, or during the early postoperative period. Hydrodissection in cases of fibrotic compression of a peripheral nerve significantly alleviated pain in the early postoperative period; however, pain intensity could increase over time, necessitating repeated procedures. Injection therapy demonstrated a good analgesic effect, although gradual exacerbation of pain was observed in some cases, potentially requiring repeated injections or subsequent surgical intervention.

In our study, the use of platelet-rich plasma resulted only in modest and temporary improvement; in 8% of cases, it led to a marked increase in pain intensity, which may be attributed to differences in preparation techniques and a predominance of pro-inflammatory factors. Botulinum toxin injections produced a sustained positive effect; however, recurrence of pain was frequently observed in the long-term follow-up period.

Surgical management of gunshot injuries to peripheral nerves generally produced a stable and predictable outcome in most cases. However, in the long-term follow-up period, an increase in pain intensity may be observed due to the development of regenerative pain associated with reinnervation of skeletal muscles (***Fig. 7***).

Overall, peripheral nerve neurolysis is characterized by a progressive but gradual reduction in pain intensity over a period of up to 6 months following surgery. Peripheral nerve reconstruction (either direct nerve suturing or autoneuroplasty) may lead to a marked reduction in pain during the early postoperative period as a result of neuroma resection. Nevertheless, in the long-term period, regenerative pain originating from reinnervated muscles, as well as neuroma formation at the nerve suture site, may occur. These changes can provoke pain and paresthesia upon mechanical irritation.

The most challenging cohort for treatment comprises patients with painful neuromas, as pain associated with such neuromas is typically chronic and resistant to therapy (***Fig. 8***).

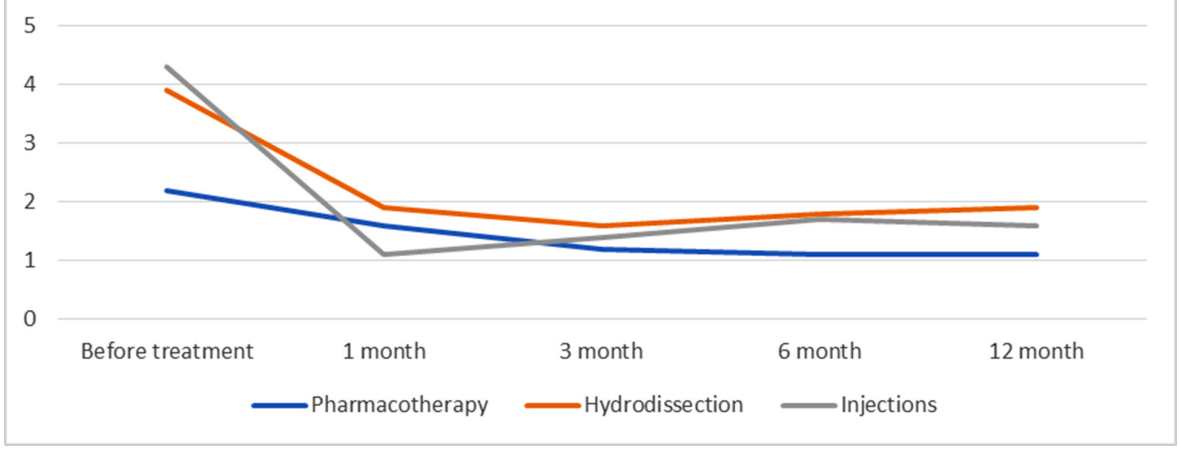

Fig. 6. Dynamics of pain intensity depending on the method of conservative treatment

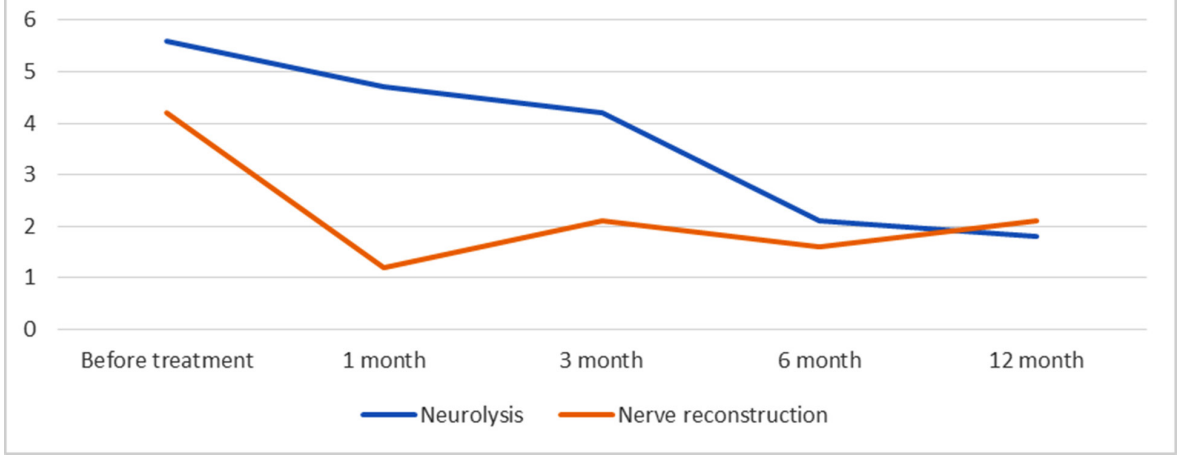

Fig. 7. Dynamics of pain intensity depending on the method of surgical treatment for gunshot injuries to peripheral nerves

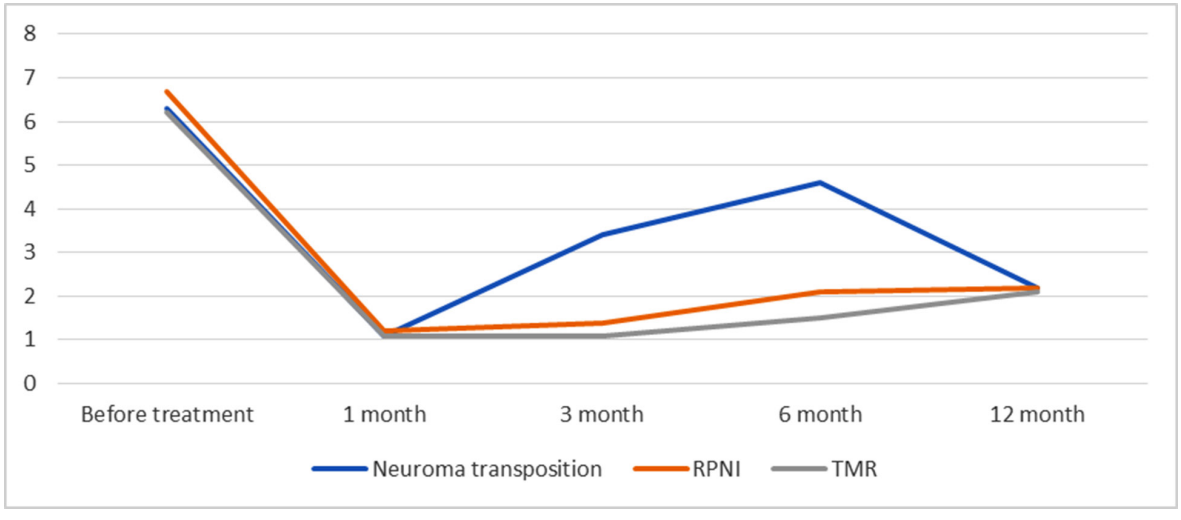

Fig. 8. Dynamics of pain intensity in painful neuromas depending on the method of surgical treatment

In recent years, there has been a global paradigm shift in the management of painful neuromas—from a passive palliative strategy involving neuroma resection or transposition (which frequently results in recurrence, even in the early postoperative period) to an active reconstructive approach, the principal objective of which is encapsulated in the concept: "provide the nerve with a target for reinnervation." In accordance with this principle, contemporary techniques such as the creation of a regenerative peripheral nerve interface and targeted muscle reinnervation have been developed. In the majority of cases (approximately 80.4%), the formation of a painful neuroma results from improperly performed limb amputation and chronic compression or irritation of the neuroma.

When discussing the concept of pain in gunshot injuries to peripheral nerves, it is essential to consider the pathophysiological mechanisms underlying the transformation of nociceptive pain—serving as a protective response to actual or potential tissue damage through stimulation of thermoreceptors, mechanoreceptors, chemoreceptors, and free nerve endings—into neuropathic pain, which is characterized by abnormal neuronal activity secondary to disease, trauma, or dysfunction of the somatosensory nervous system. Prolonged nociceptive stimulation activates both peripheral mechanisms (hyperexcitability of nerve ending membranes, ectopic synaptic discharges, and alterations in gene transcription) and central mechanisms (increased excitability of the nervous system, impaired inhibitory control of excitation, and consequent reorganization of processes and stimuli within the central nervous system). These changes may lead to sensitization of the nervous system and the development of neuropathic pain. Therefore, timely intervention aimed at reducing nociceptive stimulation following injury is crucial to prevent the formation of a neuropathic pain focus. In this context, the concept of timing and a staged therapeutic approach is of paramount importance.

Based on the analysis of our findings and the data reported in the scientific literature, we propose a staged approach to the management of pain syndrome in patients with gunshot injuries to peripheral nerves of the extremities.

Conclusions

1. All patients with gunshot injuries to peripheral nerves of the extremities or with painful neuromas following limb amputation should undergo ultrasonographic examination.

2. In the absence of objective causes of nerve compression or irritation and with preserved anatomical continuity, treatment should begin with optimization of pharmacological therapy; if necessary, hydrodissection of the nerve trunk or injection therapy with steroidal anti-inflammatory agents or botulinum toxin should be performed.

3. In the presence of an objective cause of nerve irritation, significant compression, anatomical disruption, or failure of conservative treatment within 6 weeks, surgical intervention should be recommended.

4. The application of contemporary reconstructive techniques for painful neuromas (RPNI and TMR) provides superior and more durable pain control compared with classical techniques of neuroma resection or transposition.

5. The use of multimodal anesthesia in the early postoperative period—including perineural catheter placement, administration of lornoxicam, and anti-edema therapy (dexamethasone)—makes it possible to minimize the need for opioid analgesics and contributes to interrupting the pathological mechanisms underlying the development of neuropathic pain.

Disclosure

Conflict of interest

The authors declare no conflict of interest.

Ethical approval

All procedures performed in studies involving human participants were conducted in accordance with the ethical standards of the institutional and national research committees and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent

Written informed consent was obtained from each patient or a family member prior to surgery.

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